BRAIN MECHANISMS AND CONSCIOUSNESS

A SYMPOSIUM
organized by
THE COUNCIL FOR INTERNATIONAL ORGANIZATIONS OF MEDICAL SCIENCES
Established under the joint auspices of UNESCO *and* WHO

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August 23rd-28th, 1953

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* Dr. W. R. Hess was prevented at the last minute from attending the meeting. He was represented by Dr. R. Hess, Jr.

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FOREWORD

By

J. F. DELAFRESNAYE
Executive Secretary, C.I.O.M.S.

Each year the Council for International Organizations of Medical Sciences sponsors an international symposium in connection with certain selected international congresses. The conjunction of the Third International Congress of EEG and Clinical Neurophysiology and the Nineteenth International Physiological Congress afforded a rare opportunity for holding such a meeting on the North American Continent. A chalet in the Laurentian Mountains provided an ideal setting for an informal meeting where each member would have unrestricted opportunities to give expression to his views. The meeting was purposely kept small and no audience was invited.

The symposium was planned around the general theme of 'Brain Mechanisms and Consciousness'. Research workers in the fields of neuroanatomy, neurophysiology, neurosurgery, psychology and psychiatry were invited to review present-day thinking regarding the functional significance of the brain stem reticular system about which so much has been written during recent years.

The attempt to bring together individuals from so many fields to discuss a subject at the focal point of so many disciplines was a challenge in itself. Credit for organizing a select international team which worked in complete harmony must go to Dr. H. H. Jasper who presided over the meeting and spared no effort to make it a success.

To the distinguished group of research workers were added younger men who willingly undertook certain tasks to help the meeting along.

The discussions were transcribed immediately with the assistance of Drs. Green, Livingston, Courtois and Ajmone-Marsan who also compiled the index. Dr. Buser supervised the

recording of the discussions while Dr. Ingvar acted as projectionist. On behalf of the Council, I would like to thank them all.

This monograph is the record of the conference held at Ste-Marguerite, Quebec, Canada, August 23rd-28th, 1953. I would like to express my indebtedness to the Consulting Editors and especially to Dr. H. H. Jasper. My thanks also go to Dr. A. Fessard who advised me on many points. It is our hope that these proceedings will be helpful to those who are interested in the problem of cerebral integration and the neurological basis for conscious mental processes and behaviour with special reference to the brain stem reticular system.

INTRODUCTION

by

HERBERT H. JASPER

IT was with Dr. Henri Gastaut and Dr. J. F. Delafresnaye at Unesco House in Paris, during the month of June 1952, that the plans were laid for this Symposium on Brain Mechanisms and Consciousness. It was first known as 'The Laurentian Symposium on the Electrical Activity of the Cortex as Affected by the Brain Stem Reticular System in Relation to States of Consciousness'. Prejudiced perhaps by our own interests, we could think of no development in neuro-physiology during recent years of such far-reaching significance.

Discovery of the remarkable functional properties of the extensive core of grey matter lying adjacent to the principal afferent and efferent pathways in the brain stem and diencephalon has stimulated new conceptions of the integrative action of the brain as a whole. Curiously, at the very start, in the natural history of this development, relationships were found between the activity of this 'reticular system' and states of consciousness, sleep or wakefulness. We are thus plunged immediately into the most complex problems of brain and mind: fields of thought and research into which only the naive or the tough-minded scientist dare enter. You may find examples of both in the pages that follow.

Selection of contributors to this Symposium was guided somewhat by the desire for international representation. More important was the need to bring together a small group of outstanding workers who would approach the problem of brain mechanisms underlying conscious mental processes and behaviour from different points of view; representatives of different scientific disciplines who could help to establish our discussion upon firm foundations of objective data derived from various methods of observation. In addition we have been particularly fortunate in being able to stimulate these same scientists to speculate well beyond available facts, to reconsider traditional viewpoints with

open minds, and to propose new hypotheses which may serve as a guide to research in this field for years to come.

The enthusiastic co-operation of the contributors to this Symposium has made the task of organization an easy one. The problem was not one of finding sufficient material but rather one of trying to restrict the programme within reasonable limits. In doing so I regret that it was not possible to invite many who would have made equally important contributions if time and space had allowed. We hope that our many colleagues who should have joined us will profit by this rather complete account of our proceedings.

The complete manuscripts of each of the principal contributions were circulated to all members of the Symposium before the meeting at Ste. Marguerite. Consequently, presentation of additional material and discussion occupied most of our time during the week-long sessions in this inspiring mountain setting. All discussions were recorded verbatim. Those following each communication were considerably condensed for publication though, we hope, without omitting important questions raised and points of view expressed. The final general discussion is presented in full, with very little editing, so that the considered views of many of the participants could be fully recorded after they had benefited from preceding presentations and discussion. We hope that, in this manner, our readers may share in some measure the exciting spontaneity and sincerity of the interchange of ideas which made this Conference most memorable to all of us privileged to attend in person.

The formal presentations are published, with a few exceptions, as they were prepared before the Conference, and in many instances before the authors had received the communications of others. This has resulted in a certain amount of repetition which, we hope, will only serve to clarify the rather difficult subjects under review. The same facts, expressed in a different way, often gain new meaning. One exception is the treatise of Dr. Fessard which has been revised somewhat to provide a critical and comprehensive statement of the basic issues of this Conference. This paper might be recommended to the readers either as an introduction to the whole Symposium, as a summary, or perhaps as both.

The order of presentation is also the same as given in the Conference. This may not provide the most logical sequence but it was necessary for the continuity of the discussion.

On behalf of all those who took part in this stimulating adventure as guests of C.I.O.M.S., I wish to express our most sincere appreciation to Dr. J. F. Delafresnaye and his Committee who, with the support of W.H.O. and Unesco, have organized this meeting in such an efficient manner, and who have undertaken its publication.

Though few problems have been solved, the record of progress marked by this Conference is a significant advance, more important for the guidance it may give to future work. New conceptions of brain function have been put forward, supported by a wealth of new data, which serve, at least, to clarify that ever-intriguing problem of how conscious experience may be related to neuronal mechanisms in the intricate circuits of the brain.

THE ASCENDING RETICULAR SYSTEM AND WAKEFULNESS

By

H. W. MAGOUN*

When the history of neurophysiology is examined, it can be noted to have passed through periods when investigations of reflex and of sensorimotor functions were of paramount concern. Added to these today is increasing study of neural activity associated with behaviour and with related mental activity. Although the present symposium on consciousness is doubtless something of a milestone in this development, enthusiasm may well be tempered by appreciation of the head-shaking sympathy with which future investigators will probably look back upon the groping efforts of the mid-twentieth century, for there is every indication that the neural basis of consciousness is a problem that will not be solved quickly.

It is not easy, in 1953, for the physiologist to put his finger upon consciousness, though it is present abundantly and for long periods. The present investigative programme has capitalized upon its characteristic periodic interruption, in exploring the contrasting features of central neural activity, common to animals and man, in the cerebral mutation between wakefulness and sleep. Pronounced alterations in consciousness obviously accompany the transition from sleep to wakefulness and records of the electrical activity of the brain provide objective data which are at least associated with this change.

Without further acknowledgment of the obliquity of approach, it can be said that this work began with the chance observation that direct electrical excitation of the reticular formation of the brain stem induced changes in the EEG seemingly identical with those observed in awakening from sleep, or alerting to attention, and which have been referred to variously as activation, desynchronization, EEG arousal or the blocking reaction (Moruzzi

* Aided by grants from the Commonwealth Fund, the National Institute for Neurological Diseases and Blindness, United States Public Health Service and the Eli Lilly Company.

and Magoun, 1949; Moruzzi, 1952b; Magoun, 1950, 1952a, 1953; French *et al.*, 1952; Ingram *et al.*, 1951, 1952, 1953). The effect was most pronounced against a background of EEG synchrony (Fig. 1, midde record) and little added influence was apparent in the already aroused electrocorticogram (Fig. 1, upper record). The alteration was generalized over the cortex and persisted for long periods after cessation of the stimulus initiating it,

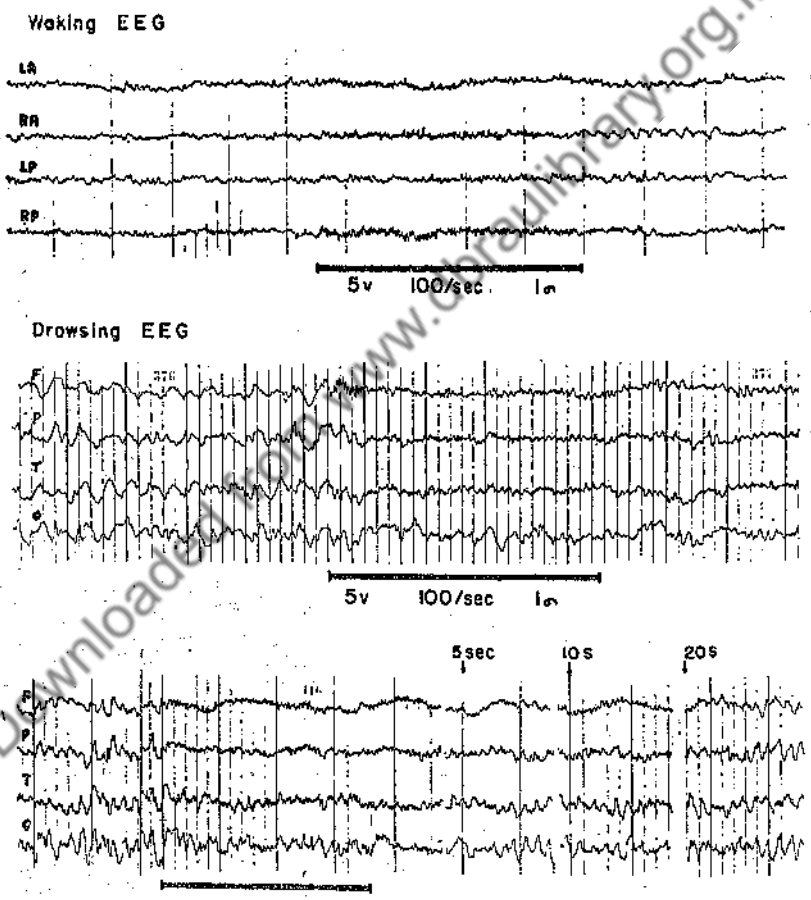


FIG. 1

Effect of stimulating the brain stem reticular formation (heavy line) upon the electrocorticogram of the monkey. Channels are: F, frontal; P, parietal; T, temporal; O, occipital. From French *et al.*, 1952, AMA *Arch. Neurol. Psychiat.* 68: 577.

being most pronounced and enduring longest in the anterior part of the hemisphere (Fig. 1, lower record).

The regions of the brain stem from which such EEG arousal could be induced included the reticular formation and tegmentum of the lower brain stem and, in the diencephalon, the subthalamus together with the dorsal hypothalamus and ventromedial thalamus (Fig. 4). There is indication that influences leading to desynchronization are transmitted to the cortex both by way of an extra-thalamic route from the subthalamus to the

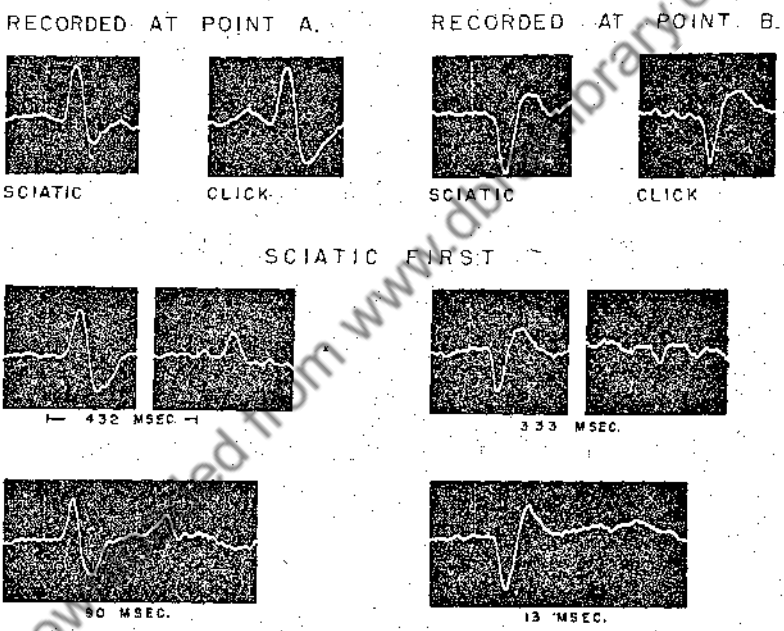


FIG. 2

Records of potentials evoked in the reticular formation of the monkey's brain stem by sciatic and auditory stimuli. Point B was 2 mm. below point A. From French *et al.*, 1953, AMA *Arch. Neurol. Psychiat.* 69: 505.

internal capsule, as well as through the non-specific and possibly other thalamic nuclei which, for the most part, however, lie dorsal and lateral to the most excitable zone (Starzl *et al.*, 1951a, b).

Since the EEG changes evoked by stimulating this reticular system resembled so closely those of arousing peripheral stimuli,

it became of interest to determine whether afferent paths made connections with the reticular mechanism in the brain stem. When, in the unanaesthetized brain, recording electrodes probed the central region, marked responses were evoked by clicks and sciatic shocks (Figs. 2, 4). This discharge had a long latency and a wave-like rather than a spike-like form, suggesting multineuronal organization (Starzl *et. al.*, 1951a, b; French *et al.*,

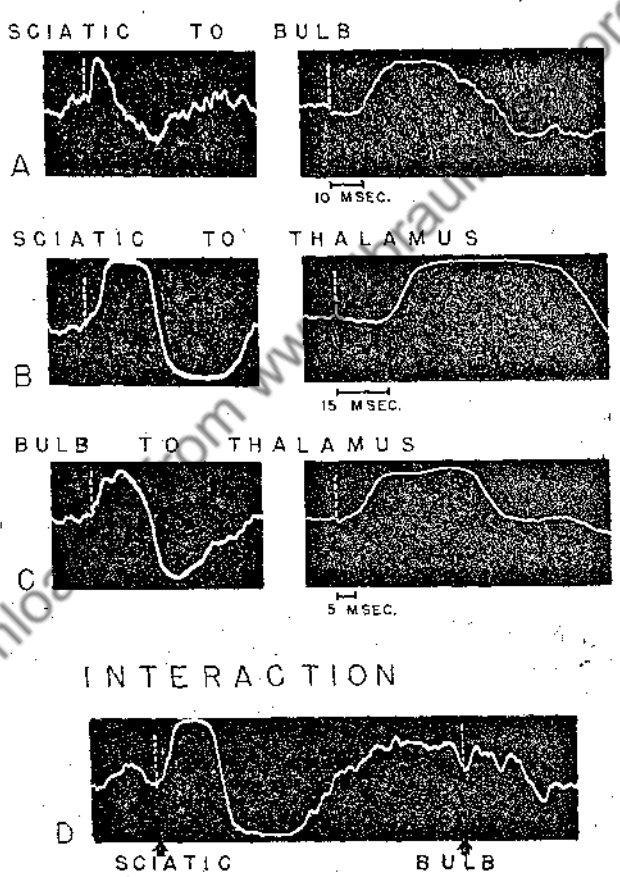


FIG. 3

Records of potentials evoked in the monkey's bulbar reticular formation and thalamus (centre median) by sciatic stimuli. The thalamic response to bulbar stimulation is also shown. From French *et al.*, 1953, AMA *Arch. Neurol. Psychiat.* 69: 505.

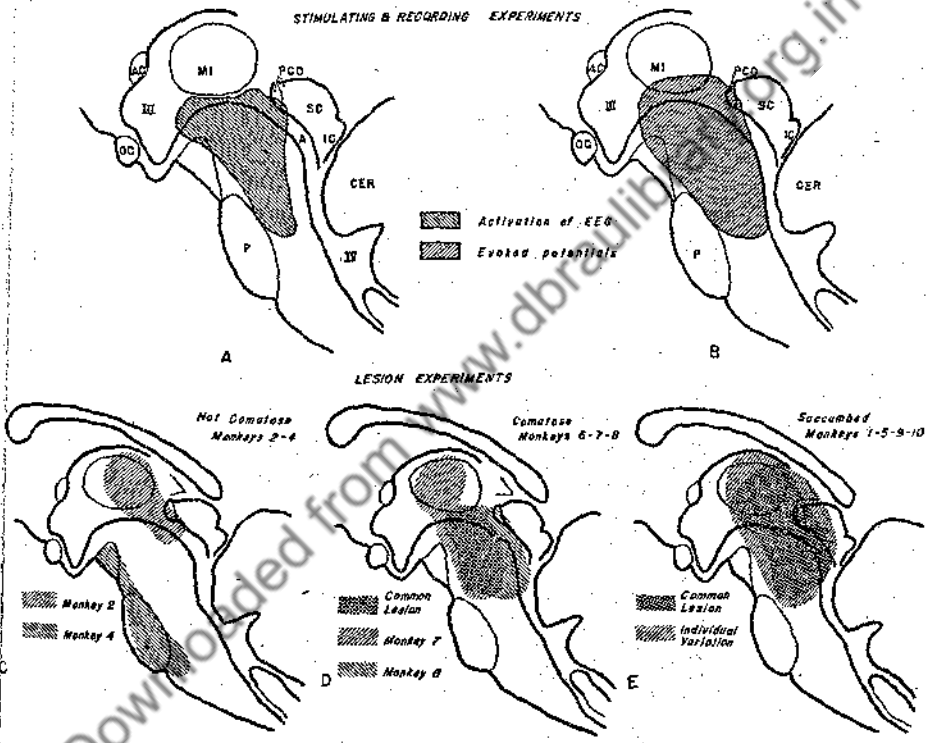


FIG. 4

Reconstructions of the mid-saggital plane of the monkey's brain stem upon which are projected the regions whose excitation desynchronizes the EEG (A) and in which responses are evoked by afferent stimulation (B). The distribution of lesions is shown in C-E, those in *D* and E being followed by coma. Abbreviations are: A, aqueduct; AC, anterior commissure; CER, cerebellum; IC, inferior colliculus; MI, massa intermedia; OC, optic chiasma; P, pons; PCO, posterior commissure; SC, superior colliculus; III, third ventricle; IV, fourth ventricle. From French *et al.*, 1952, AMA *Arch. Neurol. Psychiat. 68*: 591.

1953b). Equivalent potentials were induced at the same recording site by these contrasting modalities, reversing in phase as the focus was traversed (Fig. 2, upper records). When paired shocks were delivered, one to each of the two peripheral sources, attenuation and occlusion occurred in the brain stem, as the second stimulus approached the first, demonstrating further that common reticular elements were fired (Fig. 2, lower records). In agreement, potentials evoked at cephalic levels of the central brain stem by afferent stimuli could be shown to interact with those induced by direct excitation of the bulbar reticular formation (Fig. 3). From the additional studies of Amassian (1951, 1952b), Dell (1952), Arduini and Moruzzi (1953a) and Livingston, Haugen and Brookhart (1953) it is now clear that afferent paths subserving all sensory modalities make connections with the central reticular activating system. These connections have been designated collateral, in the sense that they are diverticula from direct paths to receiving areas of the cortex and without morphological connotations.

The great functional importance of this non-specific reticular system in the brain stem is indicated by the consequences of lesions in its cephalic part (Fig. 4). Monkeys with such experimental injury remained throughout survival in a comatose state, in which the absence of all behaviour associated with wakefulness contrasted sharply with the alertness and activity which this animal normally displays (Fig. 5). The EEGs of such preparations were chronically hypersynchronous and could no longer be affected by peripheral stimuli (Fig. 6), emphasizing the importance of collateral over direct corticipetal paths in EEG arousal induced by afferent stimulation (French and Magoun, 1952). Results in general similar to these have followed injury to the cephalic brain stem in the cat (Lindsley *et al.*, 1949, 1950) and man (Penfield, 1938; Jefferson, 1944; Thompson and Nielsen, 1948; Jefferson and Johnson, 1950; French, 1952; Cairns, 1952; Jefferson, 1952) and the findings are in good agreement with Bremer's fundamental observations that transection of the upper brain stem leaves the cerebral hemisphere in a state of sleep, with which current investigations of this problem may be said to have begun (Bremer, 1935, 1936, 1937, 1938b, 1951a, 1953c).

The chronic loss of wakefulness following injury to the central

FIG. 5
Photographs of monkey with extensive injury to the central cephalic brain stem. From French *et al.*, 1952, AMA *Arch. Neurol. Psychiat. 68*: 591.

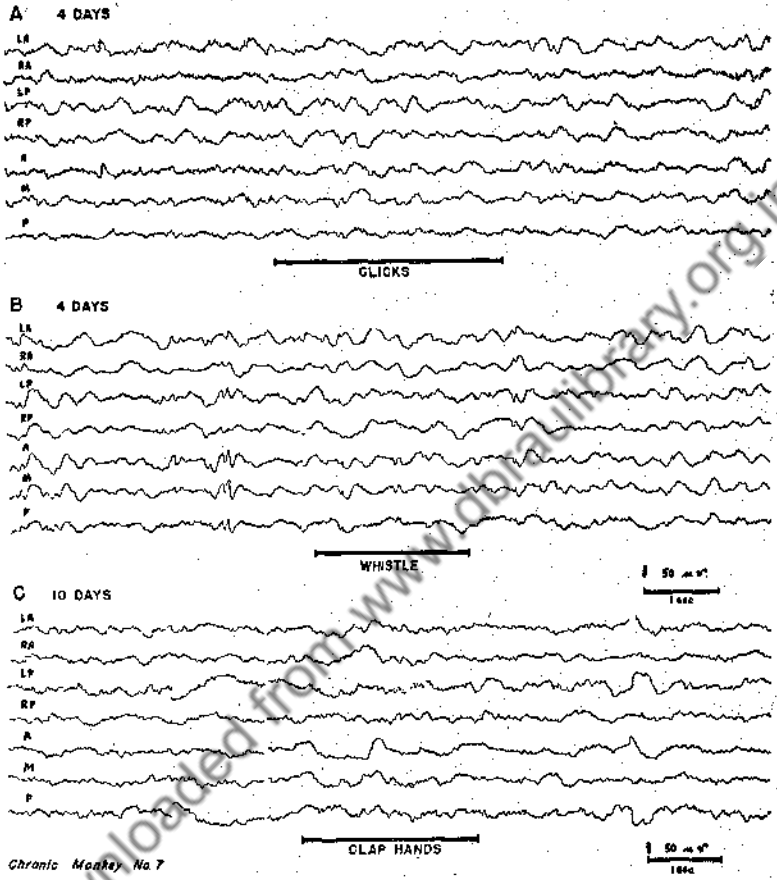


FIG. 6
Post-operative EEG records from monkey with lesion seen in Fig. 4, D. Note persistent synchrony and absence of arousal reaction on afferent stimulation. From French *et al.*, 1952, AMA *Arch. Neurol. Psychiat.* 68: 591.

cephalic brain stem raised the question of whether a reversible reduction of activity in this region might account for the transient loss of wakefulness in anaesthesia (French *et al.*, 1953a, b). The block of EEG arousal in barbiturate sedation appeared identical whether arousal was induced by peripheral afferent stimulation or by direct excitation of the reticular formation of the brain stem

(Fig. 7). When the click-evoked discharge in the auditory cortex and the central brain stem was recorded concurrently, as in the upper and lower channels of each strip in Fig. 8, and the effects of drugs or metabolic alterations were tested, the reticular response was greatly diminished or abolished by anaesthetic agents or by interference with the oxygen or sugar supply of the brain, while the early features of the cortical response were unattenuated and might, in fact, become augmented (Arduini and Arduini, 1954).

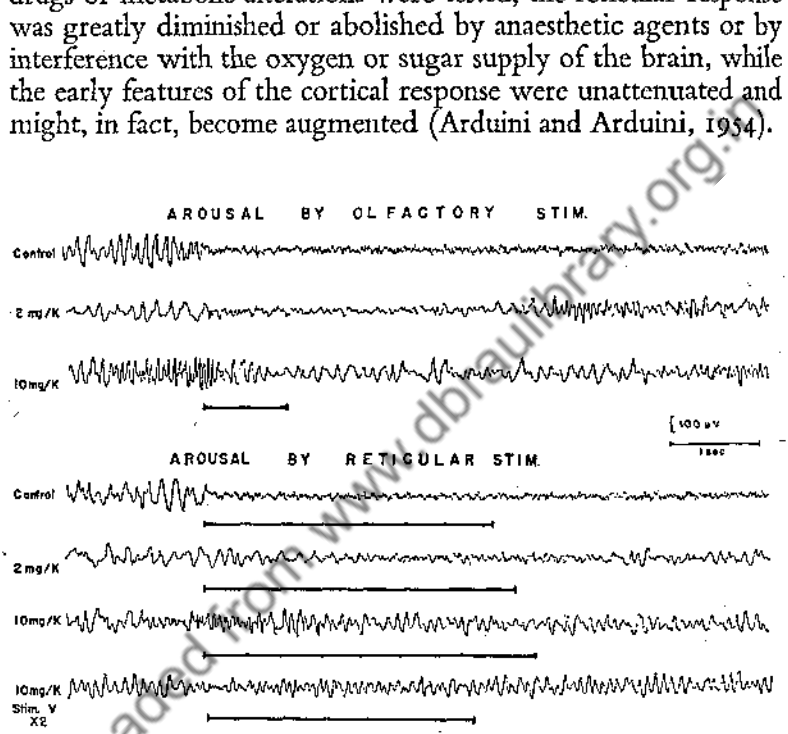


FIG. 7
Electrocorticogram of rabbit showing EEG arousal induced by afferent stimulation and direct excitation of brain stem reticular formation and its abolition by nembutal. From Arduini and Arduini, 1954, *J. Pharm. Exp. Therap.*, *110*: 76.

Similar effects of nembutal upon cortical and reticular responses evoked by sciatic shocks are seen in Fig. 9. The marked reduction of evoked discharge and simplification of the resting record at the reticular lead was associated with a loss of late components of the evoked response in the somatic cortex and with the appearance in the electrocorticogram of sensory after-discharge and of spontaneous spindle bursts (Fig. 9). It is not clear whether these alterations in cortical activity occurred independently or

were secondary to loss of ascending reticular influences, but the initial features of the evoked cortical response were unchanged (French *et al.*, 1953a, b).

Conversely, a sub-convulsive dose of strychnine led to pronounced augmentation of evoked reticular discharge, with little change in cortical excitability. The Arduinis (1954) have proposed that while pharmacologic agents, introduced systematically, obviously act diffusely upon the brain, they have a predilection for altering the activity of more complexly organized portions of the

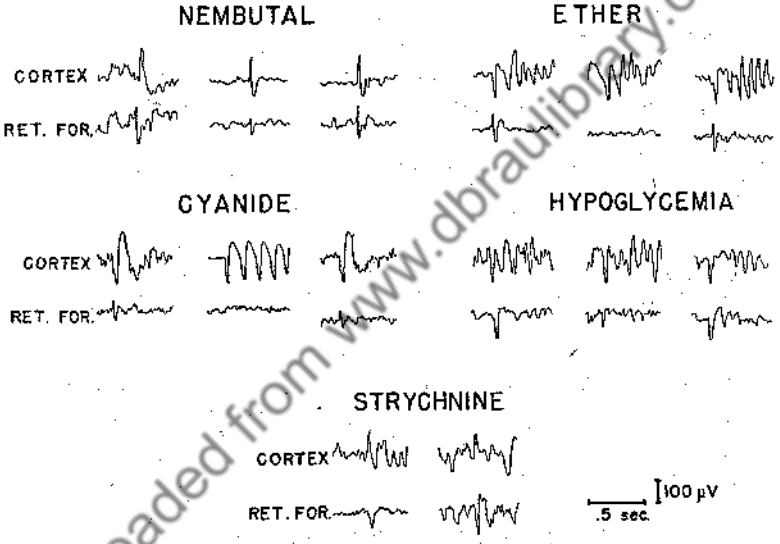


FIG. 8

Ink-written tracings from cat's auditory cortex (upper channel) and brain stem reticular formation (lower channel) showing responses to click stimulation before, during and after procedures indicated. From Arduini and Arduini, 1954, *J. Pharm. Exp. Therap.*, 110: 76.

central nervous system. This feature may explain the pronounced susceptibility of the reticular activating system, in which block of ascending conduction may provide a likely neural basis for the anaesthetic state.

A schematic view of the monkey's brain summarizes present conceptions of the functional organization of the activating system in the brain stem (Fig. 10). Its direct stimulation desynchronizes the EEG in a manner simulating awakening from sleep or alerting

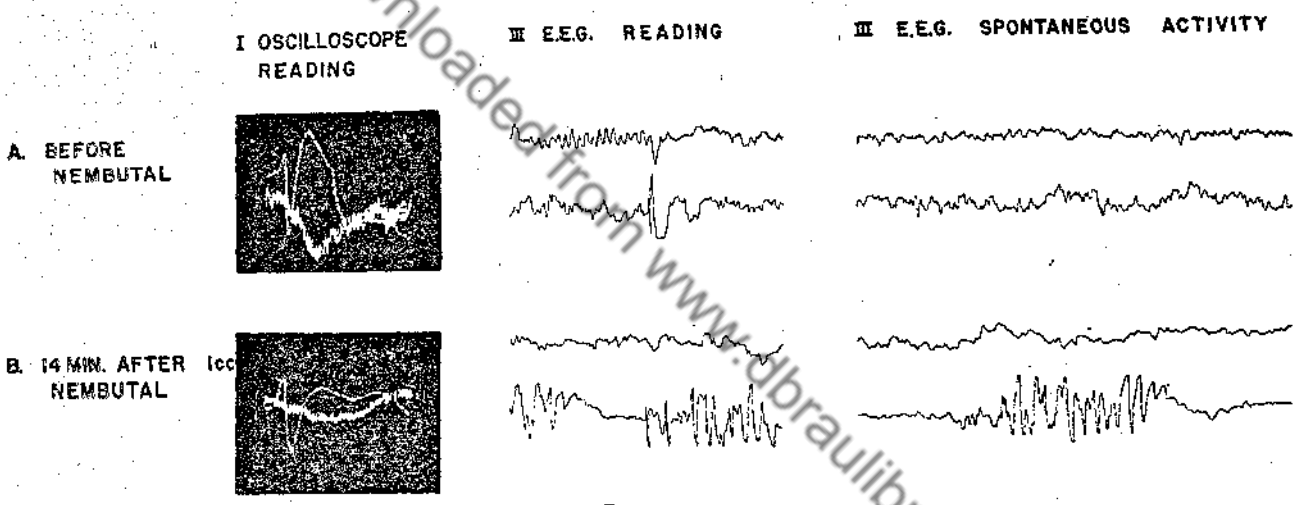


FIG. 9

Records from the monkey's sensory cortex and brain stem reticular formation showing effect of nembutal upon responses to sciatic shocks and upon spontaneous activity. In the oscilloscope tracings (left) the heavy beam records from brain stem and the light beam from cortex. In the ink-written tracings the upper channel records from brain stem and the lower from cortex. From French *et al.*, 1953, AMA *Arch. Neurol. Psychiat.* 69: 519.

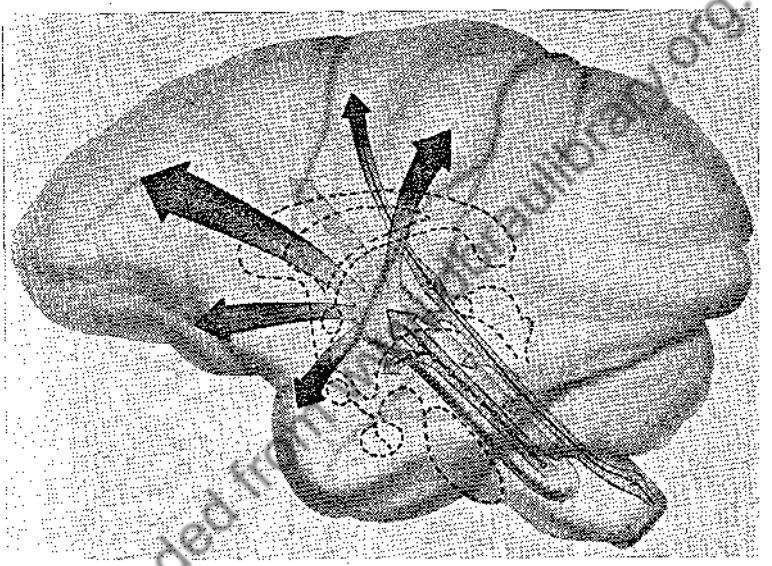


FIG. 10

Lateral view of the monkey's brain, showing the ascending reticular activating system in the brain stem receiving collaterals from direct afferent paths and projecting primarily to the associational areas of the hemisphere.

to attention. Collaterals from all afferent paths to the cortex turn into this subcortical system and EEG arousal induced by afferent stimulation can be shown to be mediated through it. Injury to its cephalic portion leads to chronic loss of wakefulness. Reversible pharmacologic block of its ascending influences upon the hemisphere may provide a neural basis for the anaesthetic state.

Time does not permit consideration now of functional relations of the ascending reticular system to the non-specific thalamic nuclei (Arduini *et al.*, 1951, 1953; Dempsey *et al.*, 1941, 1942, 1943; Hanbery and Jasper, 1953; Jasper *et al.*, 1947, 1949, 1952; Morison *et al.*, 1941, 1942, 1943, 1945; Shimamoto and Verzeano, 1953; Starzl *et al.*, 1951, 1952; Verzeano *et al.*, 1953; Whitlock *et al.*, 1953) nor of the corticifugal influences upon the central brain stem, the importance of which is beginning to be revealed by recent investigation (Jasper, Ajmone-Marsan and Stoll, 1952; Bremer and Terzuolo, 1953a; Livingston *et al.*, 1953; Buser *et al.*, 1953; Hagbarth and Kerr, 1953). Similarly neglected are relations to the hypothalamus and neuroendocrine responses to stress (Porter, 1952, 1953), as well as central brain stem influences upon the paleocortex, whose seemingly inverse arousal patterns have been opened for study by Green and Arduini (1953). The rapid course of developments in this general field suggests the desirability of holding symposia like the present one triennially, in association with each future International Physiological Congress.

GROUP DISCUSSION

JASPER: We are now afforded a rare opportunity to put Dr. Magoun on the carpet and to get him to answer many questions we have been thinking of. We have all followed his work in the literature closely and I would like to suggest we begin by addressing questions first to Dr. Magoun's own interpretation of this reticular system.

MORISON: I have never been quite clear on the evidence relating to the course of this system rostral to the midbrain. It is my impression that you feel that the impulses responsible for arousal follow the pathway of the recruiting responses. There are also alternatives which you have mentioned in your papers. One of these seems to follow much the same path as that which Dempsey and I found, in animals

under deep narcosis, to give rise to the very long latency secondary sensory response. We felt that this pathway was extrathalamic. Occasionally in stimulating subthalamic regions with high frequencies we produced a very prolonged arousal — an almost convulsive type of record — which would last about half an hour, in an animal which had previously been under very deep nembutal. Behaviourally, the animal would go from a state so deep that we might have been concerned about its respiration to one in which we had difficulty in holding it on the board. I would like you to clarify the evidence that impulses leading to this kind of reaction may go to the cortex through the intralaminar system of the thalamus.

MAGOUN: I cannot present any strictly anatomical data, though one of the Jacksonian quips that I like best is that 'anatomy should not be confounded with morphology'. Johnson, however, has been studying Marchi degeneration after lesions in the central brain stem. I saw a demonstration of his at Columbus that showed a dense collection of fibres ascending from the midbrain to the ventro-medial part of the thalamus, the subthalamus and the dorsal hypothalamus. I believe, that, anatomically, this is called the thalamic fasciculus.

The distribution of points whose excitation results in desynchronization of the EEG is similar to that just mentioned and includes the diffusely projecting thalamic nuclei, though the most excitable focus is immediately ventral to them. Green and Arduini have found that, as far as the hippocampal responses go, an excitable zone can be followed into the septal area from this region. From the point of view of lesions I do not think we can be so precise. In stimulating downstream in this system after lesions had been made towards the front, Starzl, Taylor and I thought we too could induce arousal of the EEG independently of the thalamic projections. I do not know whether these impulses might be relayed from the subthalamus and dorsal hypothalamus directly into the internal capsule or whether they might have some other route. It did appear, however, that there were extrathalamic projections, as you and Dempsey and Forbes had earlier shown.

MORISON: To be more specific, do you get identical responses from intralaminar and from subthalamic and lower brain stem stimulation? Can you really wake up an animal by stimulating the intralaminar region?

MAGOUN: Most of our experiments have been performed in immobilized animals under local anaesthesia which are unable to respond actively. We have dealt pretty largely with the EEG response of desynchronization. It is my recollection that Ingram and John Knott have aroused sleeping animals by minimal stimulation through electrodes implanted in the intralaminar structures.

NAUTA: In connection with what has just been said, I would like to say that from Dr. Magoun's earlier publications it would seem that the region of the lateral hypothalamus is in part involved in the transmission of ascending impulses from the midbrain reticular system. It is the region of the so-called medial forebrain bundle and if my assumption is correct, it is entirely possible that this fibre system contains ascending elements that will, directly or indirectly, lead to the basal and medial parts of the telencephalon, among other structures to the septal region and to the hippocampal area. Dr. Whitlock and I had the opportunity to examine the results of a very small lesion in the region of the medial forebrain bundle. We had the impression that there was a very powerful bilateral offset from this system into the intralaminar nuclei. This would provide means for impulses to pass to the thalamus and, specifically, to the intralaminar region, while an additional conduction might take place through the septum to the hippocampus.

MAGOUN: I do not know that I agree completely with Dr. Nauta about the importance of the medial forebrain bundle for EEG arousal, though it may contain extrathalamic ascending pathways going forward and up. The region that we have found most efficacious in EEG arousal includes the dorsal hypothalamus and subthalamus, the region of the ventro-medial thalamic nucleus and at least the ventral portions of the centre median, intralaminar nuclei and ventralis anterior. These latter nuclei give you beautiful recruiting responses and from them you can record burst activity. If you are going to look for a region which seems to be most important in arousal I would put it here rather than in the medial forebrain bundle, and I think this marks also the distribution of the thalamic fasciculus.

OLSZEWSKI: I would like to add that a preliminary survey of experimental material which Dr. Nashold and Dr. Hanbery are studying now in our Institute indicates that in the monkey the region indicated by Dr. Magoun shows a severe nerve cell degeneration and gliosis, following lesions in the oral part of the internal capsule and adjacent portions of the nucleus caudatus. Fibres originating in this region, which Dr. Magoun calls most important in production of arousal responses, proceed orally through the internal medullary lamina and the nucleus ventralis anterior into the internal capsule. We do not know yet what is the ultimate destination of these fibres.

JUNG: Some years ago, with Toennies, using cats with local anaesthesia, and stimulating the intralaminar structures, we got lower threshold responses in the hippocampus and the caudate nucleus than in the isocortex (Jung and Toennies, 1950). I would like to ask Dr. Magoun whether it has been confirmed in his experience that the

response appearing in the hippocampus after stimulation of the intralaminar system have a lower threshold than those appearing in the isocortex.

MAGOUN: Dr. Green has had experience with this.

GREEN: I would not like to be firm about the intralaminar system without looking back at the records, but I think that it is true for the reticular activating system that the response is found at a considerably lower threshold in the hippocampus than in the cortex.

JASPER: You are differentiating now between the intralaminar system and the reticular activating system. Do you make a distinction between the two with regard to arousal?

GREEN: We were stimulating a little more caudally in the brain stem than the intralaminar nuclei.

MAGOUN: I think the relevant thing at the diencephalic level is the frequency of stimulation employed: 10/sec. shocks give recruiting. When you get up to 25 or 50/sec. or above, you get desynchronization of the EEG. The same structures appear to be involved, at least the electrodes are located in the same sites. It seems important to know whether these are the same neurones that respond at 10/sec. with recruiting responses and that induce desynchronization at higher frequencies.

MORISON: It is my recollection that our nembutalized animals without curare gave recruiting responses on stimulation of the intralaminar nuclei at low frequencies, and that if we turned the frequency to 100 to 200 per second, we did get desynchronization; the record would be quite flat and no observable change occurred in the state of the animal. We interpreted these findings as indicating that we were driving the system so fast as to be producing what might loosely be called a Wedensky-type of inhibition of the spindle bursts, but in our anaesthetized animals nothing overtly similar to 'arousal' was seen. If stimulation was carried out a few millimetres ventrally, however, we would occasionally, but in fact not very often, get behavioural arousal and a remarkable activation of the fast activity in the cortical record. It seems possible that in animals without general anaesthesia, or under anaesthesia so light as to permit significant activity of the reticular formation of mesencephalon, high frequency stimulation of intralaminar thalamic areas by desynchronizing or abolishing the prevailing spindle bursts may allow the appearance of fast 'arousal' or 'projection activity' tonically elicited by another neuronal system. Some evidence for this view that arousal impulses reach the cortex over a system other than the intralaminar one is furnished by the fact that stimulation of the intralaminar area sufficient to produce either recruiting responses or complete desynchronization does not reduce evoked primary sensory responses, while arousal or projection activity does.

In connection with the possibility that the arousal reaction may, in part at least, involve a pathway ventral to the thalamus which can be traced to the region of the ventral medial edge of the internal capsule or the adjacent basal ganglia at about the level of the anterior commissure, it may be appropriate to recall one of the earliest papers of Fred Gibbs. Working with implanted electrodes in a large series of conscious cats he found a series of points of minimal threshold for the production of convulsions. The distribution of these points is quite similar to the pathway briefly outlined above.

JASPER: One of the causes of confusion here is the identification of the so-called 'arousal pattern', desynchronization or flattening of the EEG with behavioural arousal. Dr. Morison is speaking of a system which will flatten the cortical electrical activity without arousal, and Dr. Magoun has tended to identify these two things.

WALTER: I have been confused over a period of years by the difficulty of translating these experimental results to an understanding of human behaviour. Only this morning we have had results relating to cat, rabbit, monkey and man. It is well known that some animals react to certain stimuli by arrest and others by becoming hyperactive. I should be very grateful to Dr. Magoun and others if they would categorize these responses in a phylogenetic way. In my mind I try to visualize a sort of four-dimensional table. The animals are represented on it downward. Horizontally, one has first, not merely wakefulness but activity; then there is actual wakefulness without activity, then there is sleep, anaesthesia and various lesions as well, completing this horizontal parameter. In a third direction, you would have the recorded observations at cortical and subcortical levels. Finally, there are the problems of frequency effects just mentioned, which constitute a sort of fourth dimension. As a second issue I would like to ask Dr. Magoun to specify the nature of the response due to stimulation which acts through the brain stem mechanisms he has been discussing, in terms of latency and wave form, etc. in direct comparison with responses in the specific afferent system.

MAGOUN: Except for one instance in the rabbit, all of these data were obtained in the cat and monkey. Most of the work that Dr. Green has been doing on the hippocampus has been done in the rabbit; but he has worked also with the cat and the monkey. To my uncritical eye, the EEG arousal induced by peripheral stimulation appears identical with that induced by stimulation of the reticular activating system, including its diencephalic components. Certainly additional study may be rewarded by the establishment of clear distinctions. In working with the anaesthetized animal, if you can cause any effects, you see a wiping out of slow-wave activity and the record becomes essentially isoelectric.

When the anaesthetic is lightened, and the same point is stimulated, you see in that previously flat period, low-voltage, fast discharge. There is a question in my mind whether there are two or more phenomena involved here, or whether the anaesthetic simply modifies the appearance of one phenomenon. There is now a little data from single-unit analysis which Dr. Jasper may tell us about. Records obtained by Verzeano and Calma show units firing in groups in the synchronous stage at a regular rate and relatively infrequently, whereas during the period of EEG arousal they fire much more rapidly and without regular grouping of periodicity.

BRAZIER: Something that worries us a little is the terminology which implies that we have more knowledge of the EEG than we have. When you describe one type of record as having synchronized activity and another as being desynchronized it suggests that we know what kind of mechanism is at work.

MAGOUN: The terms are descriptive. I am both happy and unhappy to admit ignorance of the mechanisms.

BREMER: In my opinion, the wiping out of slow wave activity resulting in a flat isoelectric tracing and the low voltage fast discharge which are the cortical responses to the same reticular stimulation at different degrees of narcosis can be explained without postulating different physiological reactions. Dr. Adrian has indeed indicated that the blocking reaction of the alpha rhythm could entail a true reduction of cortical activity if one makes the plausible assumption that neuronic synchronization results – by a field effect – in a recruitment of beating units, which desynchronization abolishes. A diminution of this mass effect in arousal experiments on an anaesthetized animal may so induce, as Dr. Adrian has pointed out, a diminution of the total number of cells activated and a true reduction of cortical activity.

THE PHYSIOLOGICAL PROPERTIES OF THE BRAIN STEM RETICULAR SYSTEM

By

G. MORUZZI

The influence of the brain stem reticular system on spinal and cerebral activities was reviewed at the 1950 Meeting of the Association for Research in Nervous and Mental Diseases (Austin, 1952; Jasper and Ajmone-Marsan, 1952; Lindsley, 1952a; Magoun, 1952a) and at the 1951 Meeting of the American Neurological Association (Jasper, Ajmone-Marsan and Stoll, 1952; Magoun, 1952b). Moreover many reviews dealing with the relationships of the reticular formation with postural tonus, sleep, and EEG arousal reaction are available (Magoun, 1950; Bremer, 1951a; Moruzzi, 1950b, 1952a, b, c). Hence the basic phenomena will not be reviewed in this article, which is mainly devoted to the results of the last two years of reticular investigation. Because of space limitations, I shall restrict myself to introducing a few problems, about which I have personal experience.

I — INTRODUCTORY REMARKS

The present review will concern itself with the results of a microelectrode analysis of the reticular mechanisms and of their influences upon the cerebral cortex. Some of the observations to be reported, have already been published (Whitlock, Arduini and Moruzzi, 1952a, b, 1953; Arduini and Whitlock, 1952, 1953; Mollica, Moruzzi and Naquet, 1953a-d); for other experiments only preliminary notes have appeared (von Baumgarten, Mollica and Moruzzi, 1953a-c; von Baumgarten and Mollica, 1953a, b), the full papers being still in press (von Baumgarten, Mollica and Moruzzi, 1954; von Baumgarten and Mollica, 1954). Important contributions on these lines have been made, independently and almost simultaneously, in other laboratories: the arousal has been analysed at a cortical level by Jasper and Li (1953), the responses of the vestibular nuclei and of the lateral bulbo-reticular

formation to labyrinthine impulses have been investigated by Gernandt and Thulin (1952) and a preliminary note on the spike discharges of midbrain and diencephalic reticular neurones has been presented by Amassian (1952a) at the Annual Meeting of the American Physiological Society.

During the experiments carried on in Pisa within the last two years we have intentionally limited our investigation to only two districts of the central nervous system: the medial bulbo-reticular formation (Mollica *et al.*, l.c.; von Baumgarten *et al.*, l.c.) and the motor cortex (Whitlock *et al.*, l.c.; Arduini *et al.*, l.c.). We hope to be able to study other reticular structures and other cortical areas in the coming academic years, but we felt it advisable to simplify our task as much as possible at the beginning of our endeavours. The illustrations reproduced in this review are selected from among those belonging to papers which are still in press and which will not be published in English (von Baumgarten *et al.*, 1954).

The advantages and the limits of any single unit analysis of the central nervous system do not need to be stressed here. To know the temporal patterns of activity of a single element constitutes a step forward, although the spatial arrangement of central activity is inevitably missed with this approach. Moreover the patterns of activity within the reticular system, when recorded with coarse electrodes, are such that a microelectrode analysis appears to be particularly advantageous in this part of the brain. With the concentric Horsley-Clarke electrodes low voltage fast waves are led from the reticular formation (Eldred and Snider, 1950), and it is almost impossible to detect on this background of spontaneous activity any inhibitory response or tonic, slowly rising increase of activity. In fact the only way of modifying the electroreticulogram is to bombard the core of the brain stem with synchronous volleys, so that an abrupt, strong and transient increase of its spontaneous activity is evoked. This indeed has been done, and quite successfully, by stimulating sensory nerves or receptors (McKinley and Magoun, 1941; Starzl, Taylor and Magoun, 1951b; Dell and Olson, 1951; Bremer and Terzuolo, 1952; French, Verzeano and Magoun, 1953a, b; Morin, 1953; Arduini and Arduini, 1953a, b, 1954), the cerebral cortex (Hoefer and Pool, 1943; Lloyd, 1944; McCulloch, Graf and Magoun, 1946; Niemer

and Jimenez-Castellanos, 1950; Bremer and Terzuolo, 1952; Jasper, Ajmone-Marsan and Stoll, 1952; Livingston, Hernandez-Peon and French, 1953) or the cerebellum (Snider, McCulloch and Magoun, 1949). We shall see however that these synchronous potentials, which added so richly to our knowledge on the afferent connections of the reticular system, represent only one aspect of the responses of the individual units to the afferent impulses impinging upon them.

Mollica, Moruzzi and Naquet (1953) made the first attempt to explore with microelectrodes the activity of single units belonging to the medial bulbo-reticular formation (Magoun's inhibitory centre). Because of the circulatory and respiratory movements of the medulla, rigid glass micropipettes had to be avoided, and enamelled nichrome or stainless steel wires (12 and 37μ in diameter) were used instead. With these floating microelectrodes a single unit could be recorded for a long time, sometimes for one hour or more, and many surgical interventions were performed in distant parts of the brain without losing it. This was an essential feature for our project. A drawback was represented however by the fact that the orientation of the tip of the microwire with the Horsley-Clarke machine and its displacement with a micromanipulator were obviously impossible.

The latter difficulty is not a very serious one, if our aim is limited to leading, extracellulary, the 'all-or-none' potentials arising in the large and scattered neurones which are found in the medial bulbo-reticular formation. In fact single unit discharges were easily found by manually displacing an enamelled wire 37μ in diameter, whose recording surface was therefore many times larger than that of the glass microelectrodes. It was necessary, instead, to find a way of knowing, physiologically, if the tip of the microwire was really within the medial bulbo-reticular formation.

A parallel microwire was used for unipolar stimulation of the structures to be explored. The spikes were recorded only from reticular areas which gave upon stimulation the well-known localized inhibitory responses described by Magoun and Rhines (1946). Later on we were able to find other ways of identifying the medial bulbo-reticular formation, but the unipolar stimulation test was made, routinely, at the end of any series of records, by using the same microwire which had been utilized for leading the

spikes potentials. The material to be presented is based upon experiments in which the results of electrical stimulation were substantiated by anatomical controls (Weil), after the wire microelectrode had been utilized for producing electrolytic lesion at the recording tip (Mollica, Rossi and Venturelli, 1954).

To show that the microelectrode was within the medial bulboreticular formation does not mean, necessarily, that we are leading spikes from reticular neurones. Neighbouring ascending or descending tracts might have been recorded in this way. In view of the cerebellifugal pathways going, via the roof nuclei, from the vermian part of the anterior lobe to the medial bulbo-reticular formation (Snider, McCulloch and Magoun, 1949), a further test was introduced. Our investigations were limited to those bulbar units whose spike activity was clearly and reversibly modified by stimulating the inhibitory area of the cerebellum. Some reticular units escape cerebellar control, but the advantage of dealing with a functionally homogeneous neuronal population overruled, in our opinion, the advisability of extending the investigation to every unit belonging, anatomically, to the ventro-medial reticular formation.

These three criteria: inhibitory effects elicited by stimulation, spike discharges modified by the cerebellum, anatomical controls after microelectrolysis were adhered to strictly in all our reticular experiments. The spikes we recorded were generally negative, although occasionally positive spikes were obtained.

II — SPONTANEOUS SPIKE DISCHARGES OF RETICULAR NEURONES

Stimulation experiments have shown that impulses arising in the brain stem reticular formation impinge, through ascending and descending pathways, on both cerebral and spinal structures. Ablation experiments have suggested, moreover, that the reticular influence is tonic in nature. Hence the wakefulness has been correlated with an uninterrupted stream of ascending reticular impulses bombarding the diencephalic and cortical centres; vice versa, the regulation of postural tonus is mainly the result of a well balanced distribution of tonic discharges descending through facilitating and inhibitory reticulo-spinal pathways.

The first task of any electrophysiological investigation is there-

fore one of recording the tonic activity which is going on within the reticular formation. This was the aim of the experiments which were carried on by Mollica, Moruzzi and Naquet (1953a-d).

Both in the decerebrate cat and in the *encéphale isolé* preparation the medio-ventral reticular neurones discharge spontaneously according to three different patterns:

1. low frequency (down to 2-5/sec.) irregular discharge (Figs. 2,A; 8,A);

2. continuous discharge, occurring rather regularly, at higher frequencies (50-100/sec.) (Fig. 6,A);

3. spike outbursts at 50-70/sec., arising from a background of low frequency discharge and lasting approximately one second (these patterns are less frequently observed).

These discharges are not due to injury from the microelectrode wire, since a unit remained sometimes unmodified for one hour or more. Two or three units are often simultaneously present in the record, but they can be easily identified because of their constant size and, sometimes, through the notches occurring at a given level of the rising or declining phase of their spike potentials (Figs. 1, 7).

These reticular discharges are called 'spontaneous' because they occur without any intentional stimulation of sensory receptors or of central structures. They are not necessarily 'automatic', since the activity of the reticular neurones might be either driven or evoked by impulses arising in the cerebellum, in cerebral structures or in the sensory neurones of the cranial nerves; moreover, in the decerebrate preparation the reticular activity is under the influence of ascending discharges arising in the proprioceptors. But whatever the results of future experiments, we can safely assume that the spontaneous reticular discharges are closely correlated with the well known tonic influence of the reticular formation on spinal or cerebral mechanisms (see IV, V).

III — CEREBELLAR INFLUENCES ON BULBO-RETICULAR SPIKE DISCHARGES

Since the medio-ventral reticular formation is the second relay in the inhibitory pathways coming down from the cortex of the anterior lobe (Snider, McCulloch and Magoun, 1949), cerebellar

stimulation is the obvious choice in any attempt to modify the spontaneous reticular discharge and to investigate its relationships with the inhibition of postural tonus.

A technical drawback is represented by the stimuli artifacts, which are particularly strong when recording with microelectrodes. Mollica, Moruzzi and Naquet (1953) tried to overcome this difficulty by polarizing the vermian surface of the anterior lobe with slowly rising and slowly descending DC currents.

In their classic paper on DC stimulation of the motor cortex, Fritsch and Hitzig (1870) remarked (p. 315) that 'innerhalb der minimalen Stromstärken nur die Anode Zuckungen auslöst'. Gerard and Libet (1939), Mollica and Terzian (1950) and Goldring and O'Leary (1951) confirmed and extended these forgotten observations, by recording with macroelectrodes from frog's olfactory bulb or mammalian cerebral cortex. Moreover surface-positive polarization was reported to increase the spike discharges of the cerebellar neurones (Brookhart and Blachly, 1952, 1953) and of the Betz cells of the motor cortex (Mollica and Rossi, 1953).

The observations of Brookhart and Blachly (1953) are of particular importance in this respect. They showed that the spontaneous discharge of cerebellar units, probably to be identified with the Purkinje cells, was decreased or increased depending upon the direction of the current flow. Dendrite positivity increased the spike discharge whereas a reversal of this effect was elicited by dendrite negativity.

In order to elicit clear-cut effects in the reticular formation large neuronal masses must be polarized. It is unlikely that the response of the Purkinje cells will be uniform within the stimulated structures; the geometrical arrangement of the dendritic trees in relation to the current flow will be obviously different in the surface and within the buried layers. And yet if supraliminar currents are applied, a response is obtained only with surface positive polarization: in the decerebrate cat it is characterized by a collapse of extensor rigidity (Mollica *et al.*, 1953). Hence the tonic inhibitory discharge of the Purkinje cells must be increased with this type of stimulation, at least in the majority of the cerebellar neurones; the surface negative polarization is also effective,

but only for definitely higher intensities of polarizing current. Neurones lying in the deeper folia, having a different geometrical arrangement, are probably affected by these stronger currents.

Surface-positive polarization of the anterior lobe has a striking effect on the spike discharges of the medial bulbo-reticular neurones.

The discharge coming from an inhibitory area should increase the activity of the units belonging to the bulbo-inhibitory centre of Magoun. These predictions have been confirmed. Reticular units discharging according to patterns (*a*) and (*c*) are generally strongly increased in frequency (up to 50-70/sec.) by cerebellar polarization. The effect is particularly striking on the oscillating type (*c*) discharge, whose frequency is regularized at the top values normally attained only during the outbursts. Sometimes reticular units altogether silent are recruited by the cerebellar volleys. The strongest responses are obtained with 1.5 mA, and for these polarizing currents disappearance of rigidity in the decerebrate cat and arousal reaction in the sleeping *encéphale isolé* preparation occur (Mollica, Moruzzi and Naquet, 1953).

An unexpected finding is represented by the powerful inhibition of some spontaneously active reticular units elicited by the cerebellar polarization. The inhibitory response is obtained with lower current intensities (0.5 mA), i.e. with stimulations which are generally too weak for eliciting EEG arousal and inhibition of extensor tonus. The effect is of course particularly striking when the intensively active b units are blocked by the cerebellum and the end of the polarization is followed by a powerful rebound increase of the reticular discharge. Examples of cerebellar inhibition of reticular spike discharge are given in Figs. 1,B,E; 2,F; 4,B; 5,B,C,D; 6,B. Actually the inhibitory effects are certainly not less easily observed than the facilitatory ones.

The reticular responses are not secondary to any collateral effect of DC polarization since (*a*) some reticular units are unaffected; (*b*) following cerebellar ablation, no response is elicited by polarizing with DC current as strong as 5 mA a sham cerebellum made of wet cotton and (*c*) the response is abolished following nuclear electrocoagulation. Volleys coming down from the medial anterior lobe are responsible for the reticular effect

since they are not elicited by polarizing the neo-cerebellum with the same current intensities.

As the spike discharges recorded in the cerebellum by Brookhart and Blachly (1953), the reticular responses to cerebellar polarization are clearly non-adaptive. They may be reproduced many times, in a thoroughly predictable way, when leading from the same unit. We have been unable to obtain a reversal of the response by changing the intensity or the direction of the current flow. Hence a distinction between bulbo-reticular neurones which are inhibited and those which are excited by the anterior lobe seems justified, at least in the present state of our knowledge. The real core of the problem – a hard core, one which will be solved only by further investigation – is that of identifying the reticular units we are leading from.

The next two chapters will be devoted to an attempt made by Mollica, Moruzzi and Naquet (1953), working along these lines. It will be at once apparent that the evidence supporting the identification of the reticulo-spinal units is not altogether unsatisfactory, whereas it is unfortunately scanty and fragmentary in so far as the ascending reticular neurones are concerned.

IV — MEDIO-VENTRAL BULBO-RETICULAR DISCHARGES AND INHIBITION OF EXTENSOR TONUS

Microelectrode stimulation of the medio-ventral reticular formation in the decerebrate cat (Mollica, Moruzzi and Naquet, 1953a, b, d) duplicates most of the responses obtained from the same area with Horsley-Clarke bipolar macroelectrodes (Magoun and Rhines, 1946). Rectangular pulses 1 msec. in duration, at repetition rates of 300/sec., were delivered unipolarly through the microwire; although the shape of the stimulus was modified by the capacity of the microelectrode, localized, constant and predictable responses were obtained with only 1-1.5 volts.

When threshold stimuli are delivered through the microwire:

1. The inhibition of decerebrate rigidity and of the blink eyelid reflex is strictly ipsilateral.

2. Increase of decerebrate rigidity is observed in the contralateral hindlimb, which is inhibited if the intensity of stimulation is slightly increased.

It should be recalled here that macrostimulation of the medio-ventral reticular structures yields instead bilateral inhibition of the blink reflex and generalized inhibition of decerebrate rigidity, which is only partial for the contralateral forelimb (Magoun and Rhines, 1946). According to Sprague (1953) ipsilateral flexion and contralateral extension occur when threshold stimuli are applied to the medio-ventral reticular formation.

The spike discharges which are increased by the cerebellar polarization arise probably in Magoun's inhibitory neurones, whose somata are localized in the medio-ventral reticular formation (Niemer and Magoun, 1947). In fact (1) they are led from an area yielding inhibition upon microelectrode stimulation; (2) clear-cut correlations between type c spike outbursts and 'spontaneous' oscillations of extensor rigidity are observed; (3) inhibition of postural tonus is elicited by the same intensities of DC polarization which evoke the most striking effects on the reticular discharge; (4) if the cerebellum is polarized during one of the long pauses which are intercalated between two outbursts of a type c reticular discharge, the rate of reticular firing rises to the levels observed during the spontaneous outbursts and a collapse of decerebrate rigidity occurs. Both effects last as long as the cerebellar polarization.

The problem of the physiological significance of the reticular units which are inhibited by the cerebellar polarization is now being investigated.

V — MEDIO-VENTRAL BULBO-RETICULAR DISCHARGES AND EEG AROUSAL

Cerebellar polarization yields generalized EEG arousal, which is particularly striking when there is a background of drowsiness in the *encéphale isolé* preparation (Mollica, Moruzzi and Naquet, 1953c, d). Control experiments previously reported (see II) show that the arousal is a genuine effect, yielded by volleys of impulses arising in the stimulated area. It is probably relayed through fastigial neurones, since an EEG arousal has been elicited previously (Moruzzi and Magoun, 1949) with repetitive stimulation of the roof nuclei. Doses of intravenous chloralosane, so small (1.75 mg./kg.) that they are ineffective on the EEG activation

elicited by sensory or reticular stimuli, thoroughly prevent the arousal elicited by cerebellar polarization. This may be regarded as additional evidence that the EEG response to cerebellar polarization cannot be explained by unintentional sensory stimulations.

Many attempts were made to correlate the modifications elicited in the reticular discharge by the cerebellar polarization with the EEG changes recorded simultaneously from the animal's skull. Only fragmentary and inconclusive evidence was obtained on the reticular neurones which were inhibited by the cerebellum. For the neurones which were facilitated, an increase of the reticular discharge was often found to occur for polarization intensities which had just reached the threshold for eliciting a generalized EEG arousal. This however does not constitute crucial evidence that the cortical arousal was the consequence of the increased discharge of reticular neurones such as the one we were leading from. Any attempt to find a correlation between fluctuations of activity in the EEG and in the spontaneous reticular discharges has met, so far, with a failure.

FIG. 1

Inhibition of bulbo-reticular spike discharges elicited by cerebellar and cortical stimulations.
In this and in all the following illustrations downward deflections correspond to negative reticular spikes and to surface-positive cortical waves. Figs. 1 to 4: 'pyramidal' cats.
A – At least two units are recorded simultaneously. The large one is characterized by notches occurring in corresponding portions of the spike.
B – Surface-positive polarization of the cerebellar antetior lobe (0.5 mA) decreases the rate of firing of both units, but the large spikes are more strongly affected.
C – Rebound increase in the reticular discharge following the end of the cerebellar polarization.
D – Between C and D the motor cortex was strychninized. The lower records give the activity of this area, recorded through a wick electrode. Both types of spike discharges are inhibited whenever a strychnine wave occurs in the motor cortex. Again the large spikes are more strongly affected (longer duration of the inhibition).
E – The strychnine waves occur when the reticular discharge is already partially inhibited by the cerebellar polarization. The cortical component of the inhibitory effect is clearly visible.
F, G – Immediately (F) and few minutes (G) after the end of the cerebellar polarization. The cortical inhibition is less evident during the rebound increase of the reticular discharge.
H – Between G and H the strychninized motor cortex had been destroyed and the wick electrode was applied on wet cotton which was put at its place. The strychnine inhibitory effects are abolished, but the spontaneous spike discharge is quite unmodified.
I – It is still inhibited by the same intensities of cerebellar polarization (see the selective suppression of the large spikes).
L – Rebound discharge following the end of the cerebellar polarization.
(From R. von Baumgarten, A. Mollica and G. Moruzzi, 1954. *Pflügers Archiv*, in press.)

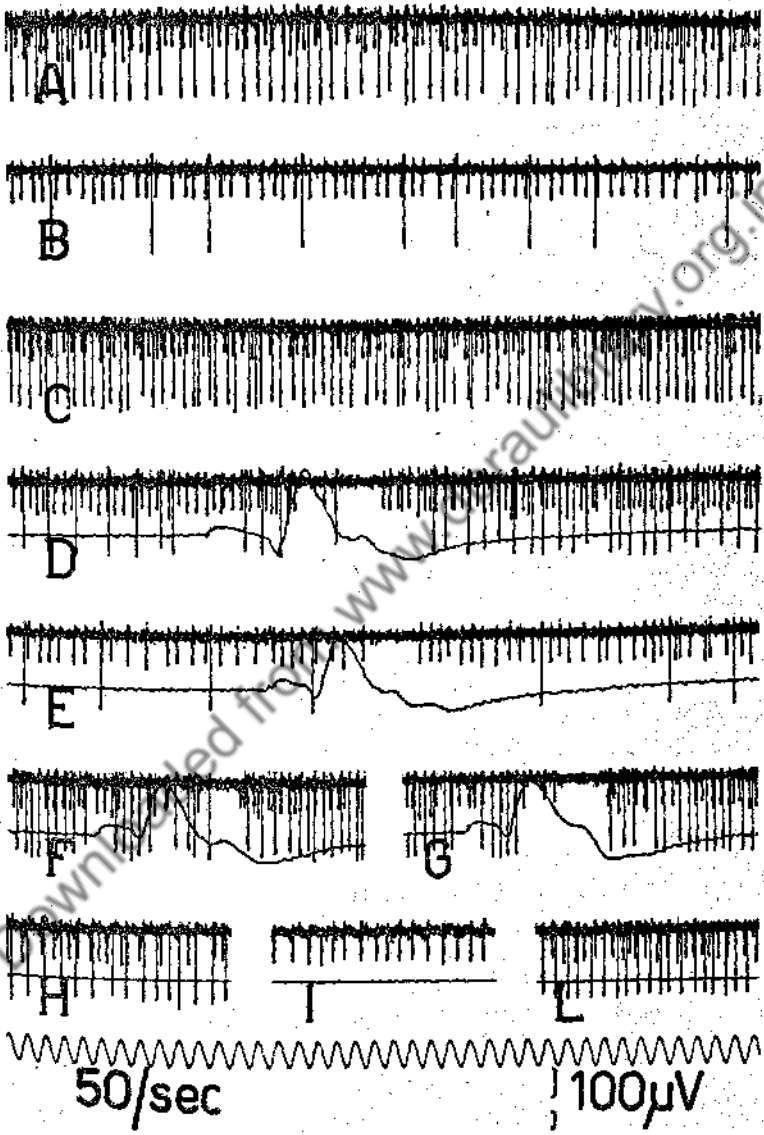


FIG. 1

It is always difficult to compare the activity of one or few reticular units with the composite response of large populations of spinal or cerebral neurones. Only whenever a very pronounced synchronization occurs, this approach is likely to yield some satisfactory results. These conditions are of course fulfilled more easily when the inhibitory reticulo-spinal neurones (which occupy a small volume of the medulla) are concerned. The bulbo-reticular formation is instead only a minor part of the structures whose stimulation yields EEG arousal and which are played upon by the cerebellum. This explains another of our negative correlations. EEG activation patterns outlasted, sometimes for many seconds, the cerebellar polarization, whereas normal patterns of discharge were recorded from the medio-ventral reticular units a few seconds after the cerebellar polarization. These facts are not surprising since the microcosm we are recording from is obviously far from reflecting the overall activity of the huge reticular system.

We believe that our negative findings should not discourage further attempts to lead ascending reticular discharges with more appropriate techniques. The Golgi I reticulo-spinal units, because of their larger size, might simply be recorded from more easily than the neurones which are responsible for the EEG arousal.

VI — INFLUENCE OF THE MOTOR CORTEX ON BULBO-RETICULAR SPIKE DISCHARGES

The problem now arises as to whether the same bulbo-reticular units whose spike discharges are so markedly influenced by the cerebellar polarization, may be driven also by the motor cortex. A positive answer to that question would raise another problem, that of the cerebello-cortical interrelations at reticular levels.

The experiments of von Baumgarten, Mollica and Moruzzi (1953, 1954) have been fully devoted to an analysis of the moto-cortical influences on bulbo-reticular spike discharges. They were performed on Bremer's *encéphale isolé* cat and on the 'pyramidal' preparation, which will be described in the last section of this report. Local strychninization (1 per cent), single electrical shocks (square pulses 1 msec. in duration), and surface positive polarization were used in order to elicit corticifugal volleys. That

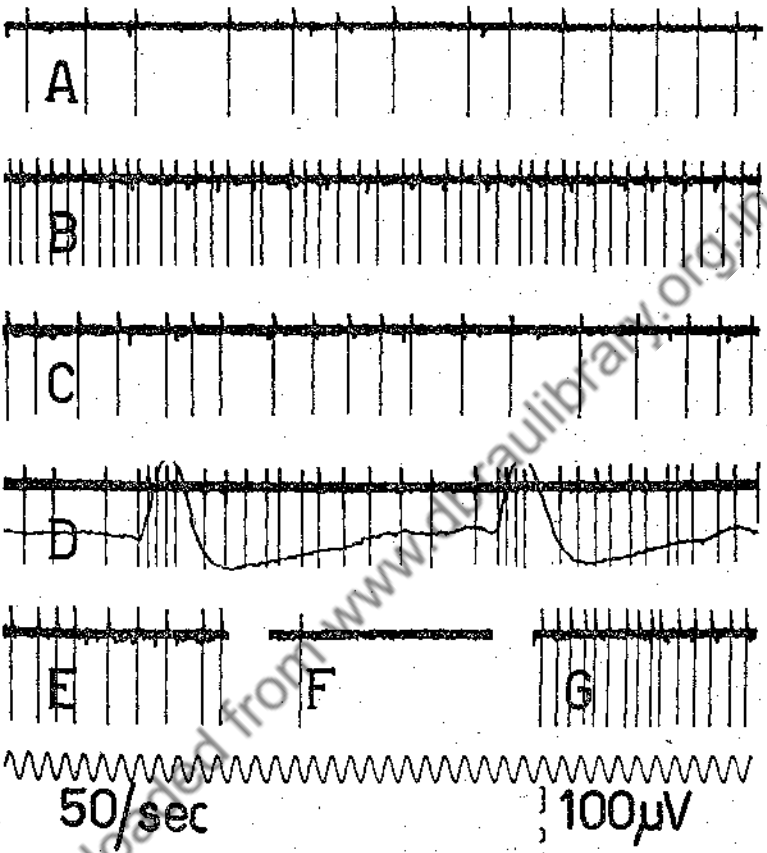


FIG. 2

Cortical facilitation and cerebellar inhibition of a single unit discharge in the medial bulbo-reticular formation.

A — Spontaneous discharge in a single unit of the medial bulbo-reticular formation.
B — Tonic increase in the rate of firing elicited by surface positive polarization (1 mA) of the motor cortex.
C — Control record, after the end of the cortical polarization.
D — Phasic modulation of the bulbo-reticular discharge occurring synchronously with the convulsive waves elicited by local application of 1 per cent strychnine on the motor cortex.
E — Following ablation of the strychninized area the cortically induced modulation is abolished, but the spontaneous reticular discharge goes on.
F — It is inhibited by surface-positive polarization of the cerebellar anterior lobe (0.5 mA).
G — Rebound increase in the reticular discharge at the end of the cerebellar polarization. (From R. von Baumgarten, A. Mollica, and G. Moruzzi, 1954. *Pflügers Archiv*, in press.)

surface-positive polarization applied to the motor cortex evokes a strong increase in the pyramidal discharge had been shown previously by Mollica and Rossi (1953).

The convulsive volleys arising in the strychninized motor area may either increase or inhibit the reticular discharges in both sides of the medulla.

Two examples of augmentative effects are given in Figs. 2 and 4. Synchronously with the strychnine waves a clear-cut increase of the rate of firing is observed; it slows down later on, but the frequency of the reticular discharge is still higher than in normal conditions, when the cortical outburst is over.

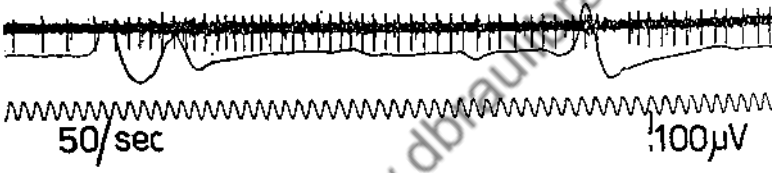


FIG. 3

Reversal in the response to corticifugal convulsive volleys correlated with a change in the background of reticular activity.
The first strychnine wave yields a long lasting increase in the reticular spike discharge. The second strychnine wave occurs during a background of increased reticular activity. A short lasting but clear-cut inhibition is observed.
(From R. von Baumgarten, A. Mollica and G. Moruzzi, 1954. *Pflügers Archiv*, in press.)

FIG. 4

Convergence of sensory, cerebellar and cortical impulses on the same unit of the medial bulboreticular formation.
In this and in the following records the electrical artifacts elicited by single shock stimulation of a nerve or of the motor cortex are shown by the black dots.
A — Strong increase in the spontaneous discharge elicited by single shock stimulation of the central end of the sciatic nerve.
B — Complete blockade of the spontaneous reticular discharge elicited by surface positive polarization (0.5 mA) of the cerebellar anterior lobe. Only two spikes are triggered by the same sensory stimulation as in A.
C — During the rebound increase in frequency, which follows the end of the cerebellar polarization, the augmentative effect of a sensory stimulation is barely visible.
D — Few minutes thereafter. The spontaneous reticular discharge is back at its normal level.
E — It is tonically increased by surface-positive polarization of the motor cortex (1.5 mA).
F — Control record.
G — Increase in rate of firing elicited by single shocks applied to the same cortical area.
H — Between G and H local strychninization (1 per cent) of the same cortical area. Synchronously with the convulsive waves, the reticular spike discharge is strongly increased in frequency. The reticular effect outlasts the electrical manifestation of the cortical outburst.
(From R. von Baumgarten and A. Mollica, 1954. *Pflügers Archiv*, in press.)

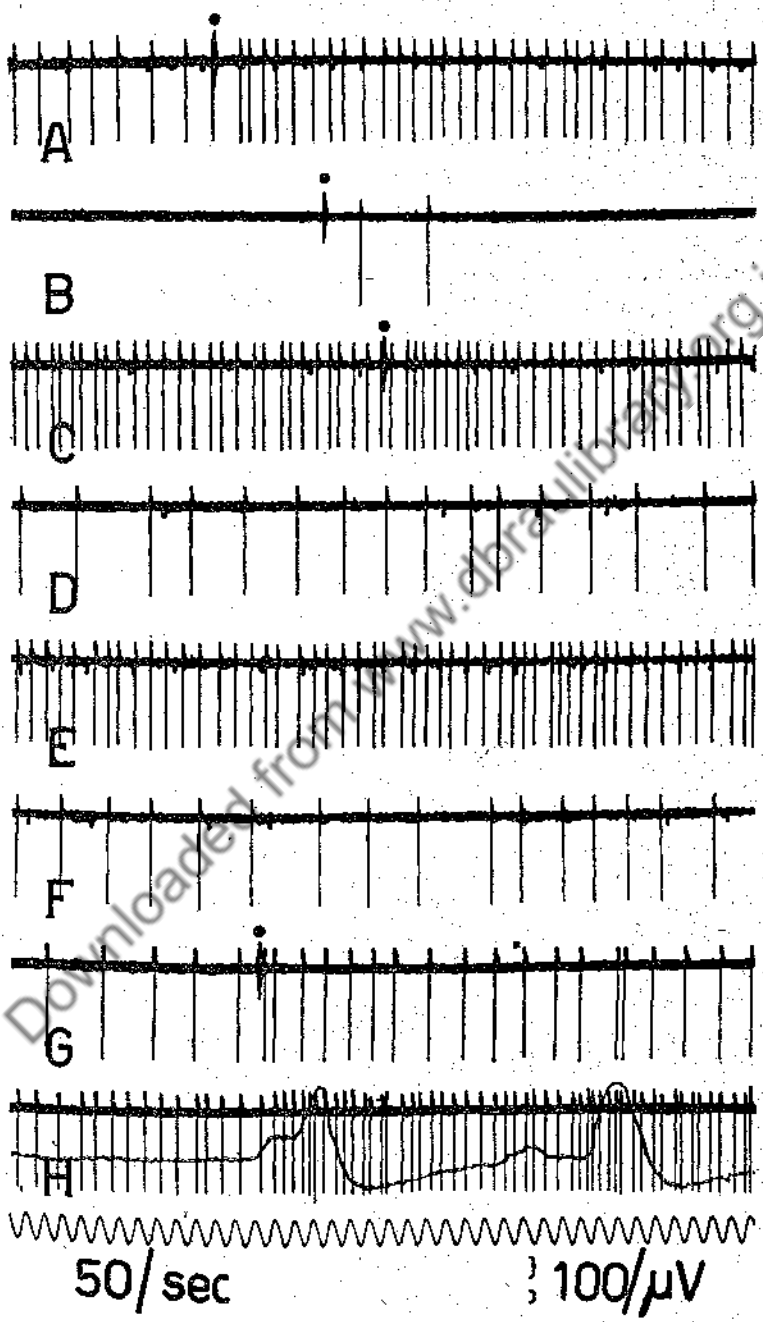


FIG. 4

There are many points which might be discussed in connection with these findings, such as the difference between presynaptic (pyramidal) and postsynaptic (bulbo-reticular) discharges, the influence of cerebellar polarization on the cortically driven reticular activity, the possible significance of an activation of inhibitory reticulo-spinal neurones occurring during the convulsive activity of the motor cortex and, finally, the identification of the pathways connecting the cerebral cortex with the reticular formation. All these problems were dealt with in the symposium on epilepsy, which was held at the Third International EEG Congress (Boston) and the corresponding illustrative material will be reproduced in the *EEG Journal* (Moruzzi, 1954). It will be enough to stress here that the strychnine responses are really due to impulses arising in the motor cortex, since they disappear altogether following its destruction (Fig. 2,E) and that the same unit which is driven by the convulsive corticifugal volleys is clearly influenced by the cerebellar polarization (Figs. 2,F; 4,B). Both the spontaneous and the cortically driven reticular discharge can be inhibited by polarizing the cerebellar anterior lobe, but the spontaneous activity offers less resistance to inhibition. In so far as the cortico-reticular pathways are concerned, it may be useful to recall that Golgi studies have given good evidence of connections between pyramidal fibres and reticular neurones (Cajal, 1909; Scheibel, 1951).

Sometimes the spontaneous bulbo-reticular discharge is inhibited whenever a strychnine wave occurs in the motor cortex (Fig. 1,D). Here too it can be shown that the inhibitory impulses arise in the strychninized motor cortex, since the effect disappears after its ablation (Fig. 1, H). The hypothesis of a proprioceptive reverberation elicited by the strychnine clonus, is not tenable in view of the fact that the response is still present when every movement is abolished following an intravenous injection of d-tubocurarine. Hence the convulsive corticifugal volleys may either inhibit or augment the activity of the bulbo-reticular units.

When single electrical shocks are applied to the motor cortex, both augmentative and inhibitory responses are again obtained. The illustrations will be found in the original paper by von Baumgarten, Mollica and Moruzzi (1954). With this technical procedure, the following new observation could be made: the

shock artifacts was followed sometimes by a short but clear-cut increase in the rate of the reticular discharge and then by a silent period which lasted more than 100 msec.

Only a tonic, non-adaptive increase in the bulbo-reticular discharge was observed as a result of surface-positive polarization of the motor cortex (Figs. 2, B; 4, E). Inhibition was never found with this type of stimulation. It would be obviously premature to draw conclusions from these negative findings. However DC polarization of the cerebellar anterior lobe, with the same technical procedure, is quite effective in inhibiting the bulbo-reticular spike discharge.

Although we have been unable so far to block a bulbo-reticular spike discharge with a surface-positive polarization of the motor cortex, it is true, nevertheless, that both facilitation and inhibition have been obtained quite easily with single shock as well as with strychnine stimulation of the motor areas. A distinction was suggested in the third chapter of the present report between bulbo-reticular elements which are facilitated and those which are inhibited by the cerebellum. To make the same classification in so far as the cortico-reticular relationships are concerned might be misleading, if proper emphasis is not placed on the following observations. First of all both the bulbo-reticular units which are augmented by the motor cortex (Fig. 2, B and D) and those which are inhibited (Fig. 1, D, F, G) may be blocked by the cerebellar polarization (Figs. 2, F; 1, B, E). Hence no clear-cut correlation can be found between the signs of the cortical and of the cerebellar influences upon reticular structures. Secondly, sometimes (although never in a predictable way), the sign of the reticular response to the corticofugal volleys was reversed depending upon the background of the reticular activity (Fig. 3).

One of the most serious drawbacks in any attempt to drive a single reticular unit by stimulating cerebellar or cortical areas is represented by the fact that a large population of functionally non-homogeneous elements must be stimulated in order to get clear-cut responses. Hence we do not know which of the elements activated by the chemical or electrical stimulation is responsible for the single reticular response we are recording. The increase in the reticular discharge may be regarded, after all, as the micro-physiological aspect of the responses led with coarse electrodes

from different regions of the reticular formation, following chemical (Hoefer, and Pool, 1943; Niemer and Jimenez-Castellanos, 1950) or single shock (Lloyd, 1950; Bremer and Terzuolo, 1952; Livingston, French and Hernandez-Peon, 1953) stimulation of the motor cortex. The inhibition of the reticular discharge had never been observed by stimulating the motor cortex. It represents a new problem, which will be eventually solved through further experiments. Finally the cerebellar inhibition of cortically driven reticular discharges shows that cerebello-cerebral inter-relations may occur also at brain stem levels. So far only the cerebral cortex (Walker, 1938; Moruzzi, 1941) and the spinal cord (Moruzzi, 1941; Snider, McCulloch and Magoun, 1949; Snider and Magoun, 1949) had been taken into account in the investigations on the cerebellar influences on cortical activity or on cortically induced movements (see Moruzzi, 1950a).

VII — INFLUENCE OF SENSORY VOLLEYS ON THE BULBO-RETICULAR SPIKE DISCHARGES

We have seen in the past chapter that cerebellar and cortical volleys converge on a single unit of the bulbo-reticular formation. The problem now arises as to whether sensory impulses of different modalities impinge upon the same unit. An attempt to answer this question was made recently by von Baumgarten and Mollica (1953, 1954) and the results of their work will be summarized in the present chapter.

Fig. 4 shows that the same bulbo-reticular unit may be influenced by sensory, cerebellar and moto-cortical volleys. These results confirm and extend previous macroelectrode experiments, which showed e.g. that the wave elicited in the midbrain reticular formation by a click was abolished whenever the acoustic stimulus was timed to occur 20 msec. after single shock stimulation of skin receptors (Bremer and Terzuolo, 1952). These and other observations (Amassian, 1952a; Livingston, Hernandez-Peon and French, 1953) suggest that cortical as well as sensory volleys of different origin share the same neurones of the midbrain reticular formation.

Although the convergence of afferent impulses of different origin on the bulbo-reticular formation is indeed tremendous,

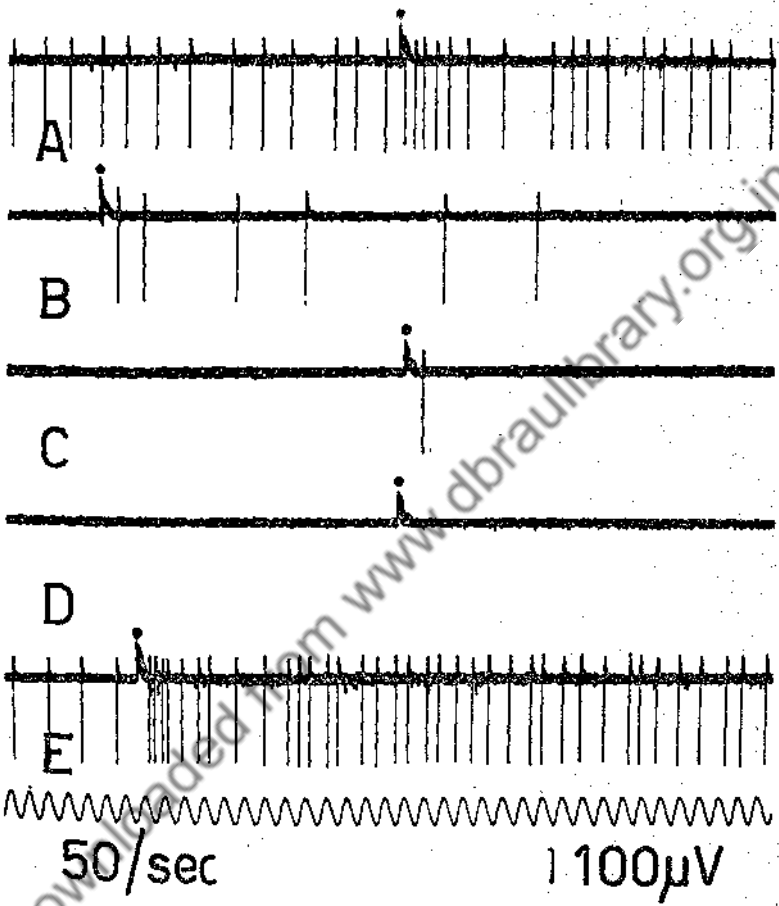


FIG. 5

Influence of increasing the intensity of the cerebellar polarization on spontaneous and on sensory driven reticular discharges.

These records and those of the following illustrations are taken from decerebrate cats.

A, E — Control records: increase in the reticular discharge elicited by single electrical shocks applied to the cornea.

B, C, D — surface positive polarization of the anterior lobe with 0.5 (B), 1 (C), 1.5 (D) mA. The lowest intensity of cerebellar stimulation is already able to block the spontaneous reticular discharge (A); but only with stronger stimuli are the sensory responses abolished altogether (C).

(From R. von Baumgarten and A. Mollica, 1954. *Pflügers Archiv*, in press.)

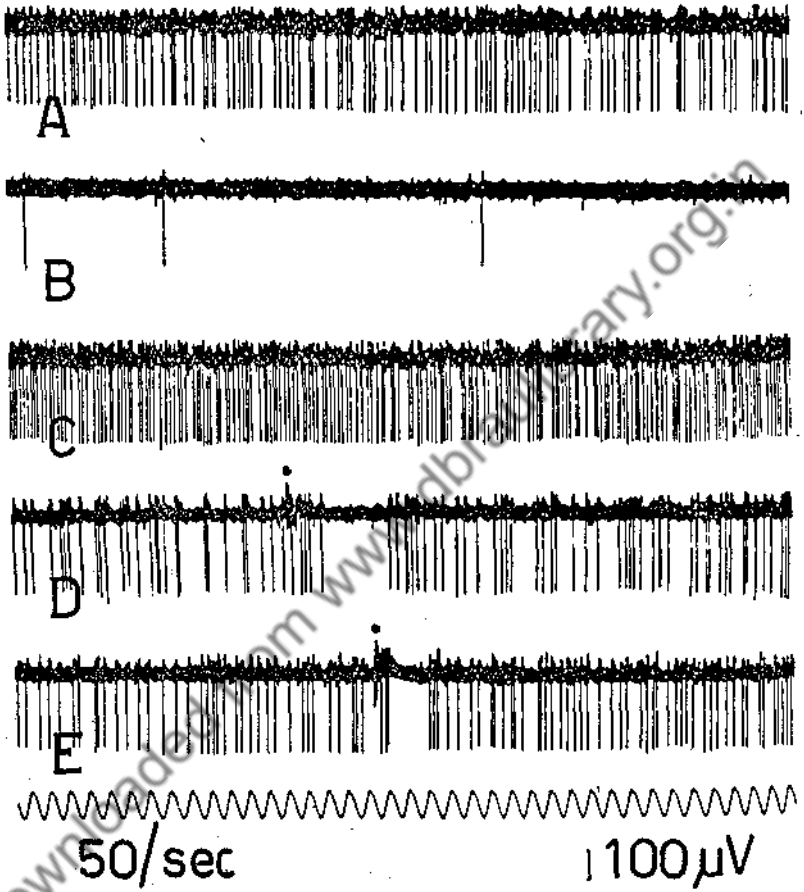


FIG. 6

Inhibition of a bulbo-reticular spike discharge elicited by cerebellar and sensory stimulations.
A — Control record: spontaneous fast discharge.
B — A powerful inhibition is elicited by surface positive polarization of the cerebellar anterior lobe (0.5 mA).
C — Strong rebound increase in the rate of firing following the end of the cerebellar polarization.
D, E — When the reticular activity is normal again, single shocks applied to the central end of the sciatic nerve evoke short lasting but complete blockade of the spontaneous discharge; the inhibitory response is not followed by any rebound increase of the reticular firing.
(From R. von Baumgarten and A. Mollica, 1954. *Pflügers Archiv*, in press.)

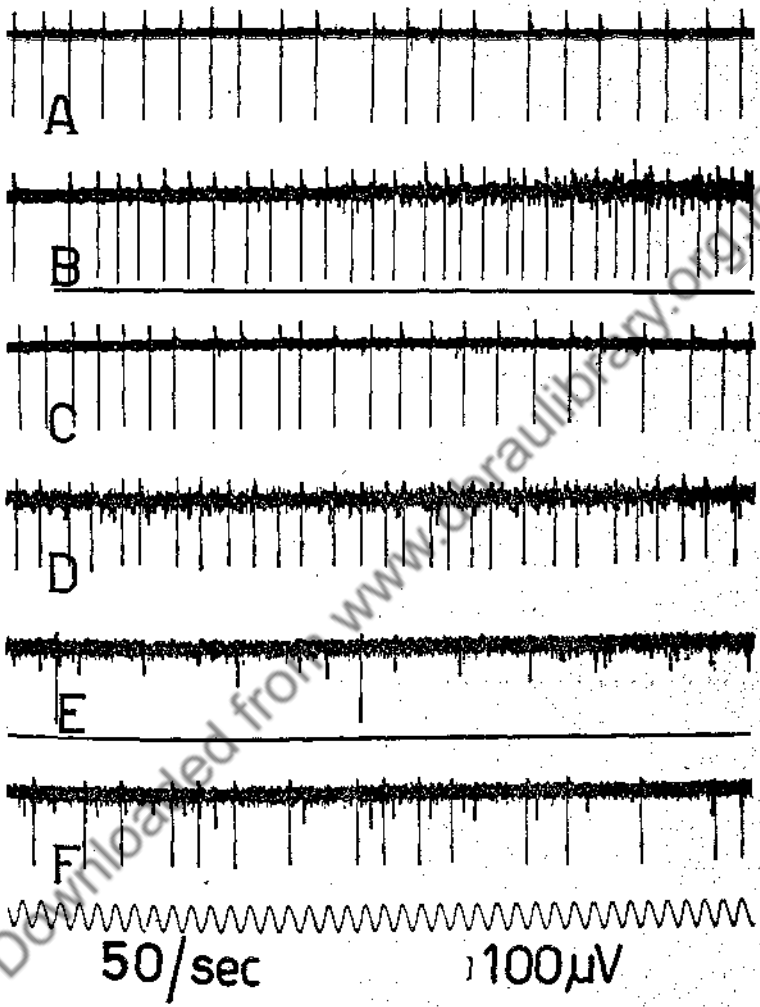


FIG. 7

Opposite results of the same natural stimulation on two different bulbo-reticular units belonging to the same preparation.

In A, B, C and in D, E, F two different bulbo-reticular units were recorded. The second one was identifiable throughout the experiment by notches appearing on the top of every spike. The first unit was increased in its frequency (B), whereas the second one was inhibited (E), by slight tactile stimulation of the cornea.

(From R. von Baumgarten and A. Mollica, 1954. *Pflügers Archiv*, in press.)

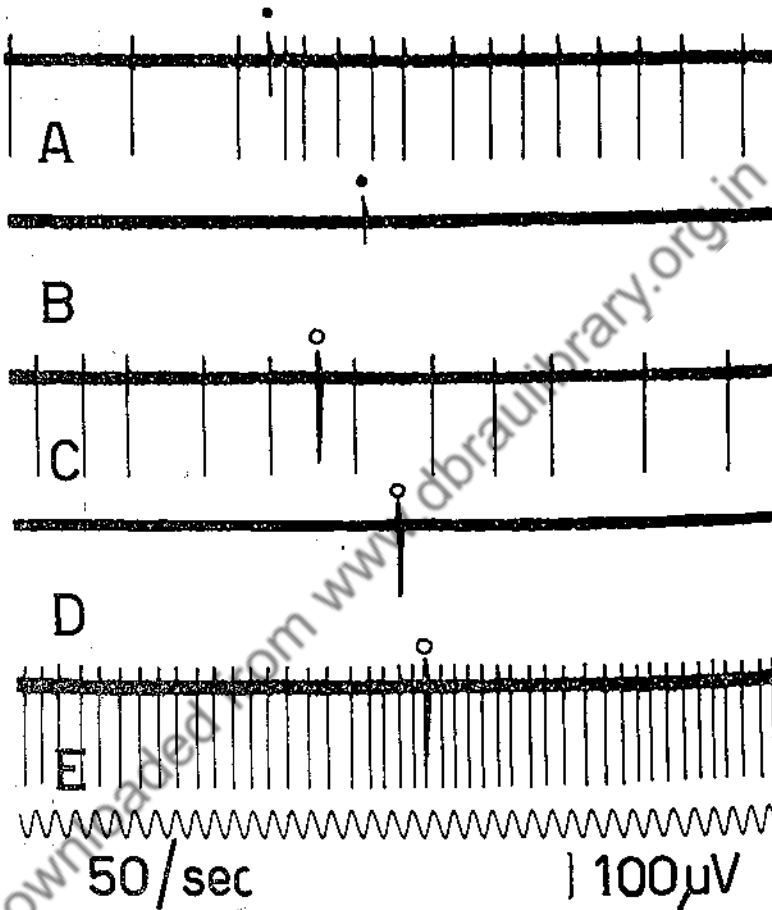


FIG. 8

Ineffectiveness of acoustic stimuli on bulbo-reticular spike discharge.
A — A slowly discharging bulbo-reticular unit is accelerated by a single shock applied to the central end of the sciatic nerve.
B — Both spontaneous and triggered spike discharges are blocked by surface positive cerebellar polarization (0.5 mA).
C, D, E — Strong acoustic stimuli (clicks: circles), eliciting large responses in the cochlear nuclei, are altogether ineffective in the control records (C), during the cerebellar inhibition (D) and during the rebound following the end of the cerebellar polarization (E). (From R. von Baumgarten and A. Mollica, 1954. *Pflügers Archiv*, in press.)

it is by no means unlimited. We see e.g. in Fig. 8 that the spike discharges of a single unit are clearly driven by single electrical shocks applied to the central end of the sciatic nerve (Fig. 8, A), but not by acoustic stimuli (clicks; Fig. 8, C). It might be claimed that the difference is one between artificial and natural stimuli. However, Fig. 7, B shows that the bulbo-reticular discharge may be clearly increased by natural stimulation of the cornea. Since acoustic responses to click have been found by many investigators in the midbrain reticular formation, one wonders if the lower reticular formation might not be divided into overlapping spheres of influence, at least in so far as its afferent connections are concerned.

As for cerebellar and cortical stimulation, the sensory volleys may also inhibit the spontaneous reticular discharge, sometimes after a short-lasting increase in the frequency of firing (Fig. 6, D, E). These inhibitory effects were obtained also with natural stimulations (Fig. 7, E).

When the spontaneous discharge of a bulbo-reticular unit is increased by the sensory volley and inhibited by the cerebellar polarization, one may wonder what the result would be if the sensory polarization were timed to occur during the cerebellar blockade. The bulbo-reticular discharges driven by the sensory volleys are reduced – both in frequency and number of spikes (Fig. 5, A) – by the cerebellar stimulation; for appropriate intensities of cerebellar polarization the induced discharge is blocked altogether and only the stimulus artifact is left (Fig. 5, D). This experiment proves, incidentally, that the inhibition really occurs at the bulbo-reticular level. If the anode polarization acted simply by abolishing cerebello-cortical or fastigial tonic discharges, only the spontaneous activity of the corresponding reticular relays might be blocked; it would be very difficult, however, to abolish their responses to synchronous volleys of afferent impulses.

There are no crucial experiments suggesting that the reticular neurones which are influenced by the sensory volleys belong to the ascending activating system. It would be important to bring such evidence, since its corollary would be that the cerebellum influences the diffuse projection system. Since the reticulo-spinal neurones are also likely to be influenced by some at least of the

sensory volleys, the main problem is one of dissociating the ascending from the descending spike discharges.

VIII — A COMPARISON BETWEEN SENSORY AND RETICULAR EEG AROUSAL

The following experiments show that the lower reticular formation is correlated with the arousal reaction and with the maintenance of wakefulness:

1. Stimulation of the reticular formation in the lower brain stem evokes EEG activation patterns, which are surprisingly similar to those recorded in an alert animal (Moruzzi and Magoun, 1949).

2. This effect is abolished by midbrain lesions destroying the reticular formation, but sparing the classical sensory pathways (l.c.).

3. The same lesions precipitate behavioural and EEG sleep patterns (Lindsley, Schreiner and Magoun, 1949, 1950).

These experiments together show that maintained wakefulness is due to tonic discharges arising in the lower reticular formation and ascending to the brain through pathways different from those of the lemniscal or spino-thalamic systems.

It is generally regarded as a corollary of the aforementioned experiments that the EEG arousal reaction elicited by sensory stimulations represents the phasic response of the reticular system, whose tonic ascending discharge would be responsible for the maintenance of wakefulness. This hypothesis is supported by the following evidence:

1. Collaterals from sensory pathways enter the lower reticular formation (Starzl, Taylor and Magoun, 1951b) and clearly influence the spike discharge of some reticular units (Amassian, 1952a; von Baumgarten and Mollica, 1953, 1954).

2. The EEG patterns elicited by natural sensory stimulation and those evoked by electrical activation of reticular structures are surprisingly similar (Moruzzi and Magoun, 1949).

3. Both types of responses are strongly affected by barbiturates (Moruzzi and Magoun, 1949) and the reticular effects are abolished by levels of anaesthesia which leave the lemniscal conduction intact (French, Verzeano and Magoun, 1953b; Arduini and Arduini, 1953, 1954).

There are, however, some other data, suggesting that more complex mechanisms are involved in the EEG arousal.

First of all, short lasting (but clear-cut) EEG activation patterns are elicited by auditory and somatic stimulation, during the deep sleep which follows the chronic interruption (at midbrain level) of the ascending reticular system (Lindsley, Schreiner, Knowles and Magoun, 1950). Collateral from sensory pathways entering the cephalic portion of the activating system (l.c.), intracortical or cortico-diencephalo-cortical spread (see Bremer, 1951a; Jasper, Ajmone-Marsan and Stoll, 1952; Bremer and Terzuolo, 1952, 1953) from sensory projection areas might explain these findings.

They show at any rate that the lower reticular formation is essential for the maintenance of wakefulness but not for eliciting an EEG arousal. It might just be a matter of intensity of stimulation: the afferent volley impinging upon the nervous centres – when the preparation is not intentionally stimulated – might be too weak to arouse the brain, if it is not properly amplified by the lower reticular system. It is nevertheless undeniable that identical EEG activation patterns may involve different subcortical mechanisms.

Second, similar EEG patterns correspond to quite different levels of individual cortical activity. In the deeply barbiturized cat, e.g., the cortical waves are surprisingly similar – as first pointed out by Bremer (1935) – to those of the *cerveau isolé* (l.c.) preparation or of any unanaesthetized cat in which the midbrain tegmentum has been interrupted (Whitlock, Arduini and Moruzzi, 1952, 1953). And yet no spike discharges are led from the cerebral cortex (Li, McLennan and Jasper, 1952) or from the pyramidal tract (Adrian and Moruzzi, 1939) in a deeply barbiturized preparation; whereas with lighter barbiturate anaesthesia (Adrian *et al.*, l.c.) or in the unanaesthetized cat (pyramidal preparation: Whitlock, Arduini and Moruzzi, 1952, 1953) the cortical spindles parallel spike discharges occurring both in cortical layers and in the pyramidal tract. It seems unlikely, moreover, that the activation patterns elicited by different stimuli are exactly the same, in terms of single unit activity of the different layers of the cerebral cortex; although they do appear to be more or less the same in the EEG records.

These considerations emphasize the importance of investigating

what is really going on in the cerebral cortex during sleep, wakefulness or the different types of arousal elicited by sensory stimuli.

This basic problem, so closely correlated with Adrian's hypothesis of neuronal synchronization, might be solved only by analysing the activity of single cortical neurones. An attempt to investigate the transition from sleep to wakefulness, by leading with a microwire the spike discharges from the cerebral cortex and from the pyramidal tract, was made recently by Whitlock, Arduini and Moruzzi (1952, 1953).

A generalized EEG arousal had been obtained previously by blowing room air into the nostrils of a *cerveau isolé* cat (Arduini and Moruzzi, 1953). This preparation was modified by sparing the pes pedunculi during the midbrain transection; this was easily and quickly accomplished by high frequency electrocoagulation of the midbrain tegmentum, through electrodes oriented with the Horsley-Clarke technique. This 'pyramidal cat' is behaviourally asleep, but movements are elicited by stimulating its motor cortex and pyramidal spike discharges can be recorded by leading with a microwire from the *decussatio* (Whitlock, Arduini and Moruzzi, 1952, 1953).

A good correlation is found between the monotonously recurring spindles led from the motor cortex of the sleeping 'pyramidal cat' and the corresponding corticofugal volleys. The pyramidal discharge disappears completely during the interspindle lulls, whereas the pyramidal outbursts which occur synchronously with the cortical spindles are not associated with any perceptible movement of the animal, though the spinal cord is completely unanaesthetized. This confirms earlier findings made under Dial anaesthesia (Adrian and Moruzzi, 1939).

When air is blown into the nostrils of the 'pyramidal cat', a typical arousal reaction occurs; low voltage, fast waves replace the EEG sleep patterns for 10 to 60 seconds. It should be pointed out, however, that during the EEG arousal the extreme myosis characterizing the *cerveau isolé* cat (Bremer, 1935, 1938) persists, so that ocular sleep patterns and EEG activation patterns are observed simultaneously on the same preparation. It can be shown, nevertheless, that the myosis – which is still present in a preparation whose optic nerves have been acutely or chronically severed (Rossi, 1953) – is more easily inhibited by hypothalamic

stimulation, when the cerebral cortex is aroused by olfactory stimuli (Rossi and Steffanon, 1953). Hence the dissociation between EEG and ocular patterns is simply due to the fact that (in our experimental conditions) the disorganization of brain rhythms is more easily evoked than the inhibition of the tonic activity of Edinger-Westphal neurones.

The spontaneous pyramidal discharge is completely blocked during the EEG arousal elicited by either natural stimulation of the olfactory receptors or by high frequency electrical stimulation of the ventral diencephalon (Whitlock, Arduini and Moruzzi, 1952, 1953). Also the cortical strychnine waves (Arduini and Lairy-Bounes, 1952; Lairy-Bounes, Parma and Zanchetti, 1952; Zanchetti, Wang and Moruzzi, 1952) and the corresponding pyramidal outbursts (Whitlock, Arduini and Moruzzi, 1952, 1953) are blocked, provided only supraliminar concentrations of strychnine are applied. The intrinsic units led with a microwire from the motor cortex behave in a similar fashion. Here again both reticular and natural stimulations yield the same results.

We are not concerned here with the intracortical mechanism of the blockade of the pyramidal discharge. The abolition of the spontaneous pyramidal discharge is not necessarily due to inhibition, as it might be surmised following the first Berger's hypothesis. The lack of ephaptic stimulation, which follows the abolition of the high voltage synchronous waves, might also account for these phenomena (see Adrian, 1949a).

We are interested here in the fact that reticular activation elicited by electrical stimuli duplicates the effect of *startling* sensory stimulations, at least in so far as their influence on slight convulsive activity and on spontaneous pyramidal discharges are concerned. This is not surprising, since with high frequency electrical stimulation of any part of the ascending reticular system as well as with very strong and abrupt sensory stimuli, a mass discharge of the reticular neurones is likely to occur. In both cases the experimental conditions conspire towards an avalanching spread of activity from a given reticular region to the whole of the diffuse projection system.

It would be very dangerous, however, to infer from these experiments that for milder intensities of stimulation also – such as those which are more frequently involved in the processes of

perception and attention – the ascending reticular system behaves in such 'all-or-none' manner. This is only one of the hypotheses which may be put forward. Its corollary would be that for the lower intensities of sensory stimulation or whenever no generalized EEG arousal is evoked, only the specific projection systems would be activated. There is however another possibility, which should be seriously reckoned with. For the lower intensities of sensory stimulation only some districts of the ascending reticular system might be activated and therefore a more localized (or less diffuse) ascending discharge would contribute to the processes of attention for the sensory modality involved.

The microphysiology of the central nervous system is just beginning and it is about one century younger than microscopic anatomy. There is no reason to be surprised, therefore, that many basic problems have not yet been approached experimentally and that the meaning of much of our data remains unclear.

GROUP DISCUSSION

JASPER: Dr. Moruzzi has given us a demonstration of unitary activity in the reticular formation. Such information has been needed for a long time.

ADRIAN: We must have all been excited to see these excellent records, which show what these individual units are doing. It is beautiful work. I should like to ask Dr. Moruzzi whether he knows what comes out of the cerebellum to influence the reticular formation, when the cerebellum is polarized. The fact that the cerebellum is another influence on Dr. Magoun's system seems to complicate the story a little and I do not quite see how the cerebellum fits into the picture.

MORUZZI: I would like to thank Dr. Adrian for his remarks. The reticular responses we have observed arise in the cerebellum, because if one destroys the anterior lobe of the cerebellum and places moist cotton wool in its place, a current of 3 to 4 mA. applied to the cotton wool has no effect. Secondly, the cerebellar influence is mediated by the cerebellar nuclei, since the reticular responses are abolished when these structures are electrocoagulated. Exactly what is occurring in the cerebellum is unknown. There is a preliminary note by Brookhart and Blackly (1952) which throws some light on the cerebellar response to polarizing currents. They recorded, with microelectrodes, the spike discharges from the cerebellar cortex and found a marked increase of

activity during surface-positive polarization. Apparently, the cerebellar impulses going to the reticular formation have either an excitatory or inhibitory effect according to the different types of units in the reticular formation. The alternative hypothesis of a blockade of the cerebellar activity elicited by anodal polarization is disproved by our experiments. We know that paleocerebellar ablation evokes a strong increase in decerebrate rigidity. Therefore, if anodal current blocked the cerebellar discharge we should see an increase of decerebrate rigidity. Actually, we do not; in our experiments only inhibitory effects, inducing a collapse of rigidity, were observed. I would say, therefore (*a*) that anodal polarization probably increases the activity of at least the majority of the Purkinje cells; (*b*) that the Purkinje neurones influence the medial bulbo reticular formation through nuclear relays and (*c*) that the reticular neurones are sometimes excited and sometimes inhibited by the cerebellar volleys.

WALTER: Could Dr. Moruzzi tell us the physiological size of the stimulating electrodes used on the cerebellum, and could he estimate the area of cerebellum affected by this stimulation?

MORUZZI: Large wick electrodes are used, because a smaller size would induce electrolytic lesions. The point of contact is approximately 2 to 4 mm^2. One electrode is in front of the primary fissure and the other one on the posterior vermis.

BREMER: I would like to express my admiration for the splendid work of Dr. Moruzzi and to add one simple technical remark: I would like to suggest that the use of 'anodal polarization' is misleading. I would personally prefer the term 'D.C. polarization'. 'Anodal polarization' corresponds with depression of excitability. After all it is a current passing through the geometry of the cerebellum; one does not know where the cathodic influence might take effect. I would not be surprised if it is the cathodic stimulation which affects the Purkinje cells.

MORUZZI: I entirely agree with Dr. Bremer's remark. I would say that we might properly say that a surface-positive polarization was applied and I agree that we do not know where the stimulus takes place.

JUNG: I would particularly like to ask Dr. Moruzzi about the influence of cortical potentials on the unit discharge in the pyramidal tract and the reticular formation. In the cortical strychnine waves the positive and negative components may have a different influence. When we worked on the cortex with microelectrodes we found that most neurones of the cortical upper layers were activated by surface negative polarization although you may find some discharges during a surface positive potential especially in the lower layers.

MORUZZI: Although we noted occasionally that the reticular re-

sponse occurred only with the rising phase of the strychnine wave, sometimes polyphasic strychnine waves were found to be effective not only during their negative but also during their positive components. It might be interesting to compare the activity of the strychninized motor cortex with that of the pyramidal tract and of the reticular formation.

JASPER: Those among us who have tried to interpret the electrical sign of these potential waves in a volume conductor such as the brain are impressed by the insignificance of the apparent electrical sign of this wave when we find that a positive wave at the surface may be a negative wave 1 mm. beneath. We certainly do not know whether it is anodal or cathodal in terms of the units being affected by these waves.

FESSARD: The only undisputable criterion of the true sign of a bio-electrical event is that given by the sign of the membrane potential change so that we should better speak of a hypo- or hyper-polarization of the neuronal membrane rather than of a negative or positive wave. Unfortunately, in a volume conductor, the only way to know this sign with certainty would be to record potentials with an intra-cellular micro-electrode. Moreover, in order to interpret the effect of an electric action, it is not only necessary to make sure of the true sign of the membrane potential change, but also to have some idea of the previous state of the membrane itself, at the moment when it is acted upon by an electric current of external or internal origin. For instance, an anodal polarization applied to a nerve can re-establish normal excitability in this nerve provided it had previously been in a certain state of depression associated with a diminished membrane potential.

KUBIE: My comments bear on the later part of our symposium, but it may be helpful even this early to indicate points of contact between consciousness and the nervous mechanisms involved. First of all I would like to warn against a tendency to identify inactivity with unconsciousness. Can we for instance be sure that Dr. Magoun's inert monkeys are unconscious in the human sense? Unfortunately they cannot recover and describe their state; and although self-descriptions are never conclusive data they are essential ingredients in the chain of evidence.

My second point concerns the fascinating dissociation between cortical and reticular activity, described both by Dr. Magoun and by Dr. Moruzzi. This gives rise in theory, to at least four and possibly eight or more possible combinations. That is there can be (*a*) simultaneous augmentation of cortical and reticular discharges; (*b*) simultaneous diminution of cortical and reticular activity; (*c*) augmentation of cortical with diminution of reticular activity; (*d*) diminution of cortical with augmented reticular activity. Furthermore, these com-

binations may exist both on the afferent and on the efferent sides, with that many more possible combinations. I do not know how many of these states occur in nature; but I mention them as logical possibilities; because if these different combinations influence states of consciousness in any way, they provide us with a remarkably flexible array of neurological mechanisms for understanding the various states of consciousness.

Thirdly, I would like to ask for specific data on the relative representation of different elements of the afferent systems in the ascending reticular system. Are the exteroceptive, prioprioceptive and enteroceptive systems all represented? The answer to this will have significance for the mechanisms of memory, for the sensory content of both day-dreams and the dreams of sleep, and many other problems.

Finally, for special reasons which I will discuss later, I would like to inquire about the representation of the respiratory complex in the ascending reticular formation.

JASPER: I am sure we are all glad that Dr. Kubie has helped to keep us oriented to the highest levels of discussion, even when we are dealing with unitary activity in the medulla.

RIOCH: I would like to raise the question about evidence that the immediately preceding activity of the cell apparently dictates the response of the unit. I have had this impression as a result of stimulation experiences and wonder whether you have noted the same effects in your dealing with single units.

MORUZZI: We have to consider two types of reticular responses: to cortical and to cerebellar stimulation. Whenever a unit was inhibited by cerebellar polarization, no reversal in the reticular response could be obtained, by changing the level of activity. *Vice versa* the response to cortical stimulation was clearly influenced, sometimes, by changes in the background activity. For instance in one experiment a reticular unit was caused to discharge during the first strychnine wave; if then a second strychnine wave occurred during the increased reticular activity elicited by the conditioning volley, an inhibition was observed. We tried unsuccessfully, to obtain experimental reproduction of these occasional findings.

FESSARD: Such fluctuations can be expected at the single unit level. General rules can be established only after a statistical study. In one sense, single units are misleading in that they are like trees that mask the forest.

RIOCH: At what level of the brain stem were these units?

MORUZZI: They were in the medial portion of the bulbar reticular formation. On stimulation of this region one obtains inhibition.

WALTER: One of our first tasks is to get an idea of the scale of this

problem. If we know the size and complexity of the reponses we could predict the minimum number of units necessary to account for the phenomena on a simple analogous basis. It seems to me that some of the data presented by both Dr. Moruzzi and Dr. Magoun are amenable to rather simple manipulation to determine the complexity of the systems involved.

MAGOUN: May I ask Dr. Moruzzi whether the cerebellar influence is most pronounced upon the reticular units that are working downstream or whether it acts equivalently on cephalically directed units. The reason I ask this is that one has little impression of the importance of the cerebellum in wakefulness following cerebellectomy. I have seen animals with cerebellectomy who the next morning were alert and awake and seemingly normal as regards their consciousness.

MORUZZI: It is easier to identify the descending reticular units than the ascending ones. By stimulating the cornea we can modify the activity of reticular units which are possibly directed cephalad; both the spontaneous and the driven discharges of these units are inhibited by cerebellar polarization. We can confirm that cerebellectomy does not appear to affect wakefulness or the EEG patterns. This shows that the cerebellar influence, if present, is not tonic in nature.

LASHLEY: There is good evidence that pain sensation is conducted not only by the long pathways but also by short internuncial systems. I was wondering to what extent pain conduction may be functionally distinguished from other sensations by its implication of the reticular formation.

MORUZZI: I do not know if I can answer that. Our reticular units were driven by sciatic shocks, but not by stimuli applied to a dental nerve. Indeed, some units are activated by some kinds of sensory stimuli and not by others.

MAGOUN: Dr. William Livingston has been stimulating tooth-pulp and recording in the brain stem. He finds that a few whiffs of ether will wipe out the ascending discharges in the medial brain stem, leaving activity in the classical projection, pathways unaffected.

PENFIELD: I would like to ask Dr. Magoun what he means by ascending. What is it ascending to? He describes the effect of nembutal which leaves the direct pathway intact, so that impulses reach the appropriate cortical area. One should, in reality, record the next stage of the impulse stream beyond this cortical arrival. Otherwise, it may be assumed that there is no projection beyond the cortex. Would he define his 'ascending' or retract it?

MAGOUN: I used the word loosely as I use most words. What one sees under nembutal is the arrival in the cortex of afferent impulses marked by an augmented, surface-positive wave. The succeeding

negative wave conspicuous in the unanaesthetized brain, is reduced or may even be absent. I have assumed that this latter was related to the spread of activity within cortical interneuronal paths to bordering areas or down to the brain stem for reverberation between it and the cortex. I presume that it is these later events that are blocked.

KUBIE: I have assumed that what Dr. Magoun is talking about is afferent with respect to the cortex.

JASPER: You might say that this is corticipetal thus avoiding the connotation of 'ascending'. With reference to the question of collaterals Dr. Bishop is attempting to analyse this in terms of nerve components involved both in the visual system and with regard to sciatic stimulation. He has the impression that the so-called collaterals which go into the reticular formation are not collaterals in the literal sense, but may be different fibres in the nerve bundle. This would mean that the 'non-specific system' may begin in the periphery and is conducted over different fibre pathways to the brain-stem reticular formation.

THE CYTOARCHITECTURE OF THE HUMAN RETICULAR FORMATION

By

JERZY OLSZEWSKI

INTRODUCTION

The findings which will be presented here are the result of a study which was begun in 1947 in the Vogts' Brain Research Institute in Neustadt, and has been continued, after an interruption of several years, in the Montreal Neurological Institute. In this second period I was very fortunate to have Dr. Donald W. Baxter working with me on this project and the observations reported here are the result of our combined efforts.

The territory of the lower brain stem which I propose to describe can be defined as follows. It includes all the grey masses of the tegmentum of the medulla, pons and midbrain, which do not belong either to the cranial nerve nuclei, to the relay nuclei of the cerebellar system or to the relay nuclei of the lemniscal systems. Since the title of this talk includes the term 'reticular formation', an explanation seems warranted as to why I prefer to omit this term from the above definition. There are three main reasons:

1. Anatomically, the reticular formation is a poorly defined structure.
2. The anatomical and physiological conceptions of the reticular formations do not correspond with each other.
3. The reticular formation is not a morphological unit, but is composed of many nuclei of very different structure.

Points one and two will be further discussed in the introduction, and point three will form the main part of the general discussion.

1. Anatomically, the name reticular formation has been applied to those parts of the lower brain stem which in the myelin stain are characterized by an interlacing network of fibre bundles. It

is apparent that the delineation of the reticular formation based on this definition, which dates back to the early stages of microscopical investigation of the central nervous system, cannot be precise. Further, where the myeloarchitectonic method is applied, structures should be delineated on the basis of the character and density of the background felt of single fibres. Delineation of the reticular formation is attempted by paying particular attention to the presence and arrangement of coarse fibre bundles (many of which are probably *fibres de passage*), whereas the background felt is ignored. Finally, there exists considerable inconsistency in the anatomical nomenclature. Some nuclei, which undoubtedly lie within the limits of the reticular formation and by definition form a part of it, do not bear the prefix 'reticularis' in their names. The nucleus raphae pallidus or the nucleus cuneiformis may serve as examples.

2. In recent years there has been a tendency to use the term reticular formation not only in an anatomical, but also in a physiological sense. This tendency grew from the results of experimental physiological investigation of the lower brain stem. These results indicate that central portions of the lower brain stem are the seat not only of respiratory, vascular and vegetative mechanisms, but also of systems which influence profoundly the activity of the final motor pathway and of the diencephalic and telencephalic centres. The reticular formation in the physiological sense refers to the morphological substratum of these systems. A comparison between the extent of the reticular formation in the anatomical and the physiological sense reveals some important discrepancies.

For example, the lateral nucleus of the medulla seems to be primarily a relay station for long ascending tracts to the cerebellum, and as such probably does not belong to the reticular formation in a physiological sense. Anatomically, however, it must be included in it. On the other hand, such nuclei as interpeduncularis or griseum centrale mesencephali though anatomically not a part of the reticular formation belong to it functionally. And how should we classify such structures as the red nucleus or the substantia nigra?

In addition to avoiding in this presentation the term 'reticular formation', I have also followed the practice adopted in our work

with Dr. Baxter and have omitted the prefix 'reticularis' from names of all nuclei of the lower brain stem.

Before we turn to the description of the cytoarchitectonic findings, the term nucleus should be defined. This term refers to a three-dimensional territory of the subcortical grey matter which can be distinguished from the neighbouring territories on the basis of the structure and arrangement of its nerve cells. Particular attention should be directed towards the structure of nerve cells, i.e., their size, shape and the configuration of the Nissl substance, as a distinguishing characteristic of various nuclei. There is a great difference between our approach to delineation of such structures as, for example, the red nucleus or the dorsal motor nucleus of the vagus on one hand, and the nucleus pontis centralis caudalis or the nucleus pontis centralis oralis on the other. The red nucleus is surrounded by a thick lamella and can be distinguished even with the naked eye. The dorsal motor nucleus of the vagus forms a densely packed and darkly stained cell group, conspicuous even under a low power magnifying glass. The nuclei pontis centralis caudalis and oralis have – if I may use a geographical term – no natural boundaries in many directions. In the myelin stain nothing apparent suggests their individuality. Even in the Nissl stain, delineation of these two nuclei using only low power magnification is most difficult. If, however, sufficient attention is paid to the over-all pattern of cell arrangement, the number of cell types present and the characteristic of each individual cell type, the nuclei pontis centralis caudalis and oralis may be differentiated from the surrounding structures and from each other.

By approaching the grey masses of the lower brain stem in this manner, we were able to subdivide all of them into individual nuclei. Forty-eight of the ninety-eight nuclei delineated are all within the scope of this presentation. Of these, I am going to mention only twenty-two. These twenty-two, however, represent the largest nuclei and give a good over-all picture of relations and variations of cytoarchitecture.

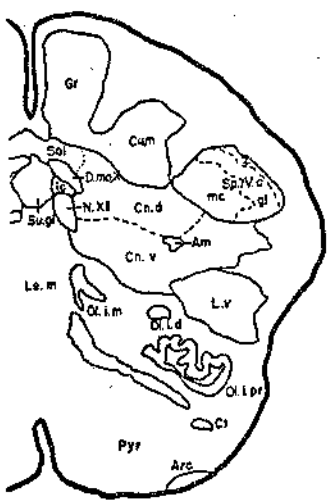


FIG. 1

Section at the level of the caudal pole of the inferior olive.

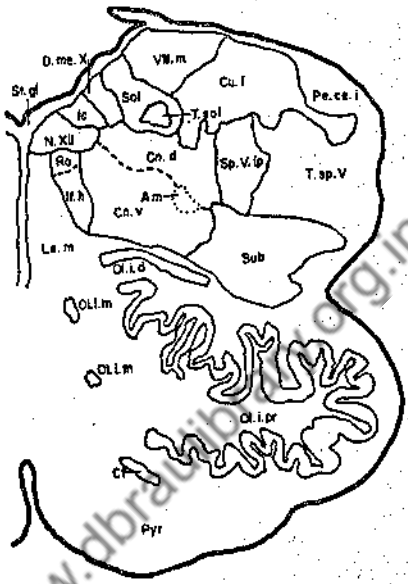


FIG. 2

Section at the level of oral one-third of the inferior olive.

Abbreviations:

Am — Nucl. ambiguus
Arc. — Nucl. arcuatus
Cn. d — Nucl. medullae oblongatae centralis, subnucl. dorsalis
Cn. v — Nucl. medullae oblongatae centralis, subnucl. ventralis
Ct — Nucl. conterminalis
Cu. l — Nucl. cuneatus lateralis
Cu. m — Nucl. cuneatus medialis
D. mo. X — Nucl. dorsalis motorius nervi vagi
Gr — Nucl. gracilis
Ic — Nucl. intercalatus
If. h — Nucl. interfascicularis hypoglossi
Le. m — Lemniscus medialis
Lv — Nucl. medullae oblongatae lateralis, subnucl. ventralis
N. XII — Nucl. nervi hypoglossi
Ol. i. d — Nucl. olivaris inferior accessorius dorsalis
Ol. i. m — Nucl. olivaris inferior accessorius medialis
Ol. i. pr — Nucl. olivaris inferior principalis
Pe. ce. i — Pedunculus cerebelli inferior
Pyr — Pyramis
Ro — Nucl. Roller
Sol — Nucl. tractus solitarii
Sp. V. c — Nucl. tractus spinalis trigemini caudalis
gl — subnucl. gelatinosus
mc — subnucl. magnocellularis
z — subnucl. zonalis
Sp. V. ip — Nucl. tractus spinalis trigemini interpolaris
St. gl — Stratum gliosum subependymale
Su. gl — Substantia gliosa centralis
Sub — Nucl. medullae oblongatae subtrigeminalis
T. sol — Tractus solitarius
T. sp. V — Tractus nervi trigemini spinalis
VIII. m — Nucl. vestibularis medialis

CYTOARCHITECTURE

The nuclei will be described utilizing semischematic drawings of representative cross sections of the lower brain stem, and photomicrographs of individual nuclei.*

Section I

In this section (Fig. 1), which passes at the level of the caudal pole of the inferior olive, we see the large nucleus centralis medullae oblongatae. The nucleus occupies the central part of the section and lies dorsal to the amiculum of the inferior olive and the nucleus lateralis medullae oblongatae, and ventral to the nucleus cuneatus medialis and the caudal nucleus of the spinal trigeminal tract. The cells of the nucleus centralis medulla oblongatae (Fig. 5) are medium-sized to small, slender, multipolar and possess long dendrites. The Nissl substance is in the form of large, darkly stained bodies in the larger cells, but the smaller cells have a pale, diffusely stained cytoplasm. On the basis of the cell size and arrangement a subdivision into dorsal and ventral subnuclei is possible.

Section II

The second section (Fig. 2) passes through the level of the oral one-third of the inferior olive. The nucleus centralis medulla oblongatae is still present. It is slightly reduced in size and its relations change to some extent, due to the widening of the central canal into the fourth ventricle, the development of new nuclei, and a shifting of previously present nuclei into different positions.

A large nucleus now occupies the ventrolateral corner of the medullary tegmentum. This is the nucleus subtrigeminalis which lies dorsal to the amiculum of the inferior olive and ventral to the spinal trigeminal tract and its interpolar nucleus. The cells of the nucleus subtrigeminalis are irregularly arranged – some are

* During the conference the presentation was illustrated by lantern slides of all representative nuclei. Due to the limited space allowed for illustrations in this publication, only a few of the most characteristic pictures have been included. For detailed description of all nuclei of the human brain stem see: Olszewski, J. and Baxter, D. (1954) *The Cytoarchitecture of The Human Brain Stem.* S. Karger Basle, New York. Distributor for U.S.A. and Canada, J. B. Lippincott, Co., Philadelphia and Montreal.

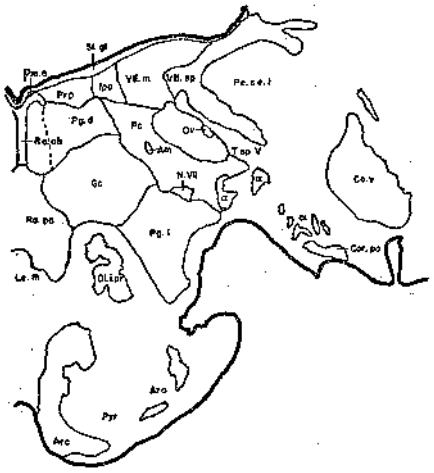


FIG. 3

Section at the level of the oral pole of the inferior olive.

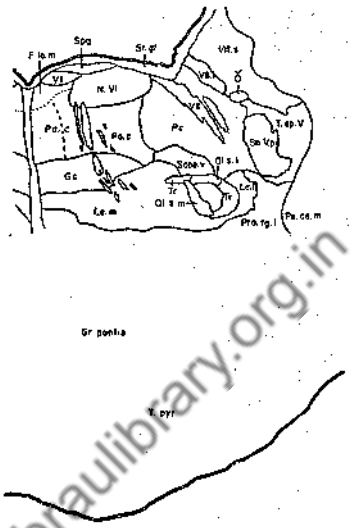


FIG. 4

Section at the level of the nucleus nervi abducentis.

Abbreviations:

Am — Nucl. ambiguus Arc — Nucl. arcuatus
Co. v — Nucl. cochlearis ventralis
Cor. po — Nucl. corporis pontobulbaris
F. lo. m — Fasciculus longitudinalis medialis
Gc — Nucl. gigantocellularis Gr. pontis — Griseum pontis
Ipo — Nucl. interpositus Le. l — Lemniscus lateralis
Le. m — Lemniscus medialis N. VI — Nucl. nervi abducentis
N. VII — Nucl. nervi facialis
O. i. pr — Nucl. olivaris inferior principalis
Ol. s. l — Nucl. olivaris superior lateralis
Ol. s. m — Nucl. olivaris superior medialis
Ov — Nucl. ovalis Pc — Nucl. parvocellularis
Pe. ce. i — Pedunculus cerebelli inferior
Pe. ce. m — Pedunculus cerebelli medialis
Pg. d — Nucl. paragigantocellularis dorsalis
Pg. l — Nucl. paragigantocellularis lateralis
Pm. o — Nucl. paramedianus dorsalis oralis
Po. c — Nucl. pontis centralis caudalis
Prp — Nucl. praepositus hypoglossi
Pro. tg. l — Processus nuclei pontis tegmentosus lateralis
Pyr — Pyramis Ra. ob — Nucl. raphae obscurus
Ra. pa — Nucl. raphae pallidus
Scoe. v — Nucl. subcoeruleus, subnucl. ventralis
Sn. V. pr — Nucl. nervi trigemini sensibilis principalis
Spg — Nucl. suprageniculatus
St. gl — Stratum gliosum subependymale
T. pyr — Tractus pyramidalis Tr — Nucl. trapezoidalis
T. sp. V — Tractus nervi trigemini spinalis
VII — Nervus facialis VIII. l — Nucl. vestibularis lateralis
VIII. m — Nucl. vestibularis medialis
VIII. s — Nucl. vestibularis superior VIII. sp — Nucl. vestibularis spinalis

aggregated into dense clusters, some are loosely scattered. Predominantly they are medium-sized, plump and oval with dendrites of medium length, eccentric nuclei and peripheral Nissl bodies. A few cells are slender, multipolar or spindle-shaped, and the Nissl bodies are evenly distributed.

Section III

The third section (Fig. 3) cuts the oral pole of the inferior olive, at the level just caudal to the junction of the medulla and pons. As compared with the last section, the cytoarchitecture of the medullary tegmentum has changed considerably; the nuclei described above have disappeared and several new nuclei are present.

The nucleus gigantocellularis occupies the central position among these new nuclei, lying dorsally to the oral pole of the amiculum of the inferior olive. The cells of the nucleus gigantocellularis are of three main types (Fig. 6).

A. Most numerous, and found throughout the whole length of the nucleus are very large multipolar cells with conspicuous dark Nissl bodies. In the oral portion of the nucleus these cells are predominantly elongated or spindle-shaped, with their long axes oriented horizontally.

B. Less numerous, and present in the caudal half of the nucleus only, are extremely characteristic cells. They are large, irregularly formed, plump and possess short dendrites. The nucleus is eccentric. The Nissl substance is arranged in the form of large irregular clusters which lie on the periphery of the perikaryon. The edges of these cells are characteristically ragged. In certain cells of this type the Nissl bodies show a tendency for concentric arrangement around the nucleus. Due to their peculiar appearance, I have suggested that they be called 'onion-skin' cells.

C. Small to medium-sized, spindle-shaped or triangular cells, with varying amounts of Nissl substance and dendrites of medium length.

Dorsomedially and ventrolaterally, the nucleus gigantocellularis is accompanied by two nuclei, which bear some morphological resemblance to it. The nucleus paragigantocellularis dorsalis is composed of a smaller variety of cell type A and numerous cells of type C. Some of the cells of type A possess extremely

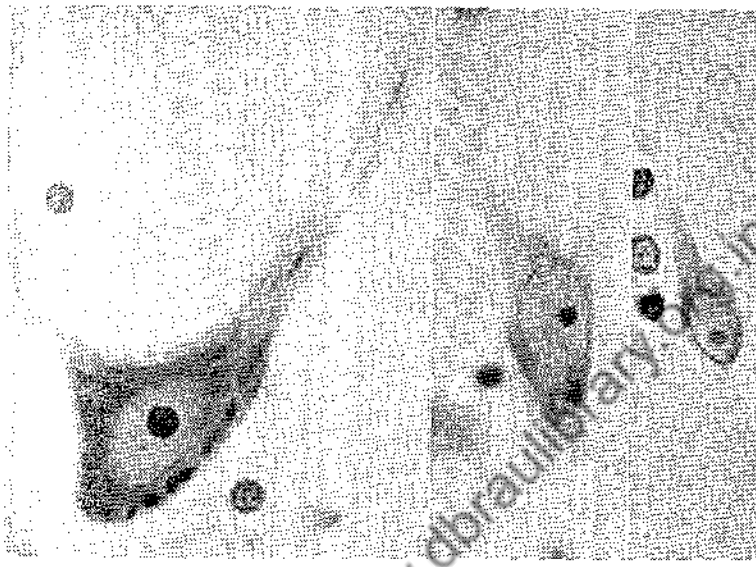


FIG. 5
Three cells from the nucleus centralis medullae oblongatae.

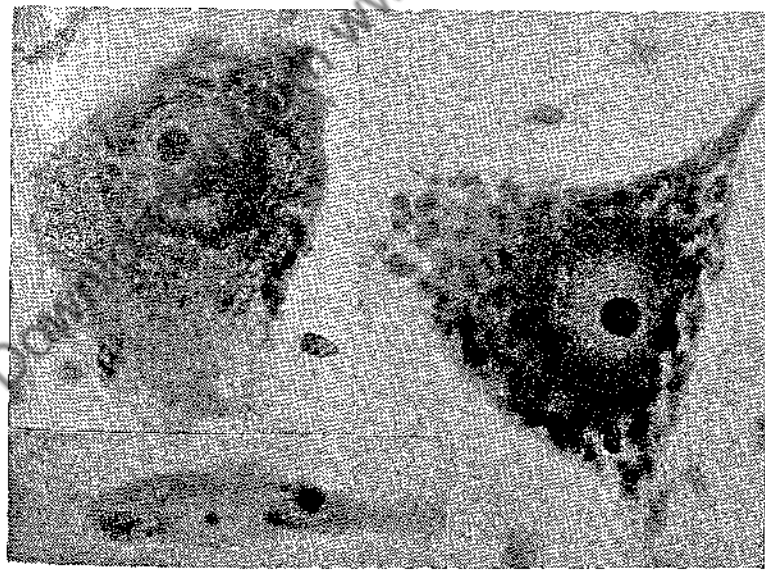


FIG. 6
Three cell types found in the nucleus gigantocellularis. See text for description.

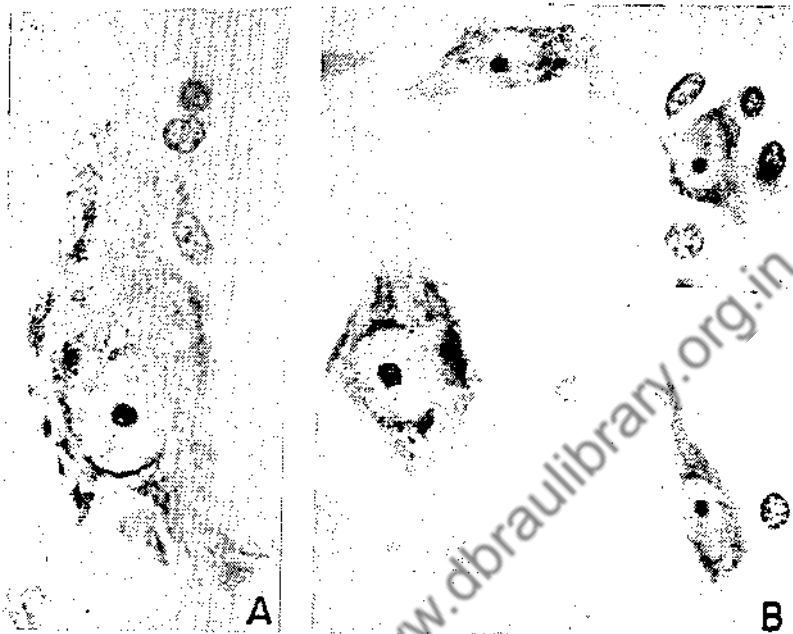


FIG. 7

A. A cell from the nucleus raphae pallidus. B. Cells from the nucleus parvocellularis.

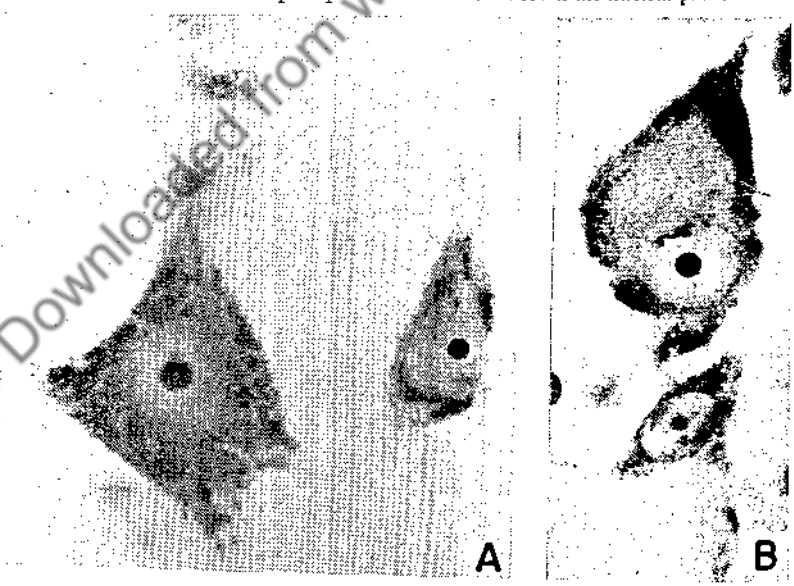


FIG. 8

A. Two cell types found in the nucleus pontis centralis caudalis.
B. Two cell types found in the nucleus pontis centralis oralis.

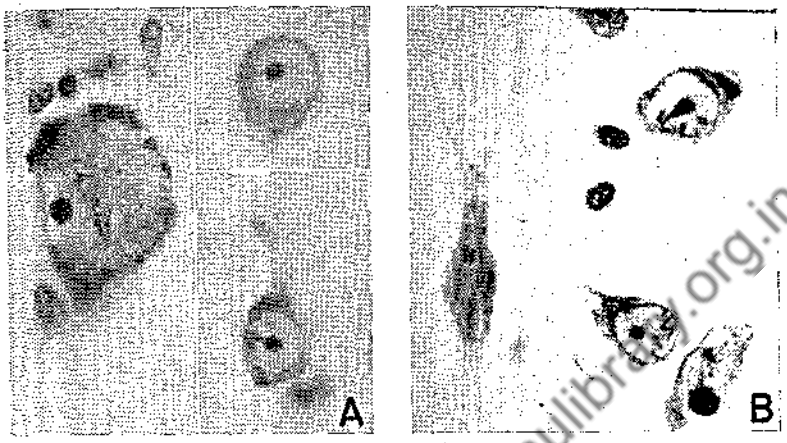


FIG. 9
A. Two cell types from the nucleus centralis superior.
B. Cells from the central grey matter.

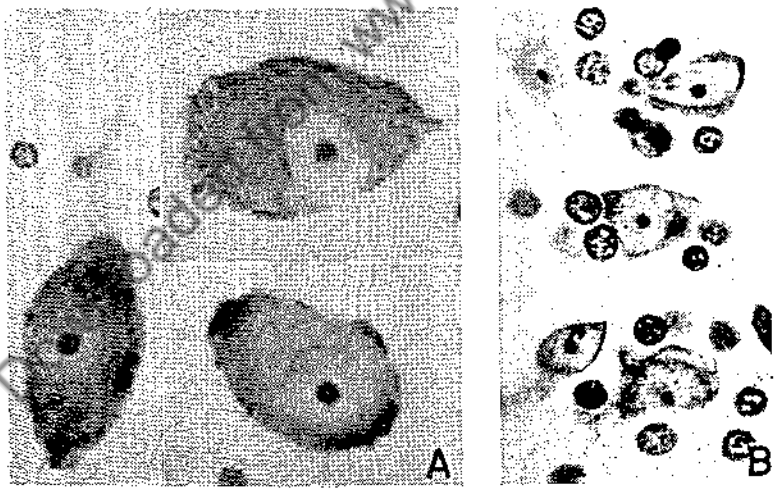


FIG. 10
A. Cells from the nucleus tegmenti pedunculopontinus:
Two cells with excentric nuclei and peripherally arranged Nissl substance, and one cell with evenly distributed Nissl bodies and more centrally placed nucleus.
B. Three cells from the nucleus cuneiformis. Note intense glial satelitosis.

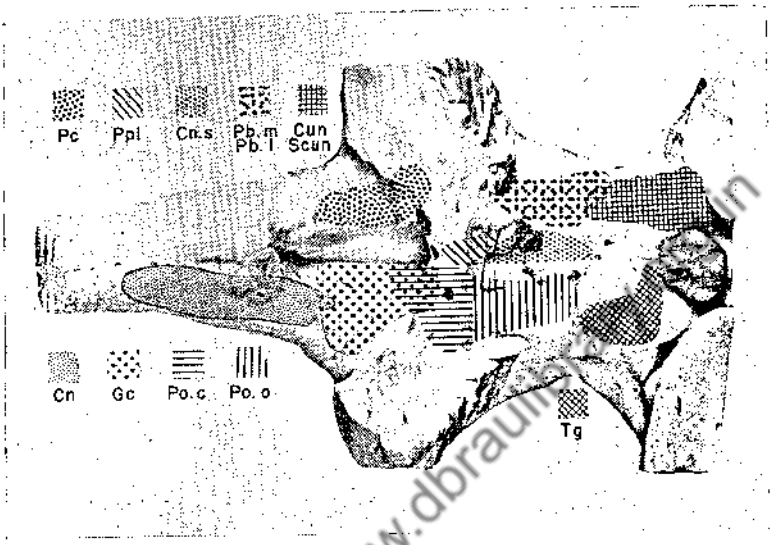


FIG. 11

Horizontal projection of certain nuclei of the lower brain stem.

Abbreviations to Figs. 11 and 12:

Cn — Nucl. centralis medullae oblongatae
Cn. s — Nucl. centralis superior
Cun and Scun — Nuclei cuneiformis and subcuneiformis
Gc — Nuclei gigantocellularis and paragigantocellulares
Gr. cn — Griseum centrale
Ip — Nucl. interpeduncularis
Pb. m and Pb. l — Nuclei parabrachialis medialis and lateralis
Pc — Nucl. parvocellularis
Po. c — Nucl. pontis centralis caudalis
Po. o — Nucl. pontis centralis oralis
Ppl — Nucl. papillioformis
Ra. pa — Nucl. raphae pallidus
Ru — Nucl. ruber
Str — Nucl. supratrochlearis
Su. n — Nucl. substantiae nigrae
Sub — Nucl. subtrigeminalis
Tg — Nucl. tegmenti pedunculopontinus

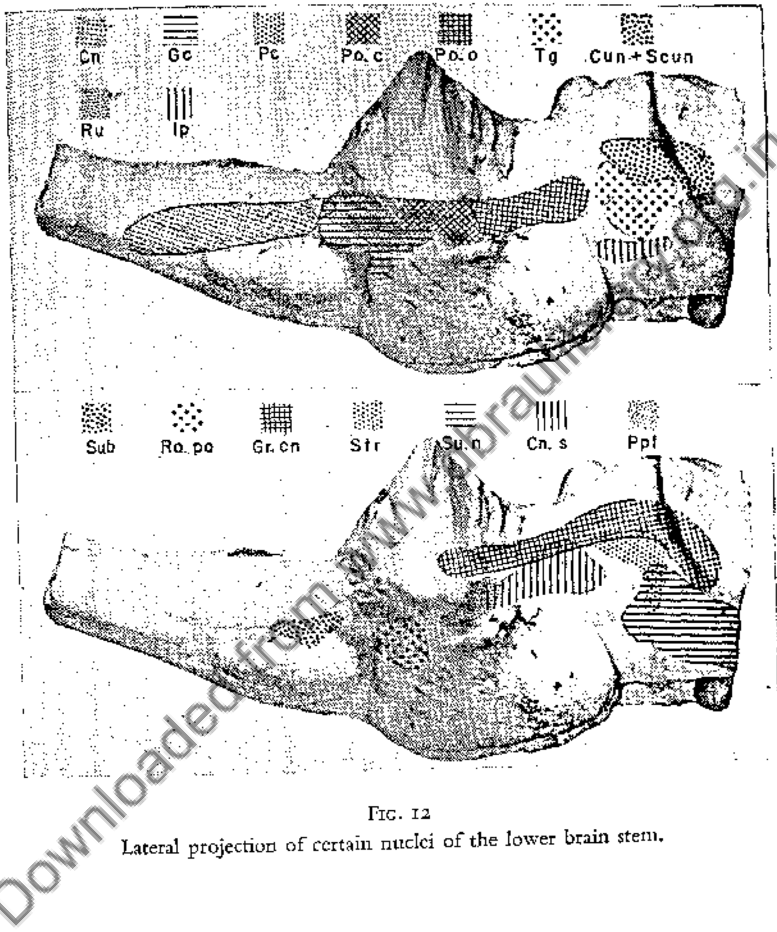


FIG. 12
Lateral projection of certain nuclei of the lower brain stem.

long dendrites and a very slender perikaryon. An occasional 'onion-skin' cell may be present. The nucleus paragigantocellularis lateralis is composed of similar, but slightly larger cells than the latter. In addition, a few medium-sized cells with peripheral Nissl bodies are seen.

The space between the nucleus gigantocellularis of each side is occupied by the nucleus pallidus raphae, which is formed by elongated, medium-sized cells with a very pale cytoplasm, and a few small peripherally arranged Nissl bodies (Fig. 7). These cells are very characteristic, and are not found in other nuclei of the brain stem. A few 'onion-skin' cells are regularly present in this nucleus.

Dorsolateral to the nucleus gigantocellularis, the nucleus parvocellularis occupies a large kidney-shaped area, in whose hilus lies the oral nucleus of the spinal trigeminal tract. The nucleus parvocellularis is composed of small to medium-sized, loosely arranged cells with medium-sized, moderately dark Nissl bodies, and long dendrites. Numerous glial satellites are usually accumulated around the cells (Fig. 7, B).

Section IV

The fourth section represents the level of the nucleus nervi abducentis (Fig. 4). The nuclei parvocellularis and gigantocellularis are still present. The nucleus parvocellularis has enlarged somewhat and is now traversed by the descending root of the facial nerve. The nucleus gigantocellularis has diminished in size and its elongated cells are oriented horizontally. This characteristic appearance of the oral portion of the nucleus gigantocellularis prompted Ziehen to call this region piscina.

The large area between the nucleus gigantocellularis ventrally and the nucleus nervi abducentis dorsally is occupied by the nucleus pontis centralis caudalis. In its main part this nucleus is composed of small lightly stained multipolar or spindle-shaped cells, among which lie single large multipolar cells with dark, regular Nissl bodies (Fig. 8, A).

Section V

This section (Fig. 13) passes through the level of the lingula of the cerebellar vermis, and cuts through many new nuclei which we must mention.

The central portion of the pontine tegmentum is occupied by the nucleus pontis centralis oralis. This nucleus is less cellular than those described above. It is composed of numerous small multipolar triangular or fusiform cells stained with medium intensity and a few medium-sized cells with eccentric nuclei, ragged edges and peripherally arranged Nissl substance (Fig. 8, B). The presence of this type of cell in various nuclei, alone, or in combination with other cell types, is characteristic of the tegmentum of the midbrain and oral pons.

Ventral to the floor of the fourth ventricle, which narrows now to become at a slightly more oral level the Sylvian aqueduct, lies the griseum centrale pontis composed of small cells darkly stained and compactly arranged. On both sides of the raphe, the nucleus centralis superior has just made its appearance. Its cells are of two types; very small, round or oval, lightly stained cells; and medium-sized, oval cells with eccentric nucleus and Nissl bodies accumu-

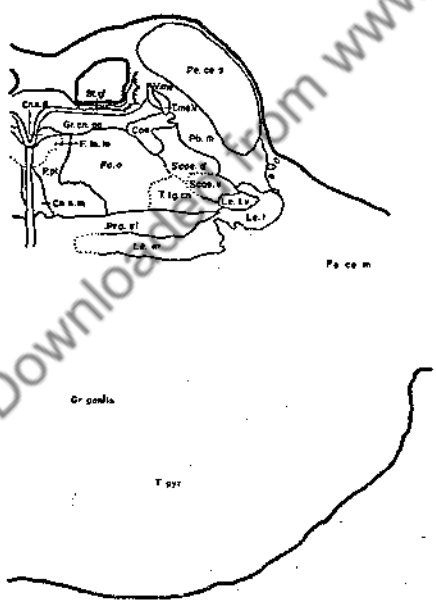


FIG. 13
Section at the level of the oral pons.

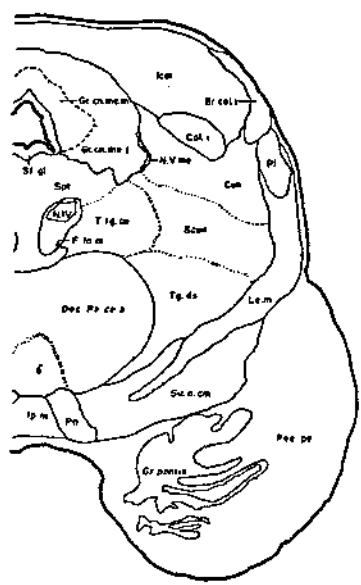


FIG. 14
Section at the level of the inferior colliculus.

Abbreviations: to figs. 13 and 14

Br. col. i – Brachium colliculi inferioris
Cn. s. d – Nucl. centralis superior, subnucl. dorsalis
Cn. s. m – Nucl. centralis superior, subnucl. medialis
Coe – Nucl. locus coeruleus
Col. i – Nucl. colliculi inferioris
Cun – Nucl. cuneiformis
Dec. Pe. ce. s – Decussatio pedunculorum cerebelli superiorum
F. lo. m – Fasciculus longitudinalis medialis
Gr. cn. me. m – Griseum centrale mesencephali, subnucl. medialis
Gr. cn. me. l – Griseum centrale mesencephali, subnucl. lateralis
Gr. cn. po – Griseum centrale pontis
Gr. pontis – Griseum pontis
Icol – Nucl. Intercollicularis
Ip. m – Nucl. interpeduncularis, subnucl. medialis
Le. l – Lemniscus lateralis
Le. l. v – Nucl. lemnisci lateralis ventralis
Le. m – Lemniscus medialis
N. IV – Nucl. nervi trochlearis
N. V. me – Nucl. nervi trigemini mesencephalicus
Ppl – Nucl. papillioformis
Pb. m – Nucl. parabrachialis medialis
Pe. cc. m – Pedunculus cerebelli medialis
Pe. ce. s – Pedunculus cerebelli superior
Pes. pe – Pes pedunculi
Pl – Nucl. paralemniscalis
Pn – Nucl. paranigralis
Po. o – Nucl. pontis centralis oralis
Pro. sl – Processus nuclei pontis supralemniscalis
Scoe. d – Nucl. subcoeruleus, subnucl. dorsalis
Scoe. v – Nucl. subcoeruleus, subnucl. ventralis
Scun – Nucl. subcuneiformis
Spt – Nucl. supratrochlearis
St. gl – Stratum gliosum subependymale
Su. n. cm – Nucl. substantiae nigrae, subnucl. compactus
T. me. V – Tractus nervi trigemini mesencephalicus
T. pyr – Tractus pyramidalis
T. tg. cn – Tractus tegmentalis centralis
Tg. ds – Nucl. tegmenti pedunculopontinus, subnucl. dissipatus
V. me – Nucl. nervi trigemini mesencephalicus

lated on the cell periphery (Fig. 9, A). Lateral to the nucleus centralis superior, the nucleus papillioformis extends from the processus suppralemniscalis pontis to the medial longitudinal bundle. Here we see only one type of cell – multipolar but rather plump cells with dendrites of medium length, and dark but indistinct Nissl bodies.

The medial surface of the superior cerebellar peduncle is covered by the nucleus parabrachialis medialis. At more oral levels, the parabrachial grey matter extends also over the lateral surface of the superior cerebellar peduncle, where it is called the nucleus parabrachialis lateralis. Both nuclei are composed of small,

elongated or spindle-shaped, densely packed cells which stain with moderate intensity.

Medial to the nucleus parabrachialis medialis and ventral to the lateral pole of the griseum centrale pontis, the locus coeruleus appears as a group of large, densely packed cells which contains abundant melanin. The locus coeruleus is conspicuous by its very high vascularization.

Between the nucleus coeruleus and the ventral nucleus of the lateral lemniscus extends a band of small cells similar to those of the nucleus parabrachialis medialis, among which lie single, medium-sized, melanin-containing cells. This is the nucleus subcoeruleus, which can be further subdivided into the subnucleus ventralis and dorsalis.

Section VI

Although a small area in between the fibres of the pes pedunculi is still occupied by the grey matter of the pons, this section lies well within the midbrain (Fig. 14). The entire pattern of nuclear arrangement as compared with the last section has changed and numerous new large nuclei are present.

The pes pedunculi is separated from the midbrain tegmentum by the nucleus substantiae nigrae. The myelin-containing, multipolar, darkly stained cells of the substantia nigra, arranged in dense nests or loosely scattered, are so well known that their further description seems superfluous.

Dorsal to the interpeduncular fossa, the nucleus interpeduncularis occupies a triangular space between the nuclei perinigrales. Its cells are very small, spindle-shaped, lightly stained and compactly arranged.

Dorsally and laterally from the Sylvian aqueduct, lies the griseum centrale mesencephali. It is composed of small, oval or spindle-shaped cells, which stain moderately dark and are compactly arranged (Fig. 9, B). A subdivision into three subnuclei can be made on the basis of cell density and slight variation in cell structure.

The area ventral to the Sylvian aqueduct and that between the medial longitudinal bundles belongs to the nucleus supratrochlearis. This nucleus is densely populated by medium-sized, oval or polygonal cells with eccentric nuclei and peripherally arranged

Nissl bodies. At a slightly more oral level, the nucleus supratrochlearis extends ventrally as a tongue-like process which lies between the superior cerebellar peduncles, just oral to their decussation and before the first cells of the red nucleus appear. In this ventral process the cells are elongated or spindle-shaped with their long axes directed dorsoventrally.

The wedge-shaped area between the decussation of the superior cerebellar peduncle medially, and the substantia nigra and medial lemniscus laterally, is occupied by the nucleus tegmenti pedunculopontinus, which in this section is represented by its subnucleus dissipatus. At a more caudal level, the subnucleus compactus – which is also known under the name of nucleus of Koelliker – lies dorsolateral to the subnucleus dissipatus. The cells of the nucleus tegmenti pedunculopontinus are medium-sized, polygonal, and possess short dendrites. The nuclei are predominantly eccentrically placed and the Nissl substance is aggregated peripherally. A lesser number of cells possess centrally placed nuclei and evenly distributed Nissl bodies (Fig. 10, A).

The nuclei cuneiformis and subcuneiformis lie between the tectum dorsally and the nucleus tegmenti pedunculopontinus ventrally. They are similar in structure in that small, light, elongated or irregularly triangular cells with many glial satellites are present in both nuclei (Fig. 10, B). The nucleus cuneiformis is composed only of these small cells; the nucleus subcuneiformis is slightly less cellular and, in addition to numerous small cells, possesses a few cells of the same type as the nucleus tegmenti pedunculopontinus.

Section VII

This is the last section which will be described (Fig. 15). It passes through the level of the caudal pole of the red nucleus. The general arrangement of the nuclei is the same as in the preceding section. The nucleus substantiae nigrae is now represented in its full size. The nucleus supratrochlearis has disappeared, and the central grey matter of the mesencephalon now surrounds the Sylvian aqueduct. The nucleus tegmenti pedunculopontinus is not present, whereas the nuclei cuneiformis and subcuneiformis have retained their previous positions.

Before closing this description, mention should be made of the

red nucleus. This nucleus, strictly speaking, lies outside the intended scope of this presentation. However, it deserves special consideration due to the important position which it occupies in the motor system.

The subdivision of the red nucleus in the magnocellular and parvocellular subnuclei is still valid for the human brain stem. The subnucleus magnocellularis is reduced in man to scattered, large, multipolar cells with long dendrites, dark Nissl bodies and centrally placed nuclei. These cells are found in the caudal part of the red nucleus, among the fibres of the superior cerebellar peduncle, caudal to, or just at the level of, the first cells of the subnucleus parvocellularis. Usually certain groupings of the cells of the subnucleus magnocellularis are observed in the dorsal and ventral regions of the superior cerebellar peduncle.

The subnucleus parvocellularis is oval in outline in all planes of sections and is surrounded by a thick capsule of myelinated fibres. Its cells are medium-sized, multipolar or irregularly triangular with long dendrites, Nissl substance which stains with medium intensity, centrally placed nuclei and a marked glial satellitosis.

To summarize the above findings, it may be advisable to project semi-schematically, the described nuclei on the dorsal and lateral aspects of the medulla (Figs. 11 and 12). In order to avoid excessive overlapping, half of the nuclei have been represented on the right and the other half on the left side of the horizontal projection, and the lateral projection has been repeated twice.

DISCUSSION

The most striking feature of the cytoarchitecture of the lower brain stem is the great variety of cell types which are found in a few cubic centimetres of volume of the mesencephalon and rhombencephalon. This variety is greater than in any other part of the central nervous system. The cells vary not only in regard to their size, shape and intensity of staining but particularly in regard to the arrangement of the Nissl substance and position of the nucleus in the cell body. The precise understanding of the functional significance of this variability is lacking. A general

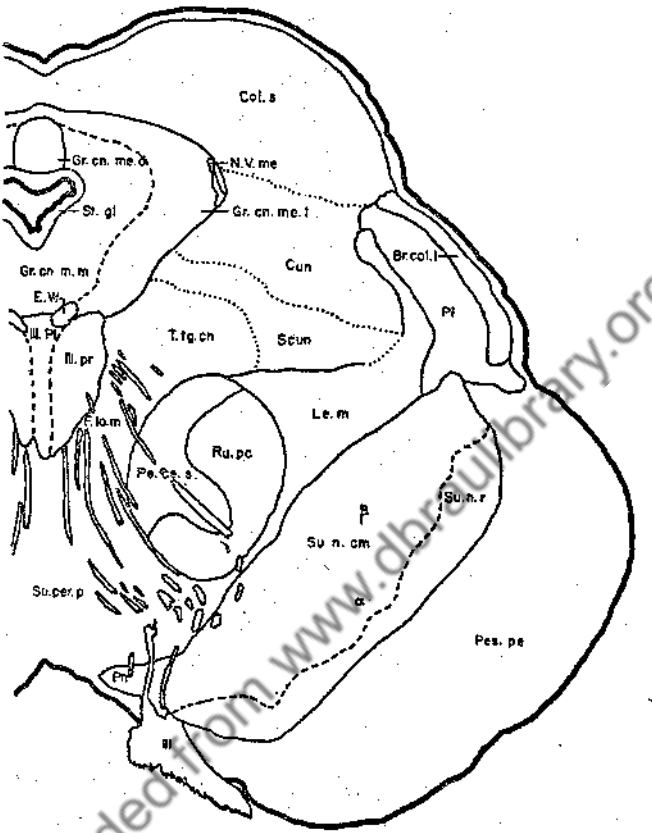


FIG. 15

Section at the level of the caudal pole of the red nucleus. Abbreviations:
Br. col. i — Brachium colliculi inferioris
Col. s — Colliculus superior Cun — Nucl. cuneiformis
E. W. — Nucl. Edinger Westphal F. lo. m — Fasciculus longitudinalis medialis
Gr. cn. me. d — Griseum centrale mesencephali, subnucl. dorsalis
Gr. cn. me. l — Griseum centrale mesencephali, subnucl. lateralis
Gr. cn. me. m — Griseum centrale mesencephali, subnucl. medialis
Le. m — Lemniscus medialis N. V. me — Nucl. nervi trigemini mesencephalicus
Pe. ce. s — Pedunculus cerebelli superior Pes. pe — Pes pedunculi
Pl — Nucl. paralemniscalis Pn — Nucl. paranigralis
Ru. pc — Nucl. ruber, subnucl. parvocellularis
Scun — Nucl. subcuneiformis
St. gl — Stratum gliosum subependymale
Su. n. cm — Nucl. substantiae nigrae, subnucl. compactus
Su. n. r — Nucl. substantiae nigrae, subnucl. reticularis
Su. per. p — Substantia perforata posterior
T. tg. cn — Tractus tegmentalis centralis
III — Nervus oculomotorius III. Pl — Nucl. Perlia
III. pr — Nucl. oculomotorius principalis

statement that it is intimately correlated with metabolic processes of the neruones is probably correct but actually explains nothing. It is interesting to note that in animals this variability is not as marked, the cells being different primarily in respect to their size and shape and only to a slight degree in respect to the arrangement of their Nissl substance. Another example that illustrates the same phenomenon is a great reduction of melanin pigment in cells of the locus coeruleus and substantia nigra in animals.

The second prominent feature of the cellular morphology of the lower brain stem is the fact that the different cell types occurring there are not haphazardly scattered over the whole area but that each cell type is limited to a given region and occurs there, either alone, or in combination with other definite cell types. This type of cell arrangement allows the subdivision of all grey masses of the lower brain stem into individual nuclei. This applies particularly to those regions of the lower brain stem which are usually included in, and described as, the reticular formation. Accordingly, the reticular formation cannot be looked upon as a morphological unity, or as a sort of ill-defined, uniform network in which, here and there, some 'nuclei' formed by accumulation of nerve cells can be recognized. Instead, the reticular formation must be considered as a collection of nuclei of very different structure. Therefore it is our opinion that the term 'reticular formation' could advantageously be dropped from both anatomical and physiological parlance, and that when speaking of any particular region of the brain stem reference should be made to the nucleus or nuclei which comprise it. An effort to correlate physiological observations with the arrangement of nuclei and fibre tracts of the lower brain stem should prove much more fruitful than the present practice of regarding the reticular formation as an anatomical entity.

An explanation of the practice of delineating the nuclei by means of lines may not be out of place at this point. This method can be applied in virtue of the fact that the transition between adjacent nuclei is usually abrupt. The advantage of such a method, rather than indicating the centre of each nucleus with a given symbol, seems to me twofold. First, this method allows a complete subdivision of a territory investigated and creates a basis on which a three-dimensional concept of nuclear arrangement can

be built. Second, it compels the investigator to much greater accuracy and precision since he must take the decisions regarding absolutely all areas, or – if I may exaggerate slightly – regarding each individual cell.

What are the functional implications of all these morphological findings? First, it may be worth while mentioning that when speaking of functional localization, we have usually in mind a combination of organological and topographical localization. The visual system (retina, geniculate bodies, visual cortex), the somathetic system (skin and visceral sense organs, relay nuclei, sensory cortex), or the motor system (motor cortex, nerve cells of the lower motor neurones, striated musculature) may serve as examples. But this type of functional localization is not the only one encountered in the central nervous system. For example, Hess has shown that our conception of localization of functions has to be modified for the hypothalamus. Instead of localization of functions of individual organs or of a single metabolic process, we are dealing with localization of over-all global reactions of the whole organism. It may well be possible that without a comparable modification of our approach to the problem of functions in the lower brain stem, the understanding of its organization will be impossible.

At the basis of our anatomical thinking lies the conviction that morphology and function are closely correlated and that the discovery of morphological differences points to the presence of functional differences. Accordingly, we may expect that future investigation will disclose functional differences between all nuclei of the lower brain stem. This is not meant to imply that these nuclei form a mosaic of functionally discrete units, such as for example an inspiratory or vasopressor nuclei. It is quite probable that either several nuclei, or a proportion of cells of a few nuclei may form a functional centre, if the word 'function' is applied in a broad sense. Physiological observations would tend to support this suggestion, since similar responses may be obtained from adjacent, but morphologically discrete nuclei. These observations do not invalidate, however, the opinion that functional differences must exist between individual nuclei. In addition to the fact that the similar responses may be partly explained by stimulation of fibre tracts, they do not indicate that the sole function of the in-

vestigated region is represented by the noted effect of stimulation. To use an analogy from another region of the central nervous system, we can consider the cortex of the pre- and post-central gyri. That movements can be obtained by stimulation on both sides of the Rolandic fissure is an observation which in no way contradicts the recognized functional distinction between these cortical areas.

No mention has been made above of fibre connections of the nuclei described. It has to be stressed before closing this discussion that these connections are largely unknown. Whereas for many years emphasis was predominantly placed on the elaboration of descending efferents, it is apparent that the discovery by Magoun of the unspecific activating system focuses a comparable, if not even greater attention on the ascending efferents. It is obvious that without a thorough knowledge of these connections, the understanding of the functional organization of regions described would be impossible. In the elaboration of these connections lies a fruitful field for many years of neuroanatomical investigation.

GROUP DISCUSSION

JASPER: Dr. Olszewski has given us an interpretation of the fine structure of this region the significance of which is not apparent from physiological studies. Some of us have seen differences in the detailed pattern of responses obtained by stimulating this area. Sometimes with a movement of the stimulating electrode of 1 mm. we see differences in response, even a change from inhibition to facilitation and differences in the accompanying patterns of behaviour. This opens a new chapter in our discussion which will be followed by Dr. Nauta and Dr. Whitlock on what we might call the thalamic extension of this system.

BRAZIER: I wonder if Dr. Olszewski would care to discuss the comparative anatomical aspects of his subject with special regard to the animals which we commonly use in the laboratory: the cat, monkey and rabbit. We know that many differences exist as, for example, in the case of the red nucleus.

OLSZEWSKI: The red nucleus is a typical example of structures which vary extensively from lower animals to man. It may be worth while to mention in this connection that — as has been pointed out many years ago by Spatz — the rubro-spinal tract which originates in the magnocellular part of the red nucleus must be very small and of negligible

functional significance in man. To my knowledge we do not have as yet any precise information about the site of termination of axons of the parvo-cellular part. The other system which varies greatly from one species to another is the griseum pontis and the associated nuclei. As we descend the phylogenetic scale, the diminution in size of these structures is very conspicuous. However, most of the nuclei which I described here are very constant and the pattern of their spatial arrangement is remarkably similar in the rabbit, cat, monkey and man. I would say that a person familiar with the architecture of the lower brain stem in any one of these animals will not be lost in any of the others.

MAGOUN: I was struck in many of the figures by the very diverse size of the cellular elements in a group which is termed a single nucleus. There might be some very large neurones and quantities of very small ones. I wonder if Dr. Olszewski would indicate for us what he feels this means? Do the large cells give rise to fibres running for long distances with heavy myelin sheaths; do the small ones represent local internuncial components within this group, or is there any generalization that he can propose from his anatomical studies as to what is the meaning of these variously sized collections of cells in what he terms a nucleus.

OLSZEWSKI: I think that we may accept as a general rule that large cells have long axons and small cells short ones. It seems that in the monkey transection of the spinal cord at a higher cervical level produces loss of large cells in the nucleus giganto-cellularis, whereas small cells remain intact. The material which I was able to study in this connection was very limited and we have to do more work in this direction, and perhaps make some cell-counts before a more definite answer to this question can be given. In general our knowledge of the connections of very small nerve cells, such as found for example in the hypothalamus or in the griseum centrale mesencephali is very limited. It is possible that such cells give origin to very fine axons, of a type which Fernandez-Moran described as submicroscopical fibres. These fibres are supposed to consist of a filament only one macromolecule thick and covered by a monomolecular sheath. The study of connections formed by such fibres will be exceedingly difficult, though the functional significance of these connections may be fundamental for many systems.

LASHLEY: My experience in this field has been confined to the cerebral cortex but conditions are probably not different elsewhere. There are certainly other factors than function which determine the shape of the cells. Where the fibres in the cerebral cortex are arranged in fascicles the cells which lie between these fascicles tend to be flattened.

As a result, when a section is cut in the plane of the fascicles, the cells appear round and when the section is across the fascicle they appear spindle-shaped. Where there are many fibres, as at the margin of the lateral geniculate body of the cat, the cells tend to be spindle-shaped and, where in the same nucleus the fibres are few, the cells are rounded.

There may be close similarities between cells, for example in the thalamus, where the function differs considerably. In the lateral geniculate of the rat there is only one type of cell and cortical destruction leads to complete degeneration, resulting after some months in cyst-formation. In the cat, on the other hand, there are two cell types, a large and a small, and the large cell alone undergoes degeneration after cortical destruction. We do not know of any differences, nevertheless, between the cat and the rat as far as the visual perception of colour or pattern is concerned. I have observed differences between the occipital and parietal cortex in both the spider monkey and macaque of a type not seen in man. Neither cell size nor cell form is a reliable index of function when unsupported by other evidence. With regard to the problem of cell size and length of axon, Lassek has shown that there are many times more fibres in the pyramidal tract than there are Betz cells in the motor cortex. These long fibres must then arise from smaller cells.

JASPER: I am sure Dr. Olszewski has encountered this argument on many occasions and will be glad to discuss it again.

OLSZEWSKI: It is very true that the shape of cells is influenced by adjacent fibres. It is also true that even the plane of section of the histological preparation may influence the appearance of nerve cells, but I do not think that Dr. Lashley would maintain that all the differences in cell structure described in my presentation are due to these factors.

The fundamental question of correlation between structure and function perhaps may be made simpler if we agree first on what we understand by the word function. For example, the human lateral geniculate body is formed by two magnocellular and four parvocellular layers. If we agree that the 'function' of the lateral geniculate body is 'vision', then the difference in cell size between different layers will be meaningless. The same can be said about the dorsal and ventral cochlear nuclei, which though fundamentally different in structure are both concerned with the function of hearing. In these two examples the word 'function' was used in a very broad sense. However, the conception of function can be narrowed if one introduces such factors as different afferent connections, number and form of axonic endings, distribution and ramification of axons, and peculiarities of metabolism of different cell types. If such a narrow conception of function is applied we may say

that two cell types, though both concerned with vision, may have different functions, because, for example, their axons may form collaterals of different distribution. I do not want to be aggressive but I would like to say: 'What is wrong with psychological methods if you cannot explain the significance of anatomical differences which are there?'

WALTER: My scepticism is due to ignorance, I hope, not prejudice. I have some acquaintance with the work being done in J. Z. Young's department by Sholl, whom you no doubt know, and he has been applying some fairly advanced statistical methods to architectonic differences such as described by Vogt in the cortex but has not, so far as I know, made any tests of subcortical structures. He has found that the differences obtained when random samples are taken of the different cellular components, using statistical devices such as superimposing many cells, tend to blur rather than clarify the laminae and cytoarchitectonic differences. He has tried these on people who claim to be able to recognize cytoarchitectonic differences and the results he has obtained are about those which might have been expected on the basis of chance. Obviously you cannot project for us all the cells which you can see, but would it be advisable do you think to apply techniques of superimposition, averaging, or possibly more advanced statistical methods to the interpretation of your findings?

OLSZEWSKI: In these studies we have used observation as the only method, and did not make cell counts. The utilization of thicker sections, which may be to some extent similar to the method of superimposition, emphasizes the cytoarchitectonic differences, as then we are more likely 'to see the forest instead of the trees'. I myself am not familiar with the cytoarchitectonics of the cortex, which is a much more difficult subject than the study of the architecture of the subcortical grey masses. If I may be permitted to use Dr. Penfield's expression, I prefer to stay at 'higher levels'.

KUBIE: In the early 1920s, the late Dr. Charles Dunlop studied cytoarchitectonic changes in many parts of the brain of schizophrenics, including the brain stem. He set himself the task of studying all the cytological changes in schizophrenia which had been reported by Mott, Hunt, Lewis, Jacob and many others. Out of all the changes, the only one which he could not reproduce as artefacts were extreme variations in cell size. Shifts in the position of the nucleus, changes in the size or colour or aggregation of the Nissl bodies around the nucleus or around the edges of the cell, changes in the cell membrane, the size of the axon, the distance it was traceable, all of these could be produced by terminal changes in body temperature, hydration, acidosis, or by such factors as variation in the angle at which the section was cut, variation in the

concentration of the fixative, the size of the tissue block in relation to the volume of fluid and the agitation of the fluid, etc.

Any factor varying the rate of penetration of the fixative altered the cytological picture. This makes me sceptical of the significance of such morphological differences as those which Dr. Olszewksi has described. But even if none of these is due to technical artefacts, it still seems to me possible that they may not be in any way related to the function of this system. Cells of quite different morphology scattered along the neuraxis might still be part of a single functional system.

RIOCH: The Nissl stain seems to me to provide data which are basic to all neurological research. The differentiation of cell types is most important, and I regret that more has not been done along the lines developed by Jakobsohn and Malone. However, the cytoarchitectonic method does not demonstrate functional organization. The complexity of the behaviour of chronically surviving decerebrate preparations suggest that there are more 'nuclei' than you have described in the reticular formation. Years ago Lorente de Nó showed me some of his Cox-Golgi preparations of this area in which quite small 'nuclei' could be identified on the basis of the distribution of the dendrites.

AN ANATOMICAL ANALYSIS OF THE NON-SPECIFIC THALAMIC PROJECTION SYSTEM

By

WALLE J. H. NAUTA and DAVID G. WHITLOCK

INTRODUCTION

DURING the past decade an impressive volume of data has accumulated concerning a particular thalamocortical mechanism, capable of producing in widespread areas of the neocortex certain modifications of existing patterns of activity, the most typical of which is commonly referred to as the 'recruiting response'. Among the students of this mechanism there appears to be general agreement that the thalamic cell groups from which such modifications of cortical activity can be evoked are situated in and near the midplane (nuclei reuniens, submedius, centralis medius, rhomboidalis, ventromedialis, medial parts of n. anteromedialis), in the internal medullary lamina (nuclei paracentralis, centralis lateralis, parafascicularis, centre median), as well as in the paralaminar part of the n. dorsomedialis, the n. ventralis anterior, and the reticular complex of the thalamus. In view of the apparently widespread nature of their connections with the cerebral cortex, these cell groups are often referred to collectively as the 'non-specific' or 'diffuse' thalamic projection system, as opposed to the association and sensory relay nuclei of the thalamus which have been shown to project to more circumscribed cortical areas.

Most of our data concerning the organization of the non-specific thalamic projection system have been furnished by electrophysiological experimentation (Morison and Dempsey, 1942a; Dempsey and Morison, 1942a, b; Jasper, 1949; Starzl and Magoun, 1951; Starzl and Whitlock, 1952; Hanbery and Jasper, 1953). The results of such studies indicate that the non-specific thalamic cell groups tend to function as a unitary system, within which, however, patterns of topical organization are likely to exist. This close functional coherence between the rather widely distributed components of the non-specific thalamic apparatus has

been attributed to the existence of a diffuse network of association fibres intrinsic to the system. Actually, some such fibre connections were disclosed by anatomical methods as early as two decades ago (LeGros Clark and Boggon, 1933).

The anatomical structures involved in the mediation of non-specific thalamic activity to vast areas of the neocortex have been the subject of intensive study. Among other hypotheses, a thalamocortical fibre system, independent of the projections from the main thalamic nuclei, has been proposed to originate in the midline and intralaminar region of the thalamus and to transmit the activity to the cortex either directly (Morison and Dempsey, 1942a) or by way of the reticular complex (Jasper, 1949). In point of fact, there appears to be good evidence that the reticular complex projects to large parts of the neocortex (Rose, 1950), and hence could conceivably be instrumental in the corticipetal mediation of non-specific thalamic activity. An alternative suggestion is that of a cortical distribution of non-specific impulses by pathways synapsing in the specific association nuclei of the thalamus (McLardy, 1951). Other possible efferent connections, such as with the caudate nucleus (Droogleever-Fortuyn and Stefens, 1951) and putamen (McLardy, 1948), might likewise be conjectured to represent parts of indirect non-specific thalamocortical projection systems, even though the existence of direct pathways leading from these structures to the neocortex is still uncertain. Moreover, there is anatomical evidence of projections from non-specific thalamic cell groups to the rhinencephalon (Rose and Woolsey, 1943) and to anteroventral parts of the cortex covering the medial wall of the hemisphere (Droogleever Fortuyn, 1950), and although no recruiting responses appear to have been recorded from the former of these phylogenetically older cortical structures, their possible function as relay mechanisms in a non-specific thalamocortical projection remains to be considered.

Up to the present time anatomical analyses of the non-specific thalamic projection system have been far outnumbered by physiological studies. Most of the available anatomical data were obtained by studies of retrograde cell changes in the thalamus following removal of parts of the telencephalon, and not more than a single study has come to our attention in which a systematic attempt was

made to trace the efferent connections of the non-specific cell groups by the aid of the Marchi technique (LeGros Clark and Boggon, 1933). In this study, no conclusive evidence of direct cortical projections from the non-specific nuclei was obtained. Since this failure might conceivably have resulted from the limitations of the Marchi technique, it appeared indicated to reinvestigate the problem with employment of more recent histological techniques. The following account is based mainly upon hitherto unpublished data obtained in collaboration with Dr. L. Schreiner in the course of an attempt to trace the efferent connections of the non-specific thalamic nuclei in the cat by the aid of silver techniques.

MATERIAL AND METHODS

Thalamic lesions were placed in adult male cats by the aid of the Horsley-Clarke stereotaxic instrument, using a fine steel electrode with an external diameter of from 0.75 to 0.2 mm. and insulated except at the tip. As a rule, focal coagulation was achieved by the passage of a direct current for a period of time suitable for the production of the desired effect. Wherever possible, the loci intended for coagulation were approached horizontally from the caudal side in order to obviate needletracks leading through cortical areas.

The animals were sacrificed 5 to 7 days after operation. Fixation was initiated by transcardial perfusion with saline followed by 10 per cent formalin, and the brains were subsequently stored in 10 per cent formalin for varying lengths of time up to 4 months. Suitably spaced frozen sections of 25 micra thickness were then stained following a modified Bielschowsky procedure, developed in this laboratory, which was found more convenient than other silver techniques in that it eliminates black impregnation in a considerable percentage of normal axons and thus facilitates identification of diffuse signs of axon disintegration.

Efferent Connections of the Median and Paramedian Region of the Thalamus

From their central position in the thalamus it is evident that surgical lesions of the intralaminar nuclei will, as a rule, be com-

plicated by the interruption of a larger or smaller contingent of the efferents from surrounding cell groups, particularly of those from the dorsomedial nucleus. Since it appeared reasonable to assume that such transit fibres will be least numerous near the median plane, it was decided first to study the effects of lesions in the median and paramedian components of the intralaminar nuclei. One of the several cases of such lesions is illustrated by drawings of representative sections in Figs. 1 to 6.

In this case a slightly paramedian lesion of slender tubular shape was produced, which extended throughout the rostroventral extent of the thalamus and involved, to varying extents, the nuclei centralis medius, submedius, and reuniens. As shown by Fig. 4, degenerating fibres tend to spread from all levels of the lesion mainly lateralwards into the internal medullary lamina with its interstitial nuclei paracentralis and centralis lateralis. Many of these degenerating fibres actually terminate in the intralaminar cell groups (Fig. 15). Terminal degeneration is profuse near the midline, and gradually diminishes in intensity with increasing distance from the median plane; the nucleus centralis lateralis appears to receive no more than a small number of fibres from the midline region. Although degenerating fibres are most abundant on the side of the lesion, a considerable contralateral spread with the same distribution is evident at all levels of the thalamus. It is important to note that on both sides only relatively few degenerating fibres can be followed to the centre median (Fig. 5).

Terminal degeneration spills over to some extent into several adjoining thalamic nuclei. The strongest of such extralaminar connections of the midline region appears to be with the ventromedial and ventrolateral nuclei (Figs. 4, 16), while a slightly less intensive association exists with the ventral, paralaminar part of the dorsomedial nucleus (Fig. 4). Not more than a few fibres spread laterally in the internal medullary lamina into the ventral part of the lateral nuclear complex (Fig. 4). Furthermore, a massive connection appears to exist with the anterodorsal nucleus (Fig. 3); however, in view of the extent of the lesion it is possible that the fibre degeneration in this cell group is caused by interruption of the interanterodorsal commissure.

Finally, degenerating terminals are observed in the medial half of the n. ventralis anterior and in the rostromedial part of the

reticular nucleus (Fig. 3). The fibres which can be followed to this most rostral thalamic territory are accompanied by a rather massive system of much longer fibres, degenerating only on the side of the lesion, which ascends as a fasciculated bundle in and ventral to the medial two-thirds of the internal medullary lamina in the ventral nuclear complex, predominantly along the lateral border of the ventromedial nucleus. This fibre system apparently represents an accumulation of fibres which course laterally from the area of the lesion and subsequently turn rostralward at varying distances from the median plane. At rostral thalamic levels these fibres continue their rostral course in the fibre layer covering the ventral aspect of the anterior nucleus as the rostral continuation of the internal medullary lamina, and subsequently curve ventralwards, partly through the medial half of the n. ventralis anterior and the rostral pole of the reticular nucleus, and partly medial to these cell groups, enclosed in the inferior thalamic peduncle (Fig. 3). Sections in front of the thalamus show these degenerating fibres in the medial angle of the internal capsule (Fig. 2).

Beginning at the level of the anterior commissure a diffuse offset of this system can be followed laterally to the claustrum and to the deep cell layers of the orbital gyrus (Fig. 2), while another group of degenerating fibres separates from the internal capsule in the ventral direction to deep-lying cells of the prepiriform cortex (Fig. 2). A further bifurcation of the degenerating fibre system in the internal capsule takes place just rostral to the septal region (Fig. 2), where a rather massive bundle detaches itself from the internal capsule, swings dorsally in front of and medial to the rostral tip of the lateral ventricle, and subsequently curves caudalwards around the genu of the corpus callosum. These fibres, which apparently constitute an important ascending component of the fasciculus cinguli, distribute to the infralimbic cortex, and to the anterior limbic cortex, particularly to the latter's preseptal strip commonly labelled area 32. Longer fibres of the same system can be traced caudally in the cingulate fasciculus to the level of the splenium corporis callosi, where they divide into two contingents, one of which distributes to the presubiculum, while the other bends ventrally in the tapetum to the entorhinal area (Fig. 6). At rostral levels (Fig. 2) degenerating fibres can be traced laterally from the cingulate fasciculus into layers VI and V of the

cortex occupying the dorsal lip of the sulcus cinguli. Such fibres appear to fan out in a caudal direction; they are still in evidence at levels represented by Fig. 4.

The remaining group of degenerating fibres in the internal capsule continues rostrally to the region of the gyrus proreus, and to the orbitofrontal cortex on the medial wall of the hemisphere (Fig. 1).

It is of interest to note that although by far the largest number of these afferents to the frontal neocortex terminate in layers IV and III and thus would correspond to Lorente de Nó's system of 'specific cortical afferents', a fair number of degenerating fibres can be followed into the plexiform layer (I) of the cortex, in which they ramify. The latter fibres are of slightly smaller calibre than those ending in layers IV and III: it appears possible that they correspond to the 'non-specific afferents' observed in Golgi material of the rat's cortex by Lorente de Nó (1933).

Less extensive lesions of the midline region of the thalamus produce results which differ from the above description in several important details. Lesions which do not extend further rostrally than frontal Horsley-Clarke plane A 11, for instance, are followed by degeneration of fibres to other thalamic cell groups, to the prepiriform, infralimbic, and limbic cortex, and to the presubiculum and entorhinal area as described above, but fail to interfere with pathways leading to the frontal neocortex. Midline lesions confined to the caudal one-quarter of the central thalamic region (frontal levels A 8 to 8.5) appear to produce degeneration of only short intrathalamic fibres, which spread to more rostral and more lateral parts of the intralaminar cell groups, to adjoining parts of the dorsomedial nucleus, and to the ventromedial nucleus, but not to the n. ventralis anterior or to the reticular complex.

These observations suggest that rostral conduction in the midline region of the thalamus takes place mainly through chains of short neurones, with extrathalamic pathways originating only in the rostral half of the system. Although such longer projections would appear to include an efferent connection with the frontal neocortex, it is obvious that involvement of fibres from the dorsomedial nucleus must be ruled out before the existence of such a projection is accepted. For this reason, the effects of partial destruction of the dorsomedial nucleus were studied next.

Efferents from the Dorsomedial Nucleus

In all cases of lesion of the dorsomedial nucleus degenerating axons were found to course mainly in rostroventral directions (Figs. 7 to 10, left half). Some fibres enter the internal medullary lamina only slightly rostral to the lesions; they accumulate in and ventral to the lamina, particularly lateral to the ventromedial nucleus (Fig. 8) and *en route* rostralwards are joined by additional degenerating elements from the dorsomedial nucleus. A considerable further contingent leaves the dorsomedial nucleus through the latter's rostral pole and cuts ventralwards through the caudal part of the anteromedial nucleus (Fig. 9). Both groups join ventral to the anteromedial nucleus, where the entire system of degenerating fibres curves ventralwards, partly through the medial half of the n. ventralis anterior and the rostromedial angle of the reticular nucleus, and partly medial to these cell groups in the inferior thalamic peduncle (Fig. 10). Some degenerating elements can be followed from the peduncle to dorsolateral parts of the anterior hypothalamus (Fig. 10), while the majority continues rostralwards in the ventromedial angle of the internal capsule to the gyrus proreus and to the medial orbitofrontal cortex. A few fibres can be followed to the inferior part of the rostral limbic cortex, but none appear to enter the cingulate fasciculus.

In the frontal neocortex degenerating terminals are abundant in layers IV and III (Fig. 19); as in cases of midline thalamic lesion, however, a few degenerating fibres ascend through all cell layers and arborize in the plexiform layer (Fig. 20).

In addition to corticipetal connections, the dorsomedial nucleus appears to emit short association fibres to midline and paramedian cell groups. These short connections include some fibres to the ventromedial nucleus, and slightly more to the centralis medius and reuniens (Figs. 8 to 10). In the greater part of the midline thalamic region such short terminal afferents do not seem to be accompanied by transit fibres from the dorsomedial nucleus. Corticipetal fibres from this nucleus do, however, accumulate rather close to the median plane at rostral thalamic levels (A 12 to 13), where they are contained in the inferior thalamic peduncle.

The above findings suggest that few if any projection fibres from the dorsomedial nucleus will be interrupted by median thalamic lesions localized behind Horsley-Clarke frontal plane

A 12. More rostral extension of the lesion, however, is likely to involve an increasing number of such transit fibres. It is significant that of all median thalamic lesions studied only those involving frontal levels A 12 and A 13 were followed by fibre degeneration to the frontal neocortex. Although contributions to the projection from the dorsomedial nucleus cannot be ruled out definitively, the present experiments have thus furnished no conclusive evidence of neocortical projections from the median and paramedian thalamic region other than such represented by relatively few fibres to peripheral parts of the orbital and lateral gyri. On the other hand, it appears justified to accept projections from the median thalamic region to older medial and basal parts of the cortex, including part of the prepiriform region, and to the claustrum. Also, there is good evidence of association of the midline region with the dorsomedial nucleus, with the nuclei ventromedialis, ventrolateralis and ventralis anterior, with the rostral pole of the reticular nucleus, and particularly with the more laterally situated intralaminar cell groups.

Centre Median

For a better understanding of subsequent sections of this paper it is necessary to deal with the centre median next. Three cases of lesions of this cell group were studied. In two of the animals the lesion had been produced by horizontal approach through the cerebellum and lower brain stem. In the third animal, the coagulating electrode had been introduced vertically through the dorsomedial nucleus; this case served as a check upon a possible interference with ascending thalamopetal fibre systems by the horizontal electrode tracks. Findings common to all three cases will be described in the following paragraphs.

A large number of degenerating axons can be followed rostralwards from the lesion into the internal medullary lamina (Fig. 12). Many such fibres apparently terminate in caudal parts of the n. paracentralis and centralis lateralis; fewer continue to more rostral parts of these cell groups. Some degenerating fibres spread medialwards in the lamina to the median thalamic region and across the median plane into the contralateral lamina medullaris interna (Fig. 12).

A slight distance in front of the lesion fibre degeneration begins

to spill over heavily into the ventral nuclear complex (Fig. 12), and from this level forward to the rostral pole of the thalamus a diffuse and rather massive system of degenerating fibres can be traced from the internal medullary lamina into the ventral nuclei. This ventral offset from the intralaminar fibre system appears to terminate mainly in the n. ventrolateralis, with slightly lesser distributions to the n. ventralis posteromedialis, ventralis posterolateralis, ventromedialis, and ventralis anterior (Figs. 12, 13). A considerable proportion of its fibres continue through the ventral nuclei into almost the entire rostral half of the reticular complex, which exhibits a diffuse terminal degeneration but for its extreme dorsolateral part (Figs. 12 to 14, 17). Still longer fibres traverse the reticular complex, perforate the internal capsule and enter the lentiform nucleus where they appear to terminate mainly in the dorsal half of the putamen and in lesser numbers in the globus pallidus and claustrum (Figs. 13, 14). No fibre degeneration can be traced to any part of the cerebral cortex.

As shown in Figs. 12 and 13, the decussating fibres noted above distribute to the contralateral n. paracentralis and ventralis. A few such fibres appear to terminate in the reticular complex of this side also.

The absence of corticipetal fibre degenerating following lesions of the centre median, considered in conjunction with the caudal position of the nucleus within the thalamus, appears to render unlikely the unintentional interruption of a significant number of efferents from specific thalamic nuclei. As will be pointed out below, such involvement does, by contrast, appear unavoidable in surgical lesions of the more laterally situated intralaminar nuclei. In order to facilitate the interpretation of the results of the latter type of lesion, their description can be profitably preceded by an account of the efferent connections of the laterodorsal nucleus.

Laterodorsal Nucleus

As illustrated in Figs. 7 to 10 (right half of Figs.), most of the fibres originating in the laterodorsal nucleus tend rostrally and laterally towards the dorsolateral angle of the thalamus where they join the lateral thalamic peduncle. Fibres originating in caudomedial parts of the nucleus travel rostralwards over some

distance in the lateral part of the internal medullary lamina before turning laterally; these fibres occupy the territory of the n. centralis lateralis and thus will be involved in any surgical lesion of the latter cell group. A considerable number of fibres, apparently originating both in rostral and caudal parts of the laterodorsal nucleus, leave the thalamus near its rostral pole, cutting through the dorsolateral angle of the n. ventralis anterior and reticularis thalami, in both of which some fibres appear to terminate (Fig. 10). A few other fibres from the laterodorsal nucleus can be traced to the ventrolateral part of the caudate nucleus.

At the cortical level, degenerating fibres are observed in the suprasylvian gyrus. Most of these terminate in layers IV and III, but a few degenerating fibres can be traced into layer I where they appear to arborize.

Lateral Intralaminar Cell Groups: n. paracentralis and centralis lateralis

As pointed out in the preceding paragraphs, the fibre population of the internal medullary lamina includes fibres of passage from the dorsomedial and laterodorsal nuclei, from the median thalamic region, and from the centre median. Obviously, the involvement of these and possibly other transit fibres will considerably complicate the picture of fibre degeneration resulting from lesions of the lateral intralaminar cell groups. With this important restriction in mind, the following observations were recorded in four cases of lateral intralaminar lesion.

In all four experiments the coagulating electrode had been introduced diagonally at frontal Horsley-Clarke level A 9.5 through the contralateral hemisphere and ipsilateral n. dorsomedialis or laterodorsalis.

1. N. centralis lateralis. In one case the lesion was found to occupy the lateral half of the n. centralis lateralis; some slight peripheral involvement of the ventral part of the n. laterodorsalis appeared likely, while additional damage to this cell group had been caused by the needle track. At and about the level of the lesion many degenerating fibres can be traced to the n. laterodorsalis and lateralis posterior, while others stream medialwards into more medial intralaminar regions; a few of the latter fibres reach the median thalamic region, but none appear to spread

across the median plane. Caudally, a fair number of degenerating fibres can be traced to the centre median; few if any distribute to the dorsomedial nucleus. Rostral to the lesion, degenerating axons are present in the lateral part of the internal medullary lamina at all frontal levels. Some such fibres terminate in the n. paracentralis and centralis lateralis, others bend ventralwards into the n. ventrolateralis, while the remaining fibres swing off lateralwards into the lateral thalamic peduncle. The most rostral elements of the last-mentioned fibre system traverse the dorsolateral angle of the n. ventralis anterior and reticularis, both of which contain scattered degenerating terminals. Most of the fibre degeneration in the lateral thalamic peduncle can be traced to the suprasylvian gyrus where degenerating terminals are present mainly in layers IV and III, while some fibres ascend through all cell layers to ramify in the plexiform layer. A rather considerable further contingent of degenerating fibres separates from the lateral thalamic peduncle and terminates in the caudate nucleus; degenerating terminals in this structure are more numerous than following lesion of the laterodorsal nucleus. Other degenerating elements can be followed to the putamen, to the claustrum, and to the ventral bank of the orbital gyrus. Finally, a considerable number of degenerating fibres enter the cingulate fasciculus in the same fashion as described for median thalamic lesions; part of these fibres distribute to the infralimbic and limbic cortex, while longer elements continue caudalwards in the cingulate fasciculus. Some of the latter fibres distribute laterally around the cingulate sulcus to the deep cell layers of the ventral bank of the lateral gyrus, which they enter as deep tangential fibres.

2. N. paracentralis. In the three remaining cases the intralaminar lesion had destroyed part of the paracentral nucleus together with a small adjacent portion of the n. centralis lateralis. As shown by earlier experiments, described above, the paracentral region of the internal medullary lamina is traversed by numerous projection fibres from the dorsomedial nucleus. Accordingly, a massive degeneration can be traced to the frontal neocortex. Additional degenerating fibres distribute to the infralimbic and rostral limbic cortex, to the orbital gyrus, the caudate nucleus, and the claustrum. Degenerating fibres running caudalwards in the cingulate fasciculus are in evidence in this case also; a rather consider-

able number of such fibres cut laterally through the white substance of the cingulate gyrus and spread as deep tangential fibres into the ventral bank of the lateral gyrus. No degenerating fibres can be traced to the suprasylvian gyrus.

Intrathalamic associations of the area of the lesion are abundant with the laterodorsal nucleus and slightly less numerous with the dorsomedial nucleus, while additional short fibres distribute to the median thalamic region and across the midplane as far as the contralateral paracentral nucleus. Finally, the degenerating projection fibres of the dorsomedial nucleus noted above appear to be accompanied by intrathalamic association fibres which distribute to the n. ventrolateralis, to the middle one-third of the n. ventralis anterior and to the adjoining part of the rostral cap of the reticular nucleus.

A comparison of the observations made in the experiments described in the two preceding sections of the present paper leaves little certainty with regard to the efferent connections of the lateral intralaminar nuclei. Thus, the findings of degenerating fibres in frontal and parietal cortical areas and in parts of the n. ventralis anterior and reticularis thalami following lateral intralaminar lesions could conceivably have resulted from interference with fibres of passage from the dorsomedial and laterodorsal nuclei (Figs. 7 to 10). Furthermore, the terminal degeneration observed in the n. ventrolateralis, ventralis anterior and reticularis, and in the putamen might have been caused by involvement of those efferents from the centre median which occupy the lateral intralaminar region. On the other hand, there appears to be somewhat better evidence of a projection from the n. centralis lateralis to the caudate nucleus. It is true that the existence of this connection also might have been mirrored through interference with efferents from both the laterodorsal nucleus and the centre median; however, the terminal degeneration observed in the caudate nucleus following a small lesion of the n. centralis lateralis was considerably more profuse than that resulting from larger lesions of the laterodorsal nucleus or centre median. This evidence should, however, be regarded as at best circumstantial, since it is often impossible to evaluate the results of small lesions on the basis of comparative size alone.

The interpretation of fibre degeneration leading from the n.

centralis lateralis to the medial wall of the cerebral hemisphere appears somewhat more unequivocal. A similar pattern of fibre degeneration was observed in cases of median thalamic lesion, but not following lesions of either the dorsomedial nucleus, laterodorsal nucleus, or centre median. Since no fibres of passage from the median thalamic region could be demonstrated in the territory of the n. centralis lateralis, it appears reasonable to accept a projection from the lateral intralaminar cell groups to the infralimbic and limbic cortical areas, with a diffuse offset to the adjoining medioventral bank of the lateral gyrus. For the same reason, the existence of a projection from the lateral intralaminar nuclei to the ventral bank of the orbital gyrus would appear likely. Finally, there is good evidence of short associations of the lateral intralaminar cell groups with the lateral nuclear complex of the thalamus.

DISCUSSION

It appears appropriate at the outset of this discussion to face a criticism that may be raised against any study conducted by direct observation of degenerating nerve fibres; what certainty exists that the degenerative changes observed are Wallerian and not retrograde or transneuronal in character? As far as the present data are concerned, several experiments not here reported have furnished satisfactory evidence that the staining technique employed in this study fails to demonstrate retrograde or transneuronal axon reactions in the cat brain after a survival time of from five to ten days. It thus appears reasonable to interpret as Wallerian degeneration all evidence of drop-like axon disintegration observed in animals which survived surgery for seven days.

Within the time limits mentioned above, a much more important source of misinterpretation would seem to be formed by the unintentional interruption of corticothalamic fibre systems, either at the level of the cortex, or along their intrathalamic trajectory. From relevant material thus far available it appears, however, that few if any corticothalamic fibres travel rostralwards within the thalamus and hence, fibre systems degenerating rostralwards from a thalamic lesion in the absence of direct cortical involvement have been interpreted as being of thalamic origin.

The fibre connections of the non-specific thalamic cell groups, as far as demonstrated by the experiments reported above, can best be discussed under three separate headings: 1. Intrathalamic associations; 2. Subcortical projections; 3. Cortical projections.

1. *Intrathalamic Associations*

The results of the present study lend support to the neurophysiological concept of multisynaptic conduction within the non-specific thalamic cell groups. Although long lines of conduction are not wholly lacking, an organization of intrinsic association pathways in the form of chains of short neurones appears to prevail both in the longitudinal and transverse directions. Judging on the basis of fibre quantity it is noteworthy that longitudinal conduction within the non-specific apparatus would seem to be potentially more intensive in the rostral than in the caudal direction.[1] This organization would tend to place the centre median, as the most caudal element, in an optimal position to produce widespread excitation within the non-specific thalamic apparatus. It may be significant in this respect that the centre median appears to have diffuse efferent connections with all remaining non-specific cell groups, including, as already observed in earlier work (LeGros Clark and Boggon, 1933), some contralateral associations, and, in addition, with almost the entire rostral half of the reticular complex of the thalamus. Furthermore, the centre median apparently emits a massive fibre system to most of the ventral nuclear complex of the thalamus, including the entire extent of the n. ventralis anterior.

The rostrally adjacent non-specific cell groups (median and paramedian region of the thalamus together with the intralaminar n. paracentralis and centralis lateralis) appear to be diffusely interconnected. A prevalence of multisynaptic conduction systems among such reciprocal associations is suggested by the small number of direct connections between the most medial and most lateral parts of the system, by the apparent absence of direct commissural associations of the lateral intralaminar cells, and by

[1] This quantitative difference might even be more pronounced than the present observations would suggest, as part of the caudally directed fibre degeneration might have been due to interruption of transit corticothalamic fibres.

the limited rostral spread of fibre degeneration observed in a case of focal destruction in the caudal part of the median thalamic region. Aside from such intrinsic associations, all of the median and intralaminar nuclei appear to possess reciprocal connections with some of the surrounding main thalamic nuclei. Connections of this sort are likely to exist between the medially situated non-specific nuclei and the dorsomedial nucleus on the one hand, and between the more laterally situated components and the lateral nuclear complex on the other hand. It will be remembered that the centre median has major efferent connections with the ventral nuclear complex. Thus, neural activity within the non-specific thalamic apparatus could conceivably spread more or less directly to those specific thalamic cell groups which project to frontal, sensorimotor, and parietal association areas of the neocortex.

Excepting the centre median, little certainty was obtained with regard to efferents from the non-specific nuclei to the reticular complex of the thalamus. Although terminal degeneration was observed in rostromedial and rostrolateral parts of the complex following lesions of the medial and lateral intralaminar nuclei respectively, the interpretation of these findings is difficult in the light of largely similar observations made in cases of lesions in the dorsomedial and laterodorsal nuclei respectively. If projections from the intralaminar cell groups to the reticular complex do indeed exist, they must be organized in a much more topical fashion than those from the centre median which appear to spread over a very large rostral part of the complex. The same remarks apply to the connections of the non-specific thalamic nuclei with the n. ventralis anterior. The latter nucleus likewise appears to receive diffuse afferents from the centre median, while afferents from the more rostral midline and intralaminar cell groups, if at all in existence, must accompany the projections from the dorsomedial nuclei and terminate in only limited parts of the nucleus.

It is of importance to note that efferents from the centre median have a widely spread thalamic trajectory, and that some such fibres are likely to be involved in stimulation or lesion of almost any part of the non-specific thalamic apparatus.

2. *Subcortical Projections*

The experiments described above have produced evidence of projections from the non-specific thalamic cell groups to the corpus striatum. Again, the most diffuse of such projections appear to originate in the centre median, from which fibres could be traced mainly to the putamen, and in lesser numbers to the globus pallidus, caudate nucleus, and claustrum. The n. centralis lateralis would appear to project to the caudate nucleus, the more medial intralaminar cell groups to the claustrum.

Although at the present time it is hardly feasible to speculate upon the functional significance of these subcortical projections, they may be of considerable importance in the light of some recent suggestions that both the caudate nucleus (Mettler *et al.*, 1952) and the putamen (Hovde and Mettler, 1953) project to the frontal cortex. It remains for further study to decide whether and to what extent such connections are involved in the corticipetal mediation of non-specific thalamic activity.

3. *Cortical Projections*

The present study has furnished little unequivocal evidence in support of the notion of widespread direct neocortical projections originating in the non-specific thalamic cell groups. Although degenerating fibres could be traced to frontal or parietal cortical areas in several cases of lesions in the midline and intralaminar nuclei, it is highly uncertain to what extent such degenerations might have been caused by interference with fibres of passage originating in main thalamic cell groups.

It is only too obvious that a technique involving the production of surgical lesions within the centrally located non-specific cell groups, such as that employed in the present study, can hardly be expected to furnish detailed information upon subtly different thalamocortical projection systems. Thus, at the present time only the following data appear to be reasonably acceptable:

1. The centre median does not project to any part of the cerebral mantle.

2. The more rostrally situated complex of midline and intralaminar cell groups projects to phylogenetically older parts of the cortex, viz. to the prepiriform cortex, to the infralimbic and limbic cortical areas, to the presubiculum and to the entorhinal area,

with additional scant projections to marginal strips of neocortex adjoining the rhinal and cingulate sulci respectively. It is interesting to note that the fibres establishing the last-mentioned connections do not seem to belong in either of the two known categories of thalamocortical fibres in that they enter as deep tangential fibres and appear to end only in the deep layers of the respective cortical fields.

3. Cortical afferents terminating in all cell layers and ramifying in layer I, probably identical with the 'non-specific cortical afferents' described by Lorente de Nó (1938), cannot be interpreted categorically as representing cortical projections from 'non-specific thalamic cell groups'. Degeneration of such fibres was observed both in lesions of specific and non-specific thalamic nuclei.

It is of interest to note that the projection from midline and intralaminar nuclei to the limbic and infralimbic cortical areas is reciprocated by considerable projections from the same areas (Niemer and Castellanos, 1950; Nauta, 1953) and indirectly from the hippocampus and septal region (Nauta, unpublished), to the non-specific cell groups. This reciprocity would suggest that the gyrus cinguli represents part of a neural circuit which might have a profound influence upon the parameters of neural activity within the non-specific thalamic cell groups.

The observations discussed above furnish little decisive information regarding the anatomical substratum for widespread neocortical transmission of non-specific thalamic activity. Until further data become available through continued physiological and anatomical experimentation, the following possibilities must be considered.

1. Cortical projection through pathways synapsing in the dorsomedial, ventral and lateral nuclei, to the granular frontal, sensorimotor and parietal association cortex respectively.

2. Transmission through the reticular complex of the thalamus (Jasper, 1949) which has been shown to project in a topical fashion to a very large part of the neocortex (Rose, 1950). Efferent connections of the non-specific nuclei to the reticular complex as demonstrated by the above experiments, however, appear to distribute only to rostral parts of the complex. Unless a secondary diffusion of non-specific impulses within the complex is accepted,

a more or less generalized cortical distribution of such impulses would therefore seem unlikely.

3. Cortical projection by intermediary of hitherto anatomically unknown pathways originating in the striatum: caudate nucleus, putamen, and claustrum. This possibility is suggested by recent findings which tend to indicate a projection of the caudate nucleus (Mettler *et al.*, 1952) and putamen (Hovde and Mettler, 1953) to the frontal cortex.

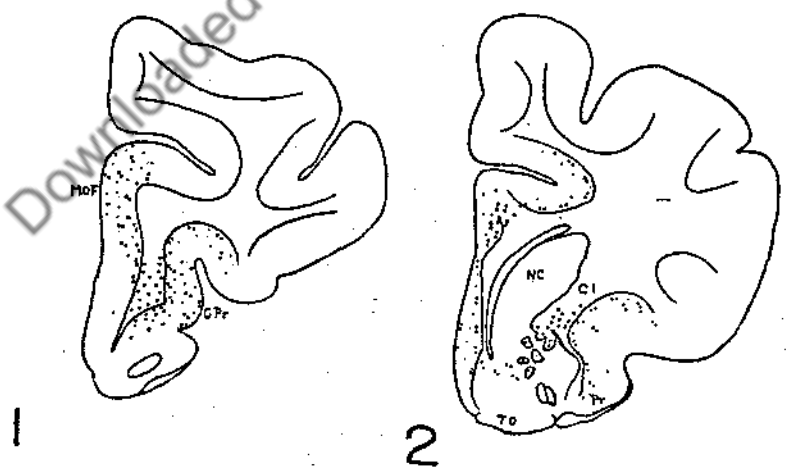
4. Intracortical or cortico-cortical spread, originating in medial and basal parts of the cortex. Associations of the limbic cortex with extralimbic cortical areas which might in part account for such diffusion have been demonstrated by both anatomical (Nauta, unpublished) and electrophysiological (McLean and Pribram, 1953) methods.

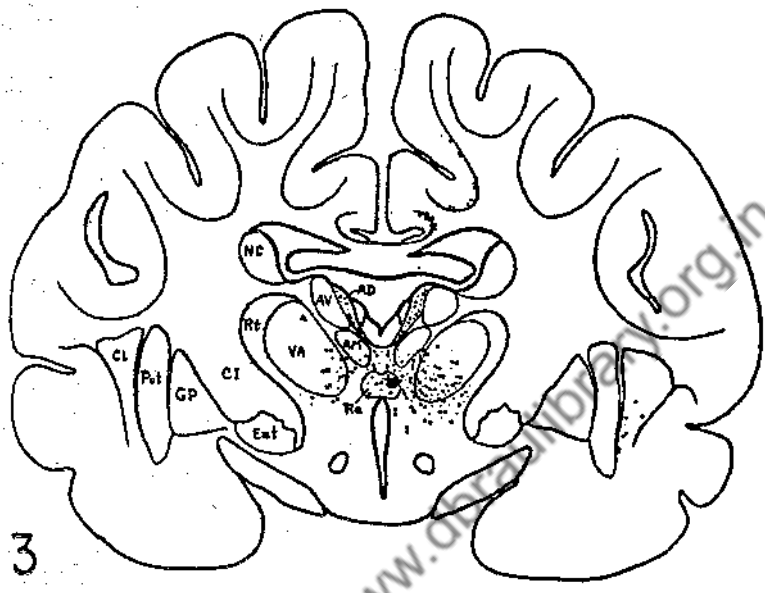
As indicated above, the existence of additional non-specific corticipetal channels cannot be excluded. The possibility must be kept in mind that several or all of the mechanisms suggested above are involved simultaneously in the corticipetal transmission of non-specific thalamic activity.

EXPLANATION OF FIGURES

FIGS. 1 TO 6

Fibre degeneration following tubular lesion of median and paramedian region of thalamus Lesion indicated as solid black area. Heavy dots represent degenerating fibres of passage small dots degenerating terminal fibres.





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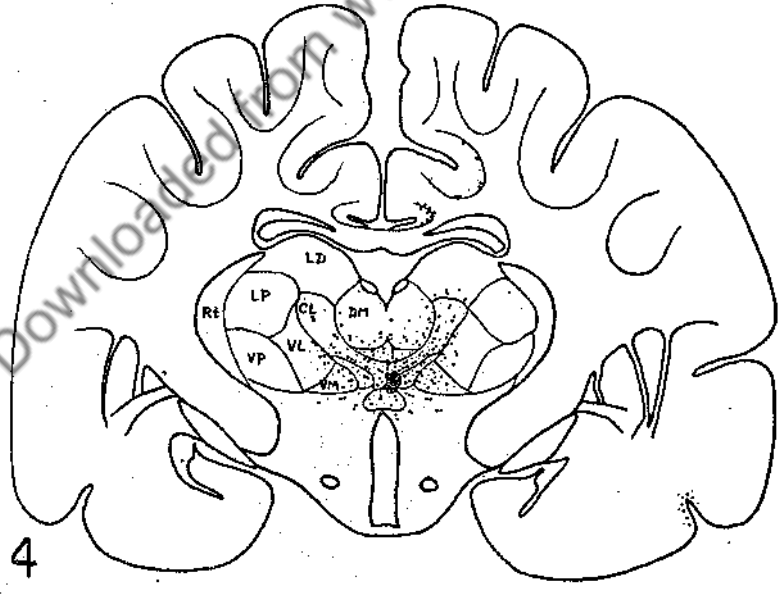

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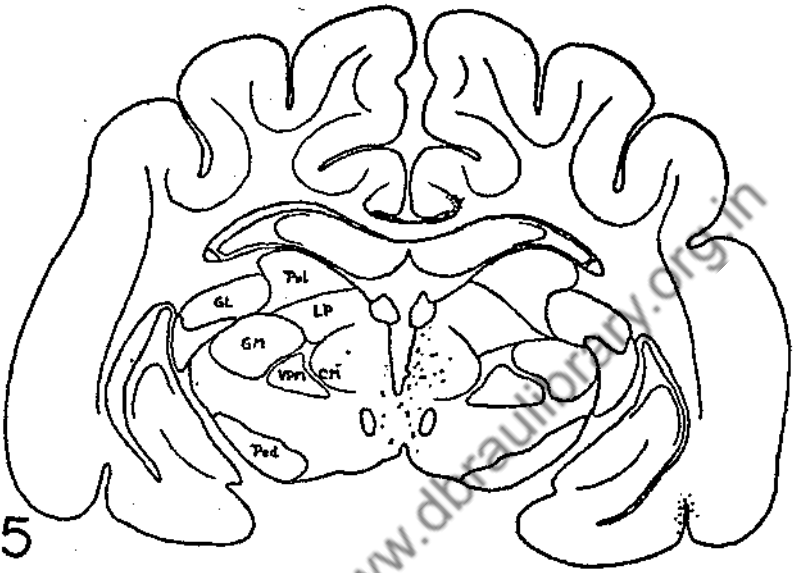

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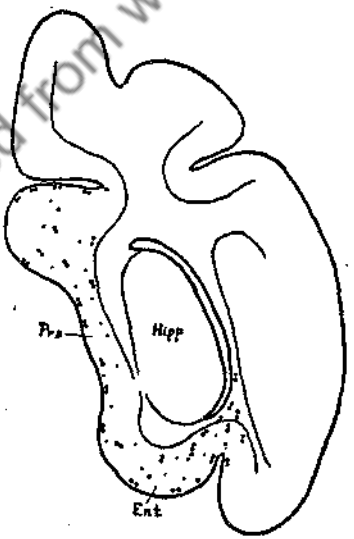

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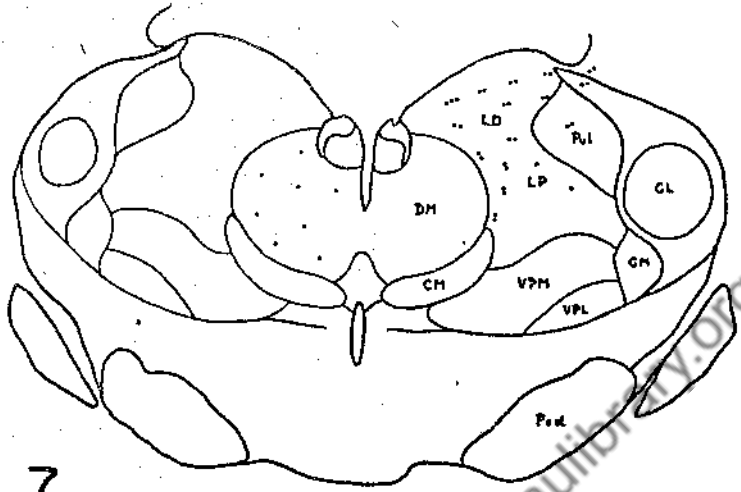
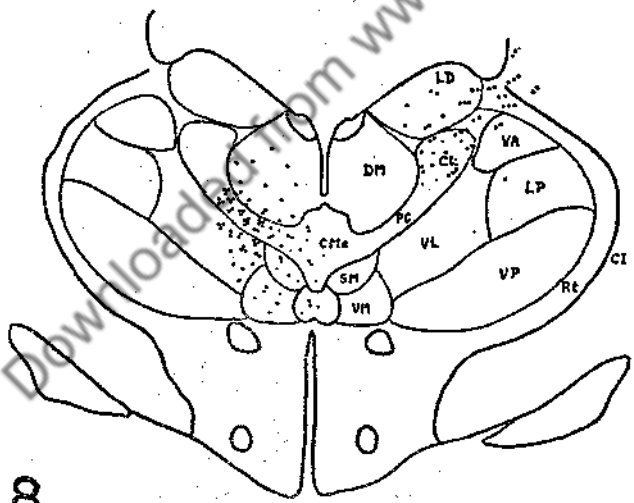
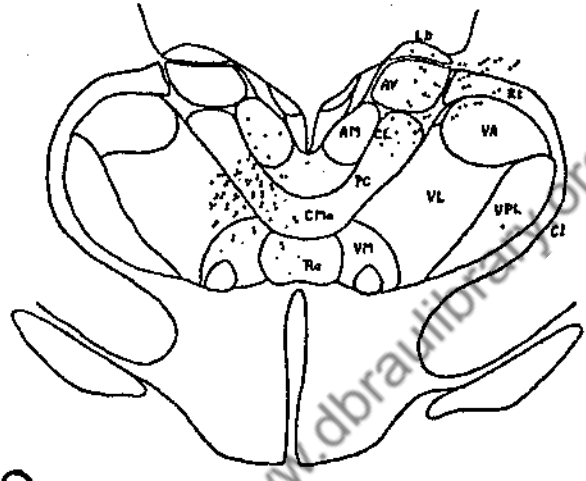




FIGS. 7 TO 10

Semidiagrammatic illustration of intrathalamic axon degeneration following lesions of the dorsomedial nucleus (left side of drawings) and laterodorsal nucleus (right side). This series of drawings represents the combined observations made in several individual cases of small lesions in different parts of the dorsomedial and laterodorsal nuclei respectively. Symbols as in Figs. 1 to 6.



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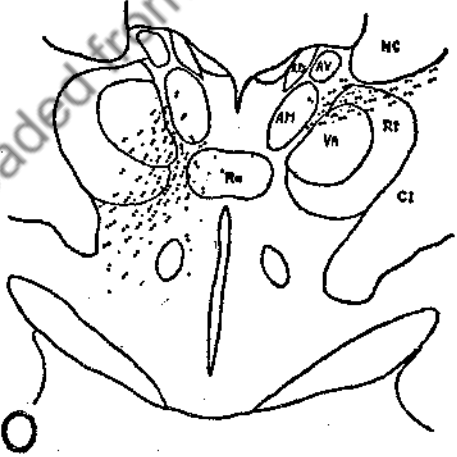

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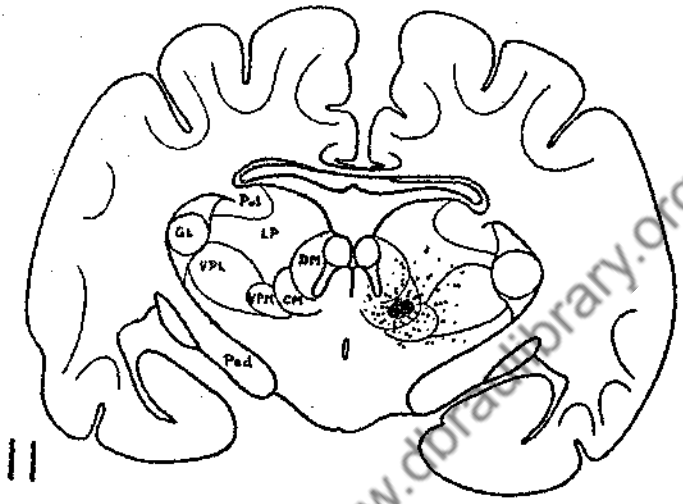
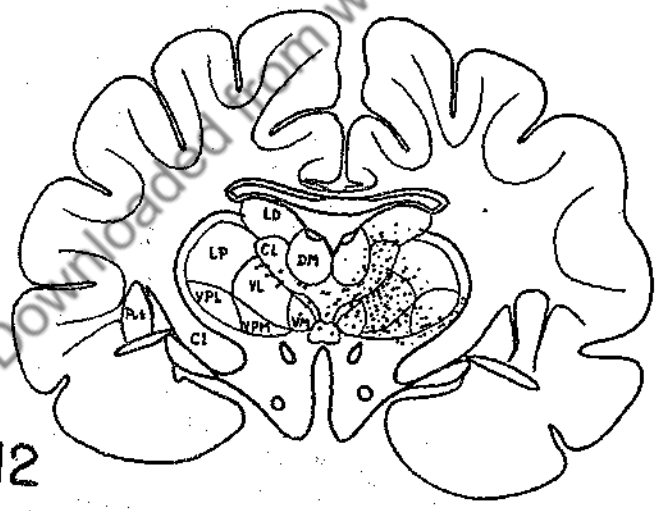
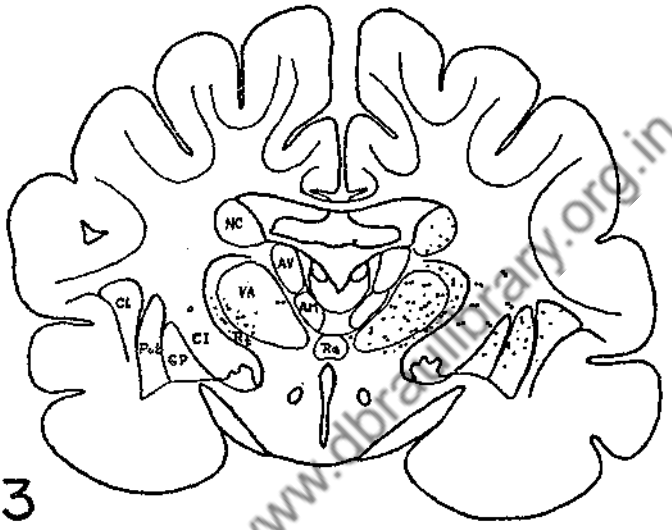




FIGS. 11 TO 14

Fibre degeneration resulting from lesion of the centre median. Symbols as in Figs. 1 to 6.



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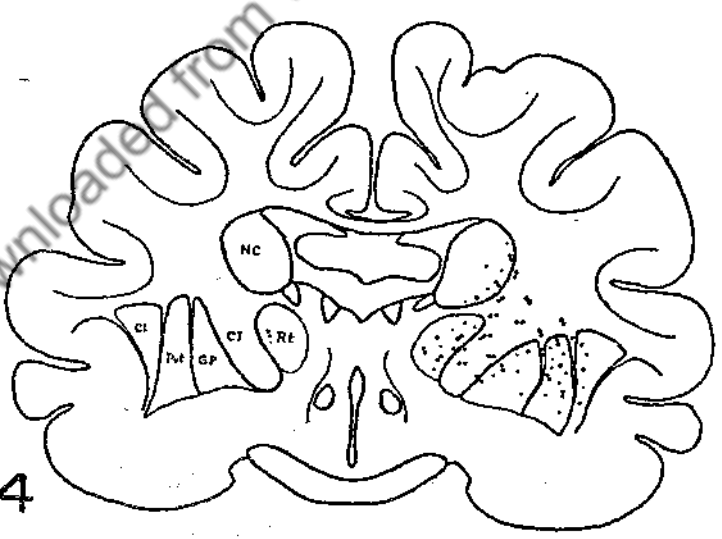

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GROUP DISCUSSION

JASPER: We have been very much interested in Dr. Nauta's work because, like other workers in the field we have been trying to analyse the connections of these intra-laminar nuclei. Dr. Hanbery and I have been doing some work in this direction and so have Dr. Ajmone-Marsan and Dr. Dillworth. I should like to ask Dr. Marsan to give us some of his results which would give a physiological parallel to the anatomical report by Dr. Nauta. Dr. Marsan will show some slides of what we consider to be 'non-specific' thalamic projection system from electrical stimulation experiments. We wish also to discuss the question of the reticular nucleus which surrounds the thalamus, the question of connection between this nucleus and the intralaminar nuclei and other parts of the thalamus.

AJMONE-MARSAN: In collaboration with Dr. Hanbery and Dr. Dillworth we have recently investigated the subcortical pathways from the 'non-specific' thalamic system, using electrophysiological methods, i.e. stimulation of the various nuclei of the system itself and cortical and subcortical recording, as well as making localized lesions in the thalamus, caudate nucleus and inernal capsule.

The intrathalamic pathway from n. centralis medialis and paracentralis, as outlined by physiological methods, closely corresponds with that obtained with anatomical methods by Dr. Nauta. Lesions of the n. ventralis anterior and of the n. reticularis are capable of abolishing the cortical recruiting responses in a more or less discrete fashion, according to the extent of the lesion; the same is observed when the anterior, inferior limb of the internal capsule is coagulated, and it is interesting to note that in these same subcortical areas, short latency responses can be recorded. Dr. Nauta feels that the concentration of degenerated fibres in this portion of the internal capsule is dependent upon lesions in the n. medialis dorsalis; in our experience, however, typical long latency, diffuse recruiting responses could be elicited by stimulation of the lateral portions of this nucleus which, at least in part, can therefore be included with the 'non-specific' thalamic nuclei.

We did not get physiological evidence in support of the hypothesis that only the limbic cortex is receiving direct fibres from the intralaminar and midline nuclei of the thalamus. In fact, most of the cingulate gyrus and the subcallosal regions do not show shorter latency responses than other cortical areas and, if destroyed, the recruiting responses in the neocortex do not seem to be affected.

The same intrathalamic pathway was observed when the n. centrum medianum was stimulated, i.e. through and/or below the midline nuclei through the n. ventralis medialis, n. ventralis anterior and n. reticularis. We failed to note any important pathway within the n.

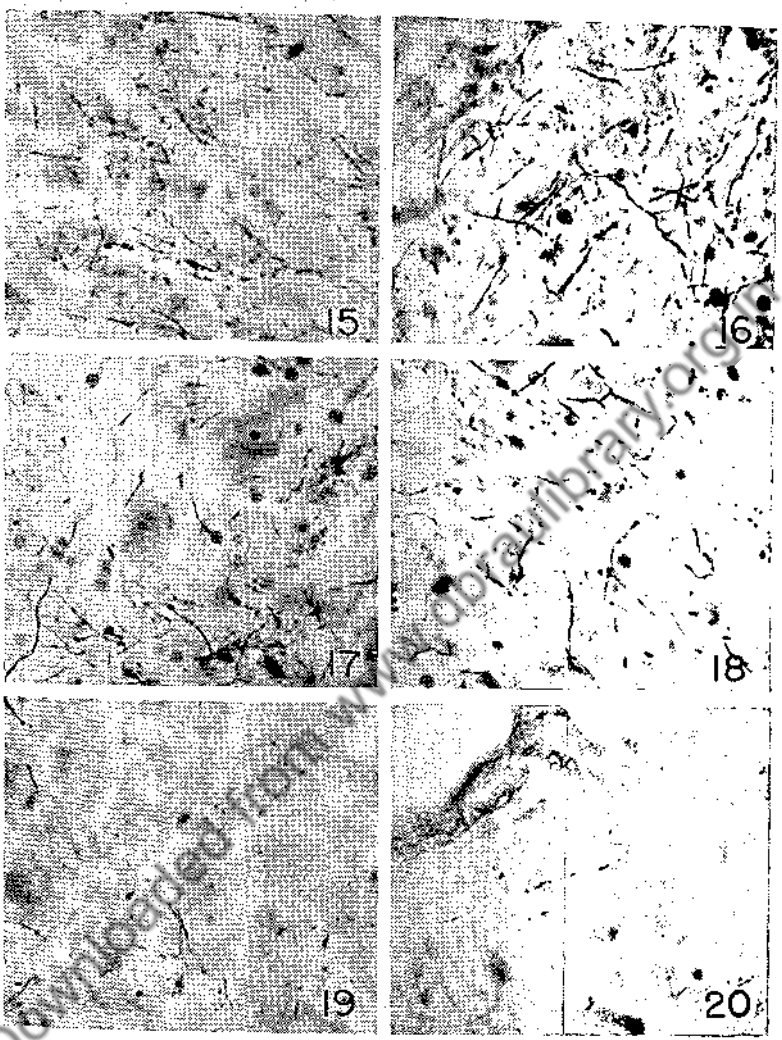
ventralis lateralis and, in addition, we do not feel that the basal ganglia play any important role as a relay between n. centrum medianum and cerebral cortex. Evidence for this has been recently presented at the Third Inernational Congress of Electroencephalography and Clinical Neurophysiology in Boston, and Dr. Whitlock himself was unable to record any recruiting response in the putamen or globus pallidus while responses could be evoked in the caudate nucleus of the cat but not of the monkey.

In conclusion, the findings obtained with physiological methods would indicate the n. ventralis anterior and/or the n. reticularis (or only the latter if the anatomical data of Rose and of Chow are also taken into consideration) as the most likely final relay nucleus for the 'non-specific' thalamic system to the cerebral cortex.

JASPER: It has been a great pleasure for us in recent months to visit Dr. Nauta's laboratory and to discuss the degree to which anatomical and physiological findings correspond in detail. We have been using electrophysiological methods to map the same pathways. The important pathway from centre median passes through the mesial thalamus goes through n. ventralis medialis and seems to end in the ventromedial part of the ventralis anterior. This pathway has been clear in many experiments and can be followed through the thalamus by both electrical recording and stimulation. Destruction methods have proven that the pathway to the cortex can be blocked by small lesions restricted to the rostral thalamus in the region of the ventro medial portion of n. ventralis anterior. It will probably take some time before the final common pathway to the cortex has been clarified. This pathway seems to us at the moment mostly from the anterior portion of the reticularis, swinging back to the rest of the cortex.

The interconnections in the thalamus that Dr. Nauta showed would merit some discussion. Perhaps Dr. Whitlock would like to discuss this.

WHITLOCK: On the basis of our anatomical studies, there would appear to be four possible routes available to the 'non-specific' cell groups for corticipetal transmission of activity. First, there is an intimate connection between the intralaminar system and the association nuclei of the thalamus. As Dr. Hanbery and Dr. Jasper have demonstrated, more or less complete destruction of the association nuclei seems to leave the recruiting response unaffected; however, there is still considerable physiological evidence indicating that the association nuclei may participate, in part, in the mediation of non-specific activity to the cerebral mantle. Second, there is an intimate relationship between the intralaminar structures and the rhinencephalon. Recent electrophysiological studies conducted in Dr. Moruzzi's laboratory



FIGS. 15 TO 20

Degenerating axons, X800.

FIG. 15

N. paracentralis, 6 days after lesion of median thalamic region as illustrated in Figs. 3 and 4.

FIG. 16

Ventromedial nucleus of same case.

FIG. 17

N. reticularis thalami, 7 days following lesion of centre median.

FIG. 18

N. ventralis lateralis of thalamus; same animal as Fig. 17.

FIG. 19

Layers IV and III of medial orbitofrontal cortex, 7 days following small lesion in dorsomedial nucleus.

FIG. 20

Degenerating axon in plexiform layer of medial orbitofrontal cortex, 7 days following small lesion in dorsomedial nucleus.

have served to demonstrate that recruiting potentials can be recorded from a portion of this region during repetitive stimulation of the intralaminar nuclei; therefore a thalamo-rhinencephalic relay must still be considered. A third possibility for the transmission of non-specific activity to the cerebral cortex would be by way of the striatum. There is some recent evidence of electro-physiological nature from Dr. Mettler's laboratory indicating that the striatum, in turn, is connected at least to the frontal regions of the cortex. On the other hand, Dr. Marsan has reported here that removal of the caudate nucleus has relatively little effect upon recruiting responses. Fourth, the intralaminar region and the centre median nucleus have rather massive connections with the more rostral portions of the reticular nucleus. Dr. Rose has reported that this reticular complex is apparently interconnected in a topographic pattern with most portions of the neocortex and hence may form the final common pathway for non-specific influence. Since up to the present time, we have studied only the effect of lesions restricted to the lateral, medial and midline nuclei of the thalamus, it is entirely possible that destruction of other thalamic regions may demonstrate connections with the more caudal portions of the reticular nucleus. It seems to me that if the reticular nucleus is involved only at its rostral pole, one must either postulate a secondary diffusion back through this nucleus or that other nuclei which we have not explored must be connected with it. In conclusion, I should like to ask whether or not stimulation of the reticular nucleus has evoked any recruiting potentials displaying a topographical distribution similar to that described by Dr. Rose in his analysis of the reticular complex.

JASPER: There is some suggestive evidence that this may be true but differentiation between specific and non-specific responses is not always clear. In experiments like this, if the electrode is in a specific nucleus, you get only specific responses from the direct projection area, and you see no effect on the rest of the cortex. This is what we mean by the specific system. We have here a discreteness of localization both in the thalamus and in the cortex which makes it an isolated system not affecting other parts. Moving just $\frac{1}{2}$ a millimetre out of that sensory nucleus, just to touch the reticularis, suddenly we bring in the more widespread recruiting responses. So, in a sense, the non-specific system is a very specific system with its particular properties which distinguishes it from other systems.

PENFIELD: But it is diffuse, isn't it?

JASPER: It is diffuse in its distribution because it overlaps projections from the specific system. In the thalamus, however, it is a very specific set of neurones which are not diffusely distributed throughout the thalamus.

MORISON: I think we were the first to use the term 'diffuse'. We did so because there are places in this system, very small places sometimes, from which the entire system can be activated. In the early exploratory studies we concentrated upon the intralaminar nuclei perhaps more than anything else; especially the rostral part of the centre median. It was from this area that the whole cortex, more or less, could be activated. Occasionally we could see two responses from the more anterior parts of the system which we interpret as some form of contamination of the responses from stimulating other pathways in the anterior part of the thalamus. Our analysis therefore confined itself more to those regions from which the widespread effects could be obtained. Stimulating the anterior part of the thalamus we occasionally observed 'primary responses' in appropriate projection areas of the thalamus, and we also observed another puzzling response, the 'augmenting response' which we had some reason to believe is different from the recruiting response. It could occur simultaneously with the recruiting response in a localized area. The fact that all three types can easily be elicited from the same or closely adjacent areas in the anterior thalamus makes interpretation of results exceedingly difficult. To be specific, there is a possibility that the localized 'augmenting response' might give a false impression of localization in the recruiting system.

In connection with the distribution of recruiting responses in the various cortical areas one must consider the possibility that the impulses leading to this response are relayed via intrathalamic connections with the projection nuclei. It was my understanding that Dr. Nauta found that the intralaminar areas have connections with the sensory projection nuclei and the lateral nuclei, except for the geniculate bodies. Is that right Dr. Nauta? If so, this fits well with Dr. Magoun's finding that recruiting responses are rare or absent in primary visual and auditory areas.

NAUTA: Dr. Morison's understanding of our findings is correct.

MORISON: This is very entertaining in view of the map which Dr. Jasper showed and the one that Dempsey and I published. If I recall correctly, the Magoun map isn't so very different from ours except that this is a little more contrasty than ours. Isn't that right, Dr. Magoun?

MAGOUN: Yes.

MORISON: We found very light projections to the cortical areas corresponding to the geniculate bodies, i.e. the auditory area and the so called visual area. As you do not find much there at all, it may turn out by using a Laplacian electrode that these responses are coming from somewhere else by just electrical spread. This finding raises to me quite seriously the possibility that the connections between the intralaminar nuclei and other nuclei in the thalamus may have an important role to

play in the production of the recruiting response. This is a possibility that we early considered but were never quite sure about. The heavy projection to the proreus may have something to do with the heavy connections between the midline nuclei and the n. medialis dorsalis. One can over-emphasize the anterior part of the recticular nucleus as important for the recruiting response.

JASPER: Are you proposing that a good deal of this response may be mediated through specific nuclei of the thalamus?

MORISON: Yes. We thought of that at the time and the interesting thing is that when you stimulate specific nuclei of the thalamus, you don't get recruiting responses, yet if you lower your electrode just half a millimetre, the picture changes entirely. This may be a question of concentration of recruiting fibres with less concentration in the centre of the specific nuclei and increasing concentration in their border lines. The coincidence between our map and the findings reported by Dr. Nauta makes me feel that we ought to keep this possibility in mind.

JASPER: The number of maps that you can plot are infinite and here is another one (slide not reproduced) showing the responses from the anterior portion of the system with bipolar stimulation of the n. ventralis anterior. As you see there are islands where there were no responses obtained. These islands were found under certain conditions, in this case in the acoustic area. I do not believe therefore that electrical spread could have played any important role because then we would not have found these areas of no response.

MORISON: I see you get many short latency responses.

JASPER: Yes that is what you get from stimulating in the region of ventralis anterior with bipolar electrodes 1 mm. apart. You don't get such short latencies with a more localized stimulus.

BREMER: It interested me to see that the region where you got no responses in this case corresponds to auditory area I.

JASPER: I think the point should be made that when in this experiment the stimulating electrode was moved to the other side of the thalamus and the laboratory at that time had quietened down, we were able to get responses in the primary auditory area on the other side in the same cat. It is our impression, therefore, that extraneous stimuli may affect the pattern of the recruiting responses especially in the sensory receiving areas.

MORISON: This highlights the difficulties which I was talking about. When you place an electrode in the anterior part of the thalamus you stimulate a good many fibres of passage and observe quite a variety of latencies in the cortical responses. It would take a little more courage than I have to call all these, recruiting responses.

JASPER: We are quite agreeable to the suggestion that in this part of the thalamus there are connections to the rostral cortex but to say that

we are stimulating fibres from the geniculate body in this region of the thalamus is asking a great deal and we had good responses from the visual cortex. The ablation experiments showed that small lesions in the anterior thalamus could block responses in posterior cortical areas, proving that the pathway goes through this region. The question of how much the specific nuclei contribute to the response has been analysed by the series of experiments by Dr. Hanbery mentioned above. I will give here an illustration of the effect of destruction of a sensory relay nucleus for tactile stimulation (cf. p. 264, Fig. 8 *in* Hanbery and Jasper, 1953). The illustration shows the responses to intralaminar stimulation as well as tactile stimulation before and after the destruction of the specific relay nucleus. It is seen that the recruiting responses are retained after destruction of the specific relay nucleus ventralis posterior but that the responses to tactile stimulation have disappeared. This kind of experiment has not given us the impression that a very important part of the pathway could go through the specific nuclei.

MAGOUN: Has it been a characteristic finding that the recruiting responses augment after destruction of a specific nucleus?

JASPER: This is quite common for the sensory nuclei.

MAGOUN: I think we are coming to a merging attitude in relation to these questions and I am inclined to agree in general with the opinion of Dr. Jasper and Dr. Marsan. There are, however, two points with respect to which we have not come to the same conclusions as they. One of these is the importance of all of the reticular nucleus as a relay by contrast with only its cephalic portion. The other point is our failure to obtain responses in the primary receiving areas of the cortex. This may have resulted from differences in technique, and the exploration of these differences may be important not for further details of maps, but as clues to the physiology of the two systems.

I was impressed by Dr. Jasper's observation that the recruiting responses could be recorded in the auditory cortex only when the laboratory noise had quietened down late in the evening and I was interested also in seeing the augmentation of the recruiting response after the destruction of a specific relay nucleus. It seems to me that one of the big problems relates to the interaction between the specific and non-specific systems. We must say that we know very little about this at the moment. I was very interested to hear Dr. Nauta describe the direct connections between the intralaminar nuclei and the n. ventralis posterior and other relay nuclei except the geniculate bodies. This opens the possibility of an interaction between the two systems at a diencephalic level and Dr. Jasper and Dr. Marsan have already shown that interaction can take place also at a cortical level, where visual

responses interact with responses from the intralaminar parts of the thalamus. Furthermore, I was interested to hear Dr. Nauta and Dr. Whitlock report connections between intralaminar nuclei and the association nuclei of the thalamus, since these latter display marked recruiting responses.

May I ask whether Dr. Nauta and Dr. Whitlock plan to extend their study to the effect of lesions in the n. ventralis anterior and the cephalic part of the reticular nucleus. They showed so beautifully, starting from behind, results of lesions in the centre median and centralis medialis that I hope they will extend their studies to the cephalic portion of the thalamus. All of us who have been working with the stimulation techniques have been grateful for this anatomical basis for our physiological studies.

GASTAUT: I have had the opportunity of investigating, first with Dr. Terzian and then with Mme Roger, the effects of stimulation of various parts of the reticular nucleus of the thalamus. We obtained recruiting responses narrowly localized on the cortex, confirming the reticulo-cortical relations already observed by anatomists (Rose, 1949; Minkowski, 1951; Chow, 1952). We particularly investigated the responses of the auditory area of the cortex during stimulation of the peri-geniculate portion of the reticular nucleus and of the supra-geniculate nucleus; in these conditions we observed recruiting responses of quite characteristic form but of very brief latency (10 to 15 m. sec.) and often preceded by a spike of opposite sign and of still shorter latency, doubtless representing the specific response of the medial geniculate body.

These observations led me to the following double conclusion:

(1) The reticular nucleus of the thalamus represents the last relay before the cortex, of the diffuse system of projection.
(2) There exist connections between the specific nuclei of the thalamus and the adjacent part of the reticular nucleus.

In 1952, Ubedda Purkiss in Madrid confirmed the soundness of this latter conclusion by demonstrating, by Golgi's method, the synaptic connections between the specific nuclei of the thalamus and the adjacent portion of the thalamic reticular nucleus.

NAUTA: Both Dr. Magoun and Dr. Gastaut suggested interesting possibilities of interaction between the diffuse and specific systems and I think that we have anatomical evidence of such connections between the diffuse and specific parts of the thalamus as well as of connections of both parts with the reticular nucleus. These might form the basis for a very close interaction between specific and non-specific thalamic mechanisms.

BREMER: Terzuolo and Stoupel have been studying the caudate nucleus with electrical stimulation in my laboratory during the last year. On the whole the findings are in agreement with those of other workers. They have concluded from latency studies that it would be most unlikely that the caudate nucleus could be a relay in the non-specific system. Regarding studies of cortical responses they were struck by the fact that the latency varied very much. Occasionally an explanation for this would be, of course, that we have stimulated direct *fibres de passage*. We have, however, been struck by the ease with which cortical responses can be obtained by caudate stimulation. We have also studied the interaction between responses to caudate stimulation and those to the sensory stimulation and our findings are in general agreement with those reported by Dempsey and Morison.

MAGOUN: I think it would be a good idea to study interaction between the specific and non-specific systems with repetitive stimulation and not simply as in previous studies, with single volleys to the relay nuclei.

Since Dr. Bremer has raised the question of the relation of the basal ganglia to the non-specific system, I should like to remark that the recent work of Shimamoto and Verzeano has been in accord with the findings of Terzuolo and Stoupel. Stimulation of the head of the caudate nucleus was able to throw the reticular system of the thalamus into activity with single shocks or low frequency stimulation. Upon higher frequency stimulation, the effect is desynchronizing upon the EEG. These findings may provide some functional data for the existence of connections between the basal ganglia and the non-specific system of the thalamus. The basis for this concept was given a decade ago by the Ransons and Papas in anatomical studies.

I think there is a generalization that can be pointed out here. The basal ganglia have traditionally been regarded as relays in extrapyramidal descending pathways in the motor system. The observations mentioned would indicate that the basal ganglia, in addition to their motor functions, may serve in much more general cerebral processes.

JUNG: I have a short comment on the rhinencephalic connections reported by Dr. Nauta. He mentioned connections between the intralaminar system and the presubiculum. These may provide an explanation for the rhythmic activity that can be evoked in this region by sensory stimuli and after stimulation of the intralaminar system. As we reported in 1938 (Jung and Kornmüller). The rhythmic activity following sensory stimuli was found not only in the hippocampus but also in the subiculum and presubiculum. I would be interested to know if Dr. Green would have some comments on this point.

WHITLOCK: In answer to Dr. Magoun's question concerning lesions

in the rostral portions of the intralaminar system, I should like to mention that we have started this work and that we have some material available at the present time. It should be realized that analysing lesions in the anterior portion of n. ventralis anterior is enormously difficult in view of the fact that one must penetrate cortical areas to get to this region and the preparations thus will be contaminated by degenerations resulting from the cortical lesion. We have gained, however, the impression that after massive destructions of this area one finds patterns of degeneration corresponding to the projection of the nucleus and to the distribution of the fibres that pass through it. Degenerating terminal fibres are found in anterior parts of the cortex, that is to say the proreus, the anterior and posterior sigmoid gyri as well as in the rostral suprasylvian gyrus. Posteriorly one finds the degeneration restricted more or less to the suprasylvian sulcus.

Dr. Hanbery and Dr. Jasper have reported a very interesting finding from stimulation of this anterior part of the thalamus. They observed that single shock stimulation of the region evoked in frontal areas of the cortex a short latency response. On repetitive stimulation, however, at frequencies corresponding to the recruiting response, a secondary complex appeared in the evoked potential. It appears to me that single shocks in this area would stimulate n. ventralis anterior among other elements of the adjacent intralaminar complex. Indeed, n. ventralis anterior has been described by Bard and Rioch and more recently by Waller as projecting to these rostral cortical areas. This would then be the specific component of the response. A repetitive stimulus would appear to mobilize the diffuse system and we would consequently get the recruiting component. I would like to ask Dr. Jasper to comment on the lesions in VA which blocked the transmission of the unspecific response.

JASPER: We are convinced, from various sources of evidence, several of which were mentioned by Dr. Whitlock, that in the VA complex there is a specific pathway to motor cortex which can be differentiated by electrical methods. This component gives a short latency response in the rostral cortex. This component disappears, curiously enough, on repetitive stimulation and does not recruit in contrast to the secondary complex of the recruiting type which develops with a long latency with this kind of stimulation. These are obviously two separate phenomena evoked from the VA system. We have thought, in line with Dr. Magoun's suggestions, that in this region we may also stimulate a pathway from striatum through VA to some unknown destination. This was established about ten years ago, I think, by the Vogts. This striato-VA pathway may have a particular significance, not related to the diffuse system in a true sense. In answer to Dr. Whitlock's question

about destruction in the VA part of the thalamus, I would like to say that this work has recently been completed by Dr. Hanbery, Dr. Marsan and Dr. Dillworth. Briefly, I should like to mention that ablations in the dorso-lateral parts of the VA complex would block responses of the recruiting type in posterior parts of the cortex. A local destruction in the ventro-medial part of the VA complex would selectively block recruiting responses in the frontal cortex without affecting the posterior responses. We have obtained the impression that from centre median the fibres pass rostrally in the region of n. ventralis anterior, then fan out so that lateral destructions for example, would destroy only the fibres going to the posterior cortical areas. This has been worked out in considerable detail. We have the impression that the posterior conduction must be through the nucleus reticularis. We were interested in Droogleever-Fortuyns's pictures of the reticular nucleus showing that specific fibres go straight through reticularis; crossing these, there were finer fibres in a meshwork which probably has given the nucleus its name. As a working hypothesis we assume that this meshwork may be the fibres of the diffuse system projecting to posterior parts of the brain.

THE DIENCEPHALIC SLEEP CENTRE

By

W. R. HESS

INTRODUCTION

In any discussion involving consciousness it is worth while considering the natural form of its alteration, as it takes place when passing from the waking state to sleep and vice versa.

The more differentiated an organism, the more it depends on conscious elaboration of, and appropriate reaction to, signals from the external world in its struggle for survival. During sleep these capacities are depressed and the individual is left defenceless. The fact that all highly organized creatures accept this risk for a considerable part of their life suggests that sleep must have a vital function. We consider it a reparative process which obviously cannot take place in the highest centres while they are active.

THE SIGNS OF SLEEP

No full description of sleep will be given here. We may refer to the monograph by Kleitmann (1939), the paper by Kayser (1949) and the more recent work by Ploog (1953). We shall mention only the points with a special bearing on our subject.

It may appear paradoxical to call sleep a function, its most obvious signs being of a negative order: reduction and eventually loss of psychomotor activity and of the ability to act in a co-ordinate way; decreased awareness of external and internal stimuli – which helps to maintain sleep, once it is established; diminished and narrowed associations, leading probably to complete loss of consciousness in deep sleep. Vegetative functions are also depressed; excitability of the respiratory centre, arterial pressure, body temperature are all lowered. Closer observation, however, shows that not all functions are depressed. The orbicular muscles of the eye are more active in sleep than in the waking state, and this becomes evident in sleeping patients with facial palsy or ophthalmoplegia. It can also be demonstrated in children who are not

easily awakened and respond by squeezing their eyes if one tries to force them open. The pupils also are contracted during sleep, even in the dark. Other sphincter muscles at least maintain their tone. With regard to internal organs, their activity is not only decreased but also altered in other ways: respiration is slowed down and changes in type; the kidneys excrete a more concentrated urine, etc.

This demonstrates, that sleep is not simply a passive over-all reduction of activity, such as coma for example, but is a complex and co-ordinated state. A functional organization has therefore to be assumed, which must have a central representation.

METHODS

Injection of ions or other chemical agents into the ventricles was considered at first but was discarded because of their rapid diffusion which would render localization impossible.

Limited destructions were used only occasionally, because of the difficulty in drawing pertinent conclusions from such experiments. This method is based on the assumption that the centres are circumscribed anatomically; it cannot be applied to anatomically widespread functional units. If lesions are small and unilateral, functions are likely to be taken over by intact tissues. Extensive destructions invariably involve several systems making it difficult to ascribe any deficiency symptom to a specific centre.

Electrical stimulation as a means of obtaining positive rather than negative evidence was considered more promising on account of its universal effectiveness but the parameters of stimuli were thought to be of importance. We tried to approximate physiological conditions so that the voltage used did not exceed greatly the threshold. Potentials applied were generally between 0.75 and 2 volts, occasionally up to 3 volts, higher voltage having an unspecific excitatory effect on the animal as a whole, irrespective of the position of the electrode. Current flow was carefully checked. The shape of the electrical impulses was considered of great importance, especially when applied to areas where different systems are represented: the steeper the potential rise, the more electively the fast reacting systems are excited, their effects masking the possible participation of slower elements. Since we were

mainly interested in the latter, we smoothed out the stimuli by slowing down their rising phase. The threshold of the fast systems was thereby raised to values more comparable to those of the slow ones. The experimental and theoretical basis for these facts can be found in the monograph by Lapicque (1926) and in our paper on experimental methods published in 1932 (Hess, 1932). Such procedure made it possible to obtain vegetative effects with less interference from sensorimotor systems, if stimulation was applied at some distance from them. Thyratron and induction coil impulses do not appear to be suitable for this purpose.

The stimulation was found to be most effective at frequencies between 4 and 12 c/sec., but 8 c/sec. was used throughout all investigations in order to make results comparable.

The condition of the animal is another important factor. It must not be hurt or hindered by the electrode arrangement and should be allowed full freedom of movement and expression. Care must be taken to avoid the after-effects of the anaesthesia under which the electrodes are placed as they obscure the results. Nitrous oxide proved most satisfactory.

The cat was chosen as experimental animal because of its fairly standardized skull, its differentiated and clearly expressed emotionality and its ability to perform skilled movements. Moreover the cat is domesticated, accustomed to man, and its spectrum of behaviour is well known. The investigations were directed to the diencephalon because of its central site and its rich connections to various parts of the brain. The diencephalon was systematically investigated and the effects of stimulation were observed and many of them filmed in order to correlate these effects with the location of the electrodes, as established by microscopic examination. (The exact location of the electrodes was identified by passing a small direct current through them at the end of each experiment, and determining the iron deposit by the prussian blue reaction.)

RESULTS

These have been published *in extenso* elsewhere (Hess, 1944b; Hess, 1949). In summary, a clear-cut depressive effect may be elicited by stimulation of a circumscribed area of the diencephalon. It is situated lateral to the massa intermedia and is limited caudally

by the habenulo-interpeduncular tract and rostrally by the mamillo-thalamic bundle, although the anterior thalamic nuclei give some good results as well. Its medial aspect lies roughly 1.5–2 mm. from the midline. A lateral delimitation cannot be given, as the thalamic radiation often causes motor effects too violent to allow depression, or sleep, although, as an after-effect, sleep may prevail.

Stimulation within the field described leads to a progressive decrease of activity. The animal sits or lies down. It often chooses a place to settle down and curls up in its natural sleeping position (Fig. 1B). Eyelids and nictitating membranes are closed. But physiological stimuli, such as loud noises or the smell of meat, will rouse the animal. Nevertheless some tendency to go to sleep again persists as a rule. Stronger or repeated stimuli, electric impulses of a higher voltage applied to any part of the brain or even weak stimuli in the 'waking centre' wipe out such remaining drowsiness and render the animal wide awake: the induced depression is therefore fully reversible.

In such states of induced depression, brain potentials show patterns which cannot generally be distinguished from those of cats sleeping normally and are astonishingly similar to the C and D-stage of human sleep. (Akert *et al.*, 1952; Hess *et al.*, 1950). In fact the sleep pattern of cat and adult man resemble each other much more than their resting records (Fig. 1A).

This sleep-like state induced by stimulation must be distinguished from two conditions which may appear similar: (*a*) atonia, in which the cat collapses and lies motionless in an unnatural position as long as the stimulus lasts. This effect is produced from the anterior lateral hypothalamus; (*b*) adynamy which is characterized by loss of initiative and spontaneous activity: it follows lesions of the so-called activation centres. This state is not fully reversible; although the animals become more lively subsequently, they do not return to their normal state and habit, they neglect themselves and remain altered in their general behaviour.

These depressing effects contrast with those elicited by stimulation in the 'dynamogenic field' which is situated in the posterior and mesial part of the hypothalamus, and extends to the central grey matter of the mesencephalon and anterior rhombencephalon.

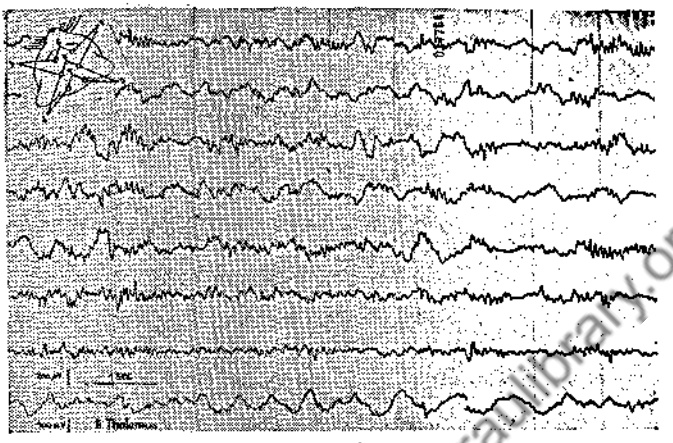


FIG. 1A

Brain potentials during sleep induced by diencephalic stimulation. Channels 1-7: Bipolar leads from cortex (see inset). Channel 8: Bipolar lead from left thalamus. High slow waves and spindle bursts remind of D stage of human sleep.

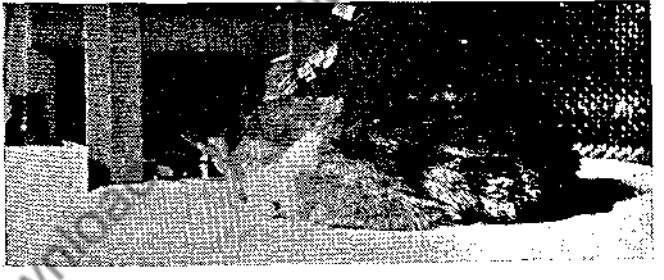


FIG. 1B

Picture taken during above state. Cat curled up in sleeping position.

Here impulses of 1-2 volts lead to a dramatic rise in excitability. The cat arches its back, and its hair standing on end, it spits and shows all signs of fear and fury.

From the same region, it is possible in anaesthetized animals to raise the blood pressure, and increase the heart and respiration rates, etc., whereas opposite effects are produced from areas which include the hypnogenic centre.

DISCUSSION

Experimentally it is a fact that electrical stimulation within a fairly limited area of the diencephalon, which is in functional connection with wide areas of cortex, hypothalamus, mesencephalon, etc., induces a diminution of the animal's activity, leads to drowsiness and eventually to a sleep-like state. This state cannot be distinguished from natural sleep by any means available: the pupils are narrowed, the nictitating membranes are relaxed, the eyes are closed and often the animal chooses a convenient place to settle down and assumes its habitual sleeping position. The condition is reversible in that physiological stimuli wake the animal up.

The reversibility is evidence against the effects being due to electrolytic destructions, which can also be ruled out by careful histological control. An inhibitory electrotonic effect of the stimuli cannot account for the effects, which are clearly excitatory in other areas of the brain with the same kind of stimulus.

The conclusion is that, in the area delimited, there exists a functional centre whose activity leads to a general depression and it appears justified to assume that this centre is in action at the onset of natural sleep. We believe its significance lies in the preservation of energetic resources and the protection of tissues from overstrain as well as in inducing a condition in which reparation of structural changes can take place; we have called it the 'trophotropic system'.

We think that this mechanism acts as an antagonist to the arousal system, which has been demonstrated by other authors (Moruzzi and Magoun, 1949) as well as by our own experiments: stimuli as weak as 1 volt may lead to a dramatic change in the animal's behaviour in the way of maximal excitement. This

system obviously tends to bring the organism in the optimal condition for dealing with the environment, especially in attack and defence. We have therefore termed it the 'ergotropic system'. Its central representation involves the posterior hypothalamus and the peri-ventricular grey matter of the mesencephalon, while the anterior extension is not perfectly elucidated.

It is evident that either of the two antagonistic centres gains influence if the other's activity declines, and the level of general excitability is accordingly altered. Experimental lesions (Lindsley *et al.*, 1950; Ranson, 1939) as well as pathological processes, as in Economo's disease (1929), lead to long lasting states of somnolence, which are only partially reversible.

There is little evidence, so far, of sleeplessness consequent to destructions in the areas of the 'sleep centre'. This might be due to the anatomical scattering of this functional unit whose elements cannot be put out of action in sufficient number by lesions compatible with life.

While the arousal system prevails in the waking state and the inhibitory centre during sleep, neither is in absolute control except in extreme conditions such as deep sleep after exhaustion or maximal activation, in attack or defence. In normal circumstances, the state of alertness – and consciousness – fluctuates between these extremes and keeps adjusted to the needs of the situation.

The fact that sleep may be induced by appropriate electrical stimulation in the described area seems therefore to be well established. But from brain regions at least overlapping with the above areas Morison and Dempsey (1942a) elicited their recruiting response, Jasper and Droogleever-Fortuyn (1949) and Hunter and Jasper (1949) induced the electrical and clinical signs of *petit mal* by stimulation. The question therefore arises whether these seemingly divergent results are due to different systems being excited by different methods of stimulation or whether some functional connection exists between the above mentioned phenomena. Impairment of consciousness is of course a common feature of both sleep and epilepsy. The activation of certain types of epileptic discharges through light sleep is another possible link. The queer coincidence that brain potentials in sleep and generalized epileptic outbursts tend to show maximum amplitude over

the same head regions as well as the similarity of some brain wave patterns in both conditions may also be taken into consideration, although it is by no means sure that these are relevant to our problem.

CONCLUSIONS

The organism's state of general excitability – which includes alertness and consciousness – is regulated by two antagonistic functional centres: the ergotrophic centre which aims at maximum alertness and readiness for defensive or aggressive action, whenever such action is needed in the struggle for survival, and the trophotropic centre which instigates inhibition of such activity, brings about sedation and eventually sleep, in order to preserve energy and allow tissues to recuperate. From absolute prevalence of the former centre to maximal predominance of the latter, shades of intermediate states exist, such as relaxation, drowsiness, light sleep and so on, each linked to a corresponding level of consciousness. These states are the result of a balance between the two antagonistic centres and conform to the needs of the environment.

GROUP DISCUSSION

JASPER: We regret that Professor Hess is unable to be with us in person but we are fortunate in having him so well represented by his son who will present both his father's opinions and his own point of view in the discussion.

PENFIELD: Which are the parameters of stimulation? Which type of electrode did you use?

HESS JR.: We used insulated steel electrodes of 0.25 mm. diameter. The stimuli were smoothed out D.C. impulses with a frequency of 8/sec. applied for 60 sec. in most cases.

WALTER: Was the stimulation bi-polar?

HESS JR.: Yes; the inter-electrode distance being 1.5 mm. Between the impulses which had a duration of 1/80th second, the direction of current was intermittently reversed with 1/10th of the voltage, so that total current flow was equal in either direction, in order to avoid polarization and lesions.

JASPER: From what I can understand the anatomical structures concerned with sleep include part of the intralaminar system as well as the

anterior nuclear group. We are all very familiar with the functional properties of this region and this fact should give us a good start for the discussion.

BREMER: When, in 1929, I first saw the film of Professor Hess, I was really impressed by it. However, in 1931, in Paris, I raised a *réserve* and I am sorry that he is not here to re-discuss with him the question. One thing I wish to underline: there is no question that the sleep induced in these cats is real sleep, neither do I reject the plausibility of the existence of a sleeping mechanism. If we admit the reality of the awakening mechanism, the very principle of reciprocal innervation should make us postulate an antagonistic mechanism.

My reservation concerns first the technical aspect of the question. The use of selective stimuli is rather attractive but there is always the danger that using slowly raising pulses, at times of high voltage, one may produce an electrotonic reversible blockage.

Then, as Dr. Hess has pointed out, the duration of sleep outlasts the stimulus. This could be explained by a mechanism of *enclenchement* but this is only an hypothesis and there is no fact to prove it.

Another difficulty concerns the inhibitory mechanism. Upon what structures does it act and what is its intimate mechanism for such long-lasting effects? Those are very difficult questions to answer but of course I don't imply that they are insoluble. We know of other examples of inhibition of long duration (Richet-inhibition for instance, well studied, in the frog by Gerebtzoff) but in these cases the inhibition never outlasts the stimulus which produces it. In Dr. Hess's experiments, as we have seen, the effect is very long-lasting after the end of the stimulus and, therefore, we find ourselves in a very uncertain position to explain the mechanism for this type of inhibition.

HESS JR.: We do not know the intimate mechanism of the described phenomenon. It is true that the area in question does not cover any definite anatomical region; the same holds for the awakening mechanism and yet the reality of it is accepted.

The very fact of obtaining excitatory effect with identical stimulation in all other areas and very clear arousal reactions in the activation areas seems to rule out the probability of an electrotonic block as a way of action.

The long duration and the outlasting of the effect just stress the physiological nature of the phenomenon: Sleep once induced tends to continue, owing to diminution of proprioceptic afferences (eyes closed, muscles relaxed, etc.), and general decrease of excitability. This is a physiological state from which the animal can be awakened with physiological stimuli. If this longlasting effect was due to an electrotonic blockade I do not think that this could be done so easily.

The electroencephalographic picture is not always consistent with a sleeping state and, while in most cases we did observe an EEG pattern characteristic of sleep, on other occasions the electrical activity was found to have waking pattern while the cat was lying in a sleeping position or *vice versa*. This, however, is not a surprising finding; we know that over-tired soldiers can march while partially asleep and it has been shown by Grüthner and Bonkalo as well as by Kleitman that over-tired people, whose EEG consists of a definite sleep pattern, may perform calculations. It was also found that a sleep pattern in the EEG can be induced by stimulation of the caudate nucleus while the clinical phenomena rather resemble a catatonic state. In these cases we are dealing with partial sleep, i.e., the cortex is asleep while the subcortical centres may possibly be active.

BREMER: Probably I was not clear in my question. I did not object to the location of the structures involved but I would like to know where do the inhibitory impulses act? With the inhibitory mechanism of sleep one must postulate a blockage of the ascending system or a generalized inhibition of the mesencephalic and cortical centres.

The long duration of the phenomenon was my second objection. I feel that it is more easy to explain by assuming that an active mechanism is put out of work on account of synaptic fatigue, and the critical point is to explain that through an active inhibitory effect which should be very long-lasting to maintain it.

Maybe the two mechanisms could be co-existent but, for the moment I feel that we have no explanation for the long-lasting inhibitory effect.

JASPER: I think that the fact of obtaining excitatory phenomena with the same stimulation in other areas is a very strong argument of its being a positive effect in the case of sleep and this Dr. Bremer has not answered.

BREMER: I agree that this is against the hypothesis of an electrotonic blockade but my chief objection still remains, i.e. to explain sleep by inhibition.

MAGOUN: I have been struck by the differences in approach to the problem which have been presented earlier today and this evening by Dr. Hess. Today we heard of studies on the alteration of electrical activity of the cortex and subcortical structures which were discussed from the point of view that they might contribute to our knowledge of the problem of wakefulness. Dr. Hess provides observations of animals going to sleep and he obviously dealt with behavioural sleep. I wonder whether he can inform us about the relation of his findings to the recruiting mechanism. While stimulating at 8/sec. the area under discussion can he record recruiting responses? If such an observation

was available, it might be possible to relate these results to the diffuse projection system of the thalamus. The 8/sec. frequency of stimulation Dr. Hess uses is close to the periodicity that this thalamic system tends to exhibit spontaneously.

During discharges at 8/sec. we usually observe in the cortex rhythmical bursts which we like to associate with sleep. This same cephalic part of the non-specific system is capable, if stimulated at 25–100/sec. of producing rapid discharges associated with wakefulness. I wonder whether Dr. Hess could produce an arousal by stimulating with higher frequency (50–100/sec.) the same system which, when stimulated at 8/sec. did produce sleep? This may at the same time, answer Dr. Morison's earlier question as to whether stimulating the intralaminar part of the thalamus can induce behavioural, as well as EEG arousal.

HESS JR.: In our experience frequency above the 8/sec. (around 20/sec.) would arouse the animal. The same was observed also if the animal was stimulated with high frequency while asleep.

Increasing the voltage of stimulation would produce a similar effect as increasing frequency. Incidentally, I must answer now Dr. Bremer's question that we never used high voltage stimulation to induce sleep, the voltage being usually 1–1.5/v.

We never recorded cortical electrographic activity during actual stimulation of the thalamus. However, Monnier did but could not to my knowledge observe any recruiting response.

WALTER: I want to stress the importance of recording during stimulation because I feel that the very first signs may be the most important, and such as can give us a clue to the understanding of the underlying mechanism. The continuance of sleep may be dependent upon much more complicated mechanisms but how sleep starts is the real question which needs to be answered; I feel that a study of the events occurring in the first seconds or even milliseconds is very important.

We cannot yet explain sleep but we could define sleep, probably, as: 'a raising of the standard of significance required of the stimuli'; in fact we know that stimuli can still reach the cortex during sleep, the K-complex is indeed a well-known phenomenon, and I wonder whether you did observe any K-complexes in your sleepy animals. A K-complex means that stimuli have reached the cortex but my feeling is that they reach it in a very 'insignificant' form.

HESS JR.: We were looking for K-complex but saw none of which we could be sure. I do not feel that the very first phenomena are the most important ones for our purpose, since we were looking for slow phenomena. I wish to point out here that one of the reasons for choosing slow rising waves instead of square waves for stimulation was

to avoid the excitation of fast systems, mostly motor or sensory, easily stimulated because of their lower threshold.

I wish to add here that sleep was usually induced only after 2–3 periods of 60 sec. stimulation at 8/sec., a slight depression only being observed after the first period of stimulation.

WALTER: If you record after the first period of stimulation, could you detect any larval sign of drowsiness in the EEG? We know that in man drowsiness is very easily detected in the electrographic tracing.

HESS, JR.: Of course we are dealing with a gradual phenomenon. In some cats which before the stimulation, were very wild and unmanageable with the EEG showing an activation pattern, we did observe after the first period of stimulation a marked change in behaviour, while in the EEG tracing 'resting' rhythms appeared and later 'spindles' suggestive of drowsiness. However we could not see any change comparable to the dropping out of the alpha rhythm in human EEG.

MORISON: Did Professor Hess find any correlation of threshold with different areas of the thalamus in the transverse dimension. As I look at his longitudinal sections it seems to me that the whole thalamus was involved. It is important to determine localization as closely as possible if we want to make any correlation with the recruiting system.

HESS JR.: Medially, this area extends to about 1 mm. from the midline. I cannot answer the question concerning the lateral extension: when stimulating laterally we always get intermixed motor phenomena, which interfere with sleep. Sometimes, in these cases, we can get sleep afterwards but this could be interpreted as a negative after-effect.

JUNG: When working in Professor Hess's laboratory I saw some of his experiments on sleep in which some motor side effects of the stimulation were present. However, I do not feel that sleep could be considered as an after-effect of these motor phenomena because when stimulating other areas in the mesencephalon sleep could not be induced even when the stimulation had been accompanied by much stronger motor activity. The most important differences between Professor Hess's and other stimulation experiments lie in the parameters of the stimuli, the very different latency and the use of anaesthetics (as in Morison and Dempsey's experiments). Otherwise I think Professor Hess, Dr. Morison and Dr. Jasper were stimulating essentially the same system.

KUBIE: Is it technically possible to record the electrical activity of the reticular system during stimulation of Hess's sleep centre? If so, the findings might throw considerable light on the relation between the two systems.

HESS JR.: Yes, it is possible. However, I don't know how much information you would get from this experiment, because a sleep pattern does not mean that an impulse is starting there and significant impulses need not be such that they can be picked up by our electrodes.

KUBIE: Let me give an hypothetical example then. Suppose that the stimulation of the sleep centre interferes with the ordinary electrical activity itself of the reticular system. Would that not be extremely suggestive at once? If, in addition, one speculates that there might be reverberating circuits in the reticular apparatus, one could then understand both the shift to sleep and the persistence of sleep after the stimulation of Hess's centre is discontinued.

OLSZEWSKI: In the experiments in which Professor Hess obtained, either sham rage or adynamia, but not sleep, was there a single period of stimulation, or more than one?

HESS JR.: Only one: this was a sudden effect. This also would seem natural since anger usually starts suddenly while the onset of sleep is slow.

BREMER: I wish to apologize and correct my objection concerning the high intensity stimulation. I was confusing it with Hunter and Jasper's paper, where it is clearly stated that sleep was obtained only with high voltages and pulses of long duration.

JASPER: We had many previous discussions on the possible relationship between Hess's sleep area, the recruiting system, and the area from which we reproduced the *petit mal*-like attack. Anatomically, it is very hard to find a distinction between these three systems of neurones if, indeed, there are any differences to be found. In the experiment with Hunter, the records were taken of the recruiting response while we were placing the electrodes, so we knew we were in this system. After a few days, stimulation of this area was performed. It is true that in special conditions (quietness of the laboratory, making the experiment at night) sleep could be obtained, but, since we were concerned chiefly in reproducing the *petit mal* syndrome, observations on sleep were only incidental. I must add that we were not using the slow rising wave of Hess but square wave stimuli. I am inclined to think that at least this part of the thalamus, giving rise to the three above-mentioned effects, can be the same. We must then think of different effects of stimulation. In other systems (cerebellum, hypothalamus, vagus) it has been shown that changing the frequency of stimulation one can reverse the effects. So I think that Hess's hypothesis is that we have a number of structures which may be stimulated in the same area and I know very well that Professor Hess's objective has always been to avoid stimulating the rapid responding systems, especially the fibre systems, by using the type of stimulus he has used. Another conceivable explanation is that

the same system can respond in a different way when activated in different manners.

To return to the discussion of this morning it seems to me that we must clarify one point; is the response obtained from this part of the thalamus a real arousal, from a behaviour point of view? The fact that we can flatten the EEG does not prove that, and in our experience we do not obtain that behavioural arousal by stimulation of the thalamic recruiting system while it is readily obtained with stimulation of the basal diencephalon.

MORISON: We agree with that. My own interpretation of Dr. Magoun's statement is that in unanaesthetized or lightly anaesthetized animals when one stimulates with high frequency in some part of the thalamic recruiting system the latter may be blocked or inhibited thus allowing the cortex to come under the influence of tonic impulses originating in other parts of the reticular system. This may result in an electrical pattern suggesting arousal. In those cases in which activity in the arousal system is low as for example deep anaesthesia or in the *cerveau isolé*, a nearly flat line may be encountered. Even in our moderately anaesthetized animals, however, we did not see behavioural changes interpretable as arousal from intralaminar stimulation, although it was occasionally observed from stimulation elsewhere.

JASPER: In the unanaesthetized animal as well rapid stimulation of the recruiting system did not produce arousal but a peculiar state that we described as the 'arrest reaction'.

MAGOUN: Are you speaking of animals which were completely awake?

JASPER: Yes. Completely awake and walking around freely.

MAGOUN: Have you ever stimulated these animals while they were asleep?

JASPER: No.

MAGOUN: Ingram and Knott have made such a study and, if I remember correctly, they state that they can awake animals by rapid stimulation of the intralaminar system. Furthermore, Dr. Hess has first told us that stimulating what is apparently the same region can awaken a sleeping animal.

JASPER: We must not forget that an animal can be awakened from sleep by stimulation of specific sensory relay nuclei of the thalamus, and, as a matter of fact, by stimulation of many other parts of the thalamus. This is probably a non-specific effect. Arousal to an agitated, aggressive or hyperactive state is another thing, however, and is most readily produced by stimulation of the posterior hypothalamus.

MAGOUN: About the 'arrest reaction. Are you sure you were not inducing a seizure?

JASPER: You may, of course, induce a seizure but this does not occur with low voltage stimulation. By slowly raising the voltage of the stimulus, the first effect we saw was the arrest reaction.

MORISON: What did the EEG show in this period?

JASPER: The EEG is flat. It is like what Dr. Magoun would call an arousal response, but this is just the point I am trying to make. We see the 'arousal pattern' also in the corticograms of epileptic patients operated upon by Dr. Penfield but this occurs often when the patient is completely unresponsive. I think it would be an error to identify normal alert wakefulness with a flat EEG record. An 'arousal' response in the EEG may not always be associated with behavioural arousal.

MORUZZI: I would like to mention here an experiment made by Whitlock, Arduini and myself (1952-53). We recorded the spike discharges from the pyramidal tract and the EEG waves from the motor cortex in a cat which was asleep because the midbrain tegmentum had been interrupted acutely. Slow waves were present in the cortex and corresponding discharges were observed in the pyramidal tract. By stimulating, the recruiting area of the thalamus at 300/sec., we found that the flattening of the EEG paralleled a blockade in the pyramidal spike discharges. After local strychinization of the motor cortex (0.1-0.2 per cent, i.e. just supraliminar) both strychine waves and pyramidal discharges were blocked during high frequency stimulation of the same thalamic system. If strychinization was stronger (1 per cent) no effect at all was observed.

JASPER: These facts seem very pertinent to the problem under discussion. I gather that you are obtaining an arrest in the motor system by rapid stimulation of the intralaminar thalamic system; certainly that could not be called an activation or arousal.

MAGOUN: I think this finding can be interpreted differently. Dr. Moruzzi has reported the blocking of a type of pyramidal discharge which appear to be closely related to slow waves at the cortical level. I wonder whether he thinks he is directly inhibiting the pyramidal cell discharge or whether he is affecting cortical activity so that pyramidal cells are no longer excited?

Dr. Jasper implies that the EEG changes produced by rapid stimulation of the thalamic intralaminar system are different from those obtained by stimulation of the lower reticular system. I have not noticed such a difference. To be clear, is it your view that the diffuse projection system of the thalamus is not a pathway to the cortex from the reticular formation?

JASPER: I do not mean to imply that the thalamic recruiting system is

not related with the lower reticular system but I am convinced that the behavioural effects may be different.

MORUZZI: I wish to add that with olfactory stimulation also one can produce both an arousal reaction and a blockade of the pyramidal discharges, so that both electrical stimulation of the thalamic system and physiological sensory stimulations seem to have the same effect upon the pyramidal discharges. I don't think, therefore, that our own experiments can be considered as evidence for dissociating the two systems.

BREMER: Another point I wish to mention here is that during an unquestionable arousal of the cortex we paradoxically observe that the acoustics response is markedly smaller than when the animal is asleep. The fast activity we observed in the cortex in the waking animal is responsible for this 'masking' effect, because the same can be observed if instead of awakening the animal we artificially produce an increasing frequency of the electrical activity of the cortex by injection of eserine. These apparent paradoxes can probably be interpreted as a phenomenon of occlusion, the neurones responding to clicks being the same as those responsible for the fast activity.

RIOCH: With regard to the problem of sleep and wakefulness 'centres', I should like to schematically review some unpublished observations. We used photographic recording taking 3 to 4 pictures at 1/sec. intervals every 10 minutes automatically by a camera mounted above the animal cage. Lights came on at each interval and remained on for about 15 sec. Otherwise the room was dark. An attendant came in once every 24 hours to provide food and water. Observations ran continuously for 48 to 72 hours. 'Sleep' was defined in the photographs as a normal sleep posture without movement in the successive pictures. Under these conditions normal cats were found to 'sleep' for 18 to 20 hours out of 24. 'Decorticate' cats 'slept' in the neighbourhood of 12 hours (which is of the same order of magnitude as found with decorticates in the open laboratory). 'Decorticate' cats which in addition had bilateral lesions of the rostal midbrain dorsal to the red nucleus only 'slept' for 4 to 6 hours.

There is a striking difference in the behaviour of cats and dogs which survive[1] transection of the brain stem at the rostral mesencephalic level as compared with those transected at the caudal margin of the mesencephalon. The former will on occasion assume the normal sleep posture and for short periods present a state of decreased spontaneous activity and increased threshold to external stimuli. They occasionally show running movements and respiratory changes similar to these

[1] The survival periods must exceed ten days for the phenomena described to appear.

interpreted as "dreaming" in sleeping normal animals.' This state is quite distinct from the state of struggling and walking activity or the states of strongly maintained bizarre postures these preparations characteristically show. The surviving post-mesencephalic decerebrate preparations show no *clearly definable* differences in states which can be regarded as analogous to states of 'sleep' and 'wakefulness'. Only relatively slight increase or decrease in decerebrate rigidity occurs. The lack of a definable sleep-wakefulness rhythm in chronically surviving decerebrate preparations was first described by Bazett and Penfield years ago.

Prolonged observations at frequent intervals over 24 and 48 hour periods of the thresholds of spinal reflexes in chronically surviving preparations with low cervical or upper thoracic transections failed to show any identifiable changes in 'state' whatever.

When the caudal parts of the neuraxis are separated from the mesencephalon they tend to maintain a continuous state which, if the thresholds for the reflexes of which they are capable are taken as indicators, is closer to the 'waking' than to the 'sleeping' states of normal animals.

Taking the behaviour of the organism in terms of its interaction with the environment as a criterion I have been forced to conclude that sleep is a positive state and that the anatomical substratum necessary for its mediation is located in the mesencephalon.

BREMER: I am surprised by Dr. Rioch's statement because, as I showed a long time ago and was later confirmed by many people, a mesencephalic transaction produces an indefinite sleep both from clinical and EEG viewpoints.

RIOCH: A high mesencephalic transected preparation is asleep 'in front' not 'behind' the transection.

BREMER: 'Sleep behind' makes no sense to me.

JASPER: What is 'Sleep behind'?

RIOCH: Absence of spontaneous activity, such as struggling, walking, running, etc. assumption of one of the normal 'sleep' postures, and increased threshold to external stimuli.

BREMER: Would you say that the cat with a high spinal section is awake because he is reacting strongly to pinching and other stimuli? Of course, this is a matter of definition.

RIOCH: No. However, I should say that we have no adequate definition of sleep based on behavioural criteria.

MAGOUN: I agree with Dr. Rioch that there is no periodicity, in the sense of a sleep-waking rhythm, at the isolated spinal level.

Hagbarth and Kerr have recently observed that stimulation of the brain stem reticular formation can affect the afferent impulses of ventro-

lateral and posterior columns at the first spinal relay. These can be diminished or even blocked. A transection of the cord produces instead an augmentation of evoked potentials below the section. In other words there is a descending influence which tends to diminish trans-synaptic conduction in afferent paths. It is possible that some of the diminution of the evoked cortical potential observed in the waking as contrasted with the ānaesthetized animal is due to the reducing influence of the descending reticular formation.

LASHLEY: Is the 'sham rage' reaction directed to any particular object, or is it a purely motor response?

HESS JR.: We prefer to call it simply 'rage', but it is not induced by an external factor and therefore has no object. It will be directed to the nearest person or object which is brought into its surrounding.

PENFIELD: It is difficult to give a definition of sleep. In observing during the night chronically decerebrated animals, Cuthbert Bazett and I noticed the decerebrate rigidity was less while the animals were quieted down – and we used to call it 'sleep'. The rigidity increased and running movements might appear when the animals were molested After all, that is like the reaction of a normal animal? Therefore, one might agree with Dr. Rioch's concept, unless we are offered a better definition of sleep. Surely there is a better concept.

BREMER: If we consider wakefulness at the spinal level we are bound to run into confusion. This is a release in Sherringtonian terminology.

WALTER: No one here has mentioned Pavlov. As you know he defines sleep as an irradiation of inhibition. I feel that sleep is probably an attitude of the animal more than just an inevitable or a necessary state. It is easier to get a description of an attitude than to give a physiological definition of a necessity.

LASHLEY: Johnson (1926) would not give any definition of sleep except in terms of objective behaviour. We have no criterion of human sleep except in activity, lack of movements or the like.

ADRIAN: Would it be possible to have a clinical definition of sleep? The sleep obtained by Professor Hess is obviously a high level sleep and what happens in other levels of the animal is really not too important.

KUBIE: I would like to suggest one direction in which definition of wakefulness and sleep may be found. First, we must differentiate them from isolated states of inhibition or excitation in fragments of the CNS. To be meaningful, the terms must be applied to the activities if not of all at least of major parts of the nervous system functioning simultaneously. Secondly, they involve some changes in the state of consciousness. Any single component of behaviour may vary during sleep

as in somnambulism. Dr. Rioch's suggestion changes so basically the use of the concept of sleep as to make it useless for either description or experimental investigation.

BREMER: If we do a high spinal transection, therefore dividing the central nervous system in two portions: a cephalic one and a caudal one, shall we define sleep from the upper or from the lower portion?

PENFIELD: After all, we must admit that there is some similarity between the quieting down of a decerebrate or spinal animal and that of a normal animal. There is a common effect of lack of stimuli and there is a common fatigue effect of continued activity that must apply to various portions of the Central Nervous System.

BREMER: Sleep goes on with a diminution of the descending impulses coming from cortex and diencephalon, so that the whole spinal cord is also asleep, but we are interested in the mechanism and not in the symptoms when we approach the problem of sleep.

JASPER: I would have agreed but now I begin to wonder if the mechanism whereby the cyclic changes in the mesencephalic section take place might give us an insight into the mechanism of the other end of the sleep mechanism. You can't deny that the same mechanism may be operating both ways.

RIOCH: When Dr. Bremer does an anterior transection, the same pupillary responses occur as in sleep. When he does a posterior mesencephalic section, then the fore brain end of the animal goes into the 'sleep' state while the caudal part of the neuraxis does not show the rhythmical changes of the sleep-wakefulness rhythm.

JASPER: Does Dr. Rioch mean that an animal with a collicular-namillary transection gets up and walks around?

RIOCH: Yes.

PENFIELD: But I don't believe they dream....

THE NEUROPHYSIOLOGICAL PROBLEM OF SLEEP

By

FREDERIC BREMER

INTRODUCTION

It is perhaps an excessively anthropocentric interpretation of the succession of periods of waking and sleep, and of the finality of this alternation, which has led us so often to seek the explanation of sleep in an active inhibition of cerebral activities. The hypothesis assumed concrete form in the admission of the existence of a central mechanism responsible for the regulation of the sleep and wakefulness alternation in Mammalia. Anatomo-clinical observations, dating from as long ago as the nineteenth century, indicated that this mechanism was situated in the grey matter of the mesencephalic tegmentum and adjacent subthalamus. The electrical excitation experiments of R. Hess (1929-49), cinematographically recorded and anatomically verified, seemed to provide direct proof of a hypnogenic 'centre' located in this region and inducing sleep by an active inhibitory process.

But in recent years it has become increasingly evident that the neurophysiological problem of sleep is rather that of the mechanism of the waking state. The vigilant activity of the brain can no longer be considered as a necessary aspect of its normal functioning; that is to say as such a natural and obligatory manifestation of this functioning that an active mechanism of inhibition must intervene in order to substitute periodically the sleeping state for the waking state. The necessity has now been shown for a continuous facilitatory dynamogenesis of the cortical and diencephalic neuronal networks in order that wakefulness may be maintained; cerebral vigilance being the condition of critical reactivity of the individual, of the spontaneity of his behaviour and of his complete adaptive and conscious integration.

EXPERIMENTAL EXCITATION AND DESTRUCTION OF THE RETICULAR FORMATION OF THE BRAIN STEM. INTERPRETATION OF THE EFFECTS OF MESENCEPHALIC-TRANSECTION

The conception of the meso-diencephalic sleep regulating apparatus as a mechanism of vigilance, which was proposed from 1890 onwards by Mauthner, obtained its first experimental support in the work of Ranson and his associates (1939) and later in the work of Miller and Spiegel (1940) and Murphy and Gellhorn (1945). Recent striking confirmation, as we know, has been provided by the work of Magoun, Moruzzi and their associates (1949, 1950, 1952) in their experiments of stimulation (Fig. 1, B) and destruction of the bulbo-mesencephalic reticular formation.

These investigations which are closely linked with those of Morison and Dempsey (1942, 1943), Jasper and his associates (1947, 1949, 1953), showing the existence in the median thalamus of a nuclear apparatus of diffuse excitation of the neo-cortex, have completed the explanation of the fact, demonstrated by the author (1935, 1936, 1937), that a mesencephalic transection, carried out behind the nuclei of the third nerve, thus respecting their cephalic connections, determines immediately and permanently a functional condition of the diencephalon and of the cortex that has the electro-corticographic and behavioural (ocular) characteristics of deep sleep. When the plane of the mesencephalic transection lies in front of the third nerve nuclei the same electro-corticographic and ocular syndromes are observed. But the last one, notably the extreme myosis, has no more the same significance for the problem of sleep. It reveals simply the interruption of the corticifugal and diencephalofugal oculomotor fibres and the liberation of the tonic activity of the Edinger-Wesphal nucleus from the continuous inhibition exerted on it by the impulses transmitted by these descending fibres.

The experiments by Magoun and his associates on the brain stem reticular formation have led them to the conclusion that the interruption of the classical sensory (lemniscal) ascending channels probably plays only a subsidiary part in determining the profound modification in cerebral functioning of the hypnic type following mesencephalic transection. But the demonstration that the phenomenon results from the blocking of impulses issued from

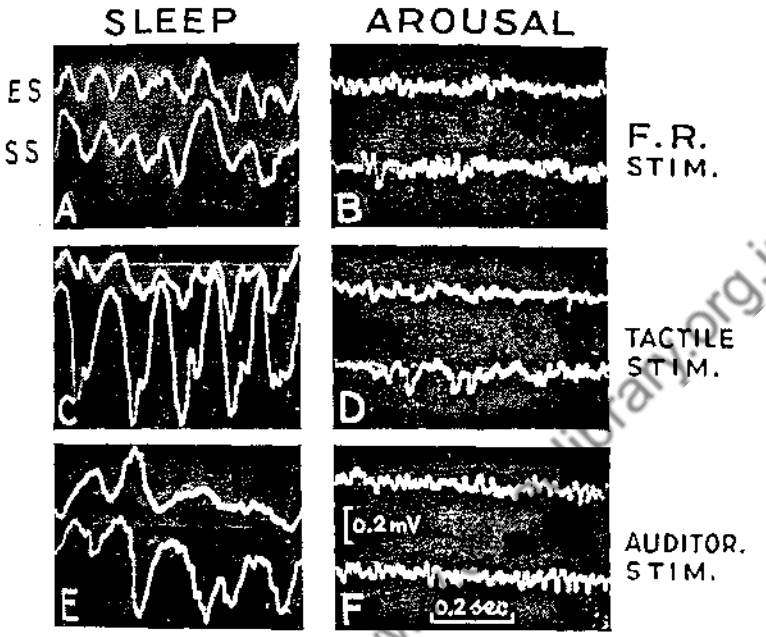


FIG. 1

Identity of electrocorticographic aspect of arousals produced by the electrical stimulation of the reticular formation and by sensory stimulations.

Cat; *encéphale isolé* preparation; monopolar leads on the middle ectosylvian and suprasylvian gyri; tracings reproduced in the order of their recording.

A, C, E: spontaneous sleep: B, arousal by a brief electrical stimulation of the mesencephalic tegmentum, ended two seconds before the recording; D and F: arousal respectively by a tactile stimulation (on the nose) and by a voice call (Bremer and Terzuolo, 1953).

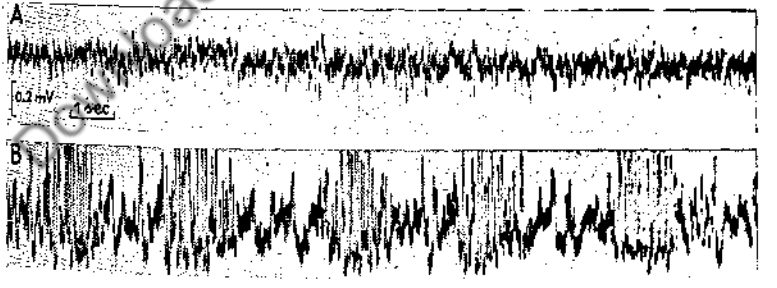


FIG. 2

Contrasting electrocorticographic features of the awake *encéphale isolé* (section at C_1) and the *cerveau isolé* (mesencephalic transection).

A, fully awake *encéphale isolé*.

B, *cerveau isolé* tracing showing the typical bursting and the slow waves between the spindles (Bremer, 1937).

the reticular formation has not invalidated the fundamental notion that a sleep-like functional depression of the telencephalon and diencephalon is linked with the suppression of the continuous flood of ascending dynamogenic impulses which, by maintaining a state of subliminal excitation of their networks, is the condition of the waking state. Besides, the tonic functioning of the reticular formation is probably inseparable from the stimulating action exerted on its cells by the impulses which are transmitted to it by collaterals of the sensory channels or by special fibres (Starzl *et al.*, 1951b). It may even mediate responses of the association areas of the cortex to single volleys of sensory impulse (French, Verzeano *et al.*; 1953a).

However, mesencephalic transection interrupts ascendant connections only of one part of the column of reticular grey matter extending from the bulb to the hypothalamus and subthalamus. It must be explained why the rostral portion of the reticular formation remaining in connection with the diencephalon and the cerebral cortex is not sufficient to maintain their state of vigilant dynamogenesis. For although it is true that experimental olfactory excitations can transitorily rouse the *cerveau isolé* (Moruzzi, 1952b), these same excitations apparently do not suffice, any more than do visual stimulations, to maintain the waking state. We may therefore describe the sleeping condition of the *cerveau isolé* as permanent. The monotony of its electrocorticographic aspect is striking, with its characteristic succession of bursts of alpha or slower waves separated by regular pauses (Fig. 2, B). The explanation of the hypnogenic efficacy of mesencephalic transection must probably be sought in the fact that the caudal part of the reticular formation which is disconnected from the telencephalon and the diencephalon, possesses, by reason of the richness and variety of its afferent connections, the greatest functional importance. In this multisynaptic neuronal system, the tonic activity of the proximal parts apparently depends upon that of the distal segment.

The conception of sleep as the consequence of a fall in reflex tonus of the diencephalon and the telencephalon, and thus of a deafferentation in the wide sense of the term, found support in the observation of the depression, much deeper than that of sleep but qualitatively – electro-corticographically – very similar, deter-

mined, for any cortical area, by the section of its fibres of projection in the corona radiata (Bremer, 1938a; Kristiansen and Courtois, 1949; Henry and Scoville, 1953). And the effect of cerebral relaxation brought about by closing the eyes, which is revealed by the regularization of the EEG of the awakened subject (Berger, 1929), may also be attributed to the fall of tonus of the thalamocortical neuronal networks resulting from the suppression of the particularly powerful activating factor represented, as shown by Adrian and Matthews (1934), by the visual perception of forms (see also Adrian, 1947). This necessity of visual perception for the maintenance of a state of complete electro-encephalographic activation introduces a psycho-physiological notion. It stresses the complexity of mechanisms of the waking-state and leads us to suspect the participation of the cortical network in these mechanisms.

THE ROLE OF THE CEREBRAL CORTEX IN THE PROCESS OF AROUSAL

An exclusively reticular theory of sleep regulation does not explain the facts of common observation which indicate the intervention of the cerebral cortex in the determination of its own awakening. It is improbable that the immense agglomeration of nerve cells, which in Mammalia is the almost exclusive depository of associative memory and of the faculty of symbolic abstraction, plays the part, in the waking state, only of a passive beneficiary of a process of activation organized on its behalf in the grey matter of the brain stem. In fact, a series of concordant experiments leaves no doubt of the reality of this active intervention of the cortex in the process of arousal.

1. The reticular formation, which responds by action potentials to volleys of the most varied sensory impulses converging on its cells (Starz *et al.*, 1951b; Bremer and Terzuolo, 1952; French *et al.*, 1952a), reacts in the same way to corticofugal volleys provoked by a single electric shock at any point (apparently) of the neocortex (Bremer and Terzuolo, 1952, 1953a; Livingston *et al.*, 1953), or resulting from convulsive activity of the latter (Niemer and Castellanos, 1950; Jasper *et al.*, 1952).

2. Sensory impulses and corticofugal impulses of various origins which attain the reticular formation may summate on the

same cells of the latter, as is shown by interference (occlusion) experiments between two heterogeneous sensory volleys, between a corticifugal and a sensory volley (Fig. 3) and between two heterogenous corticifugal volleys (Bremer and Terzuolo, 1952, 1953).

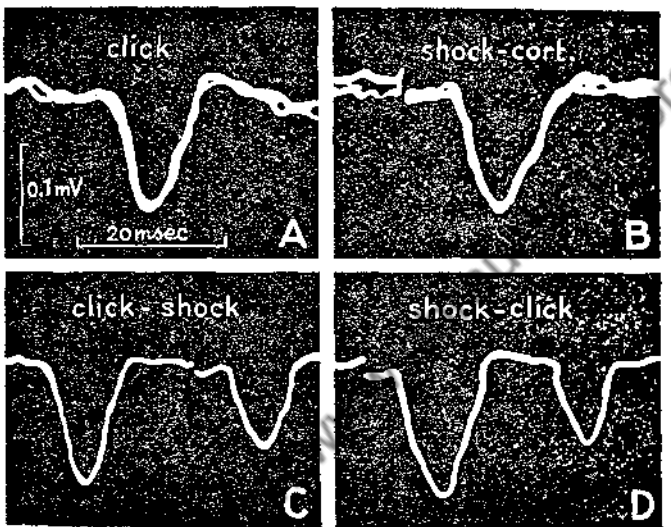


FIG. 3

Convergence and occlusion of sensory and corticifugal impulses in the mesencephalic reticular formation.

Cat; *encéphale isolé*; lead by concentric bipolar electrodes from the mesencephalic tegmentum.

A, response to a click; B, response to a thyratron shock on the anterior suprasylvian gyrus; C, click followed by shock, D, shock followed by click (Bremer and Terzuolo, 1953).

3. Brief faradization of a few seconds duration of non-convulsive intensity, at widely distant areas of the cortex, awakens the sleeping animal (Bremer and Terzuolo, 1953a; Livingston *et al.*, 1953; see also Sloan and Jasper, 1950). Our experiments have been carried out on the *encéphale isolé* preparation of the cat in such a way as to obtain information derived from the aspect and movements of the eyes in addition to recordings of cortical potentials led from the hemisphere opposite to the one stimulated. This arousal by cortical faradization, which is shown in Fig. 4,

could only be attributed to corticofugal discharges penetrating deeply, for it was still observed on the opposite hemisphere after section of the corpus callosum. The intervention of the reticular formation in this awakening is indicated by the activation pattern of its oscillogram (acceleration and desynchronization), parallel to that of the cortex.

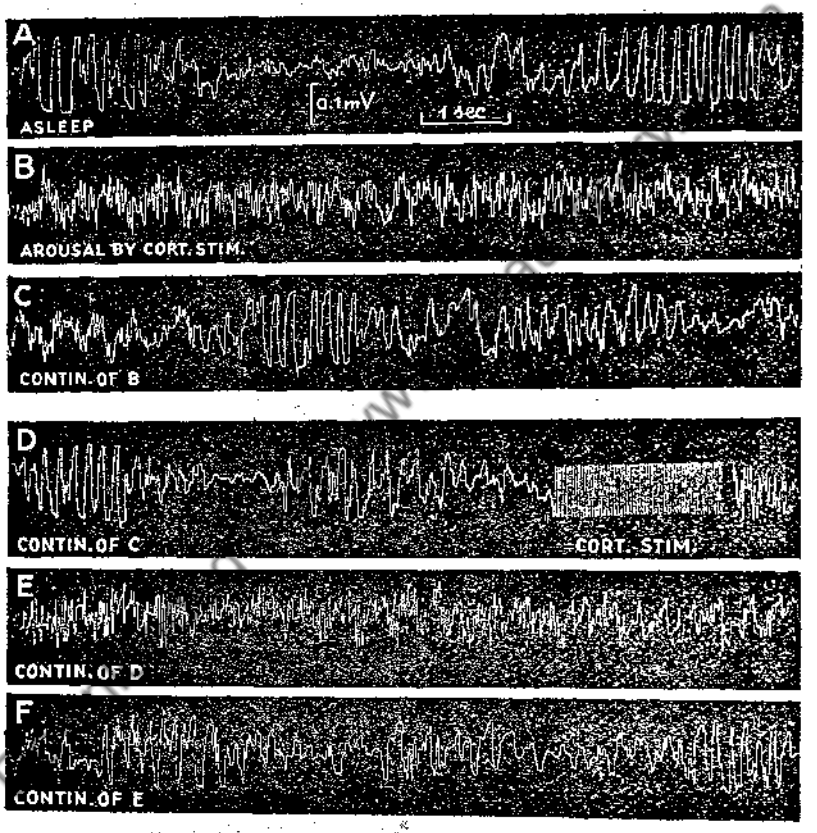


FIG. 4

Arousal by a brief non-convulsive cortical faradization.
Cat, *encéphale isolé*; bipolar lead on left middle ectosylvian gyrus.
A, spontaneous sleep, arousal following a brief faradization of the cortex pyriformis on the right side; C, continuation of B; end of the arousal; D, sleep interrupted by the faradization of the right anterior suprasylvian gyrus (duration of the stimulus indicated by its artefacts); E, continuation of D; F, continuation of E, the brain is again asleep. (Bremer and Terzuolo, 1953).

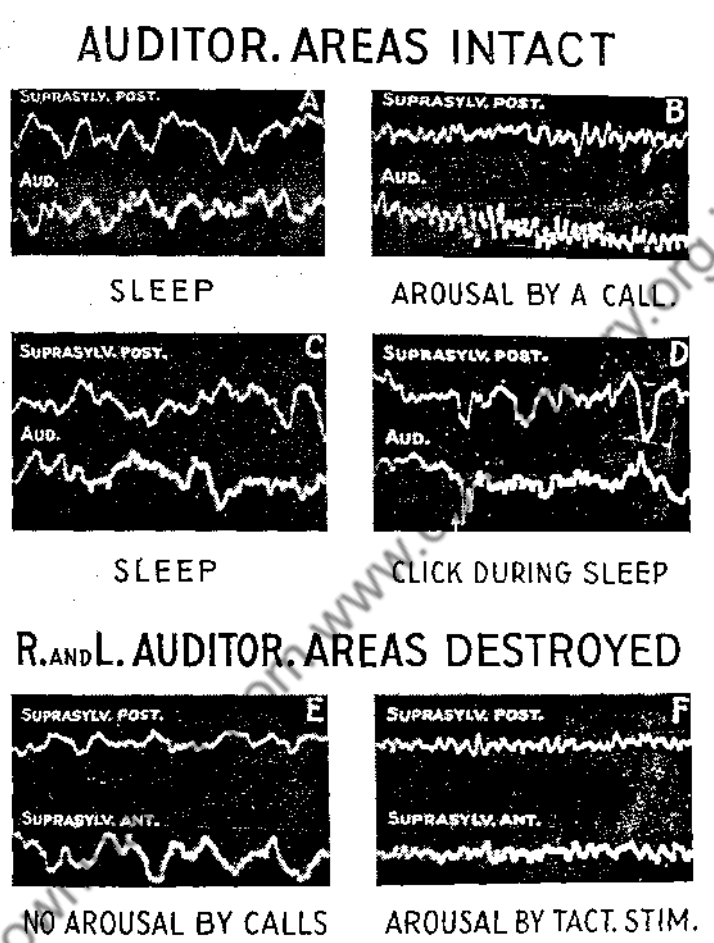


FIG. 5

Abolition of auditory arousal after the destruction of the auditory areas I and II on both sides.

Cat, *encéphale isolé*; leads from the posterior suprasylvian gyrus and middle ectosylvian gyrus (auditory area I), in A, B, C, D; from the posterior and anterior suprasylvian gyri in E and F; tracings reproduced in the order of their recording; A, C, E: spontaneous sleep; B, arousal by a voice call; D, transient arousal of the auditory area by a click; E, absence of the arousal effect of the call after the bilateral destruction of the auditory area; F, persistence of the arousal effect of a tactile palpebral stimulus (Bremer, 1952).

4. As shown by Fig. 5, the arousal of the sleeping brain by meaningful auditory excitations (e.g. by a voice call) is no longer possible following bilateral destruction of auditory areas I and II, whereas cutaneous stimuli remain effective (Bremer, 1951; cf. also Fischgold and Lairy-Bounes, 1952).

The synergic interaction of the reticular formation and of the cortex in the maintenance of the waking state may explain better than does the hypothesis of a central hypnogenic mechanism certain pharmacological data, especially that concerning the difference in the action of various hypnotics (particularly barbiturates) on the intact animal and the decorticated animal (Pick, 1930; Economo, 1929). The reinforcement of their action following extirpation of the telencephalon may be accounted for by the suppression of the continuous dynamogenesis which the latter exercises on the brain stem reticular formation.

Thus, it is as though the reticular formation centralized, amplified and diffused the arousal excitations which are transmitted to it directly by sensory channels and those which reach it after a circuit through the cortical neuronal networks.*

It seems moreover legitimate to suppose that the emission of corticoreticular impulses can have no immediate sensory antecedent. Looked at in this way, the intervention of the cortex in the process of awakening becomes a part of the fundamental problems of voluntary attention, the effort of vigilance, and psychogenetic insomnia.

This collection of experimental data, indicating the utilization of the reticular formation of the brain stem (with its thalamic and subthalamic extensions) in the process of arousal, even when the latter has its origin in the cortex, is the answer to the question, which we are justified in asking concerning the legitimacy of bestowing on this formation – already so rich in functional attributes – a special function of vigilance.

* The hypothesis of a cortico-subcortical interaction in arousal was made by Adrian (1937) many years ago: '. . . The unfamiliar noise wakes the sleeper because the afferent message reaches the cortex and is there judged as important. The cortex signals back to the diencephalon and the rapid spread of activity ensues. The facilitation is therefore between cortex and thalamus as well as between neurone and neurone.' The experimental evidence now at hand demonstrates both the reality and the importance of the mechanism suggested by Adrian 'as a pure speculation'.

MECHANISM OF THE ACTIVATION OF THE CORTEX BY THE RETICULAR-ASCENDING IMPULSES

The exact mechanism by which the reticular impulses exert their arousal effect on the cortical networks represents an interesting, but difficult, problem. The simplest hypotheses assume a continuous subliminal facilitating effect of the unspecific impulses on the operational activities of the brain, including its responses to specific sensory impulses. As one knows it, Dempsey and Morison (1942b) were unable to find an interaction between a specific sensory volley and a thalamo-cortical recruiting volley in the somatic sensory area of the barbitalized cat. However, Jasper and Ajmone-Marsan (1951), studying the unanaesthetized brain (*cerveau isolé* preparation) observed clear evidence of such interaction in the visual area. Particularly interesting is their finding that the temporal coincidence of the two volleys results in a marked facilitation of the sensory cortical response, specially of its surface-negative phase. Recent experiments in the author's laboratory have shown that the manifestations of interaction (in the somatic sensory area of the nembutalized cat), which are not discernible when the responses to the sensory and to the unspecific volley (issued from nucelus ventralis anterior f.i.) are small (cf. Dempsey and Morison), become perceptible when their amplitude is spontaneously great or when it has been increased by a local strychnization. It is as if this condition of amplitude of the response increased the overlapping of the neurone pools activated by the two volleys and the chances of convergence of their impulses on the same cortical units.

These results are thus in agreement with the hypothesis of a subliminal facilitatory effect exerted on the cortical networks by the unspecific impulses. The alpha waves, with the fluctuations of cortical reactivity corresponding to them (Bishop, 1933, 1936; Bartley, 1939, 1941; Bates, 1951; Lindsley, 1952), would be, in this hypothesis, the expression of such continuous dynamogenesis, modulated by the rhythmical properties of thalamic and cortical neurones.

However in the auditory area (and probably in other projection areas as well) the interaction between sensory specific impulses and arousal ones may be marked by a strong reduction in ampli-

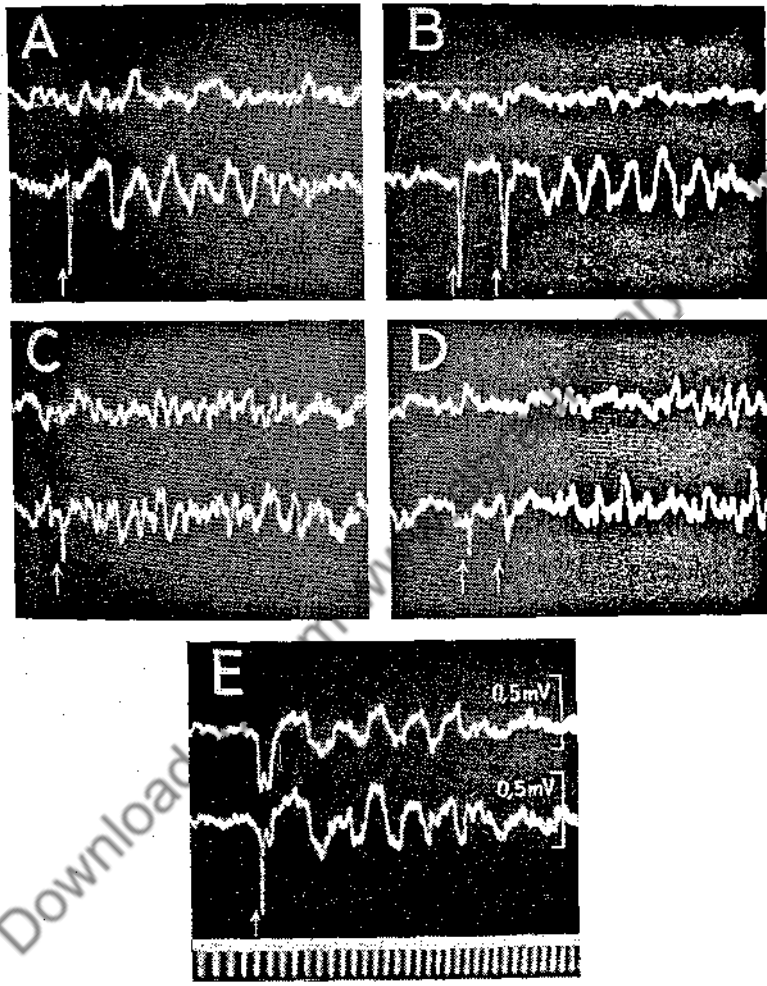


FIG. 6

Reduction of the primary response of the auditory area to a click in arousal.
Cat, *encéphale isolé*; monopolar leads on the middle suprasylvian (top tracing) and the middle ectosylvian gyri in A to D, on two different points of the middle ectosylvian gyrus in E; in A and B, the animal is drowsy; in C and D it has been just awakened by a voice call; in E it slumbers again. Time in 20 milliseconds intervals below. Other explanations in text.

tude of the primary response to a synchronized afferent volley (Fig. 6). It is as if the sensory response of the awakened and excited auditory area was partially occluded by the fast rhythmical activity of the cortical neurones which characterizes arousal. In the experiment whose tracings are reproduced in Fig. 6, the arousal of the brain had followed auditory stimuli (voice calls), but the same masking phenomenon is observed when the awakening results from an electrical stimulation of the brain stem reticular formation. The psycho-physiological implications of this paradoxical reduction of a cortical response in arousal have been discussed by the author elsewhere (Bremer, 1951b, 1953b). The phenomenon illustrates anyhow the complexity of the liaison, at the cortical level, between perception and its electro-physiological correlates.

THE ROLE OF CEREBRAL DYNAMOGENESIS AND FACILITATION NOT INVOLVING THE RETICULAR FORMATION

The fundamental necessity of a brain stem activation for the maintenance of the waking state does not exclude the contribution of cerebral facilitating interactions which do not bring into play this reticular mechanism of awakening. Many experiments suggest that full consciousness requires an incessant cross-fire of intracortical and inter-cortical as well as cortico-thalamic facilitating interactions. In this connection we may mention the following experimental data obtained in the cat and monkey: the lowering of threshold of the frontal oculo-motor area resulting from the spontaneous activity of the posterior oculo-motor area (Claes, 1939b); the mutual facilitation of masticatory areas by inter-cortical (callosal) impulses (Moruzzi, 1939); the visual inattention, simulating an hemianopsia, and the motor akinesia, which follows in the monkey (Kennard and Ectors, 1938) and in the cat (Morin, Donnet *et al.*, 1951) the destruction of the frontal oculo-motor area (area 8 of Brodman); the non-convulsive activation of the cortex which irradiates eccentrically from an area of faradic or strychnic excitation (Adrian, 1936; Moruzzi, 1939; Noël, 1941); the facilitation of the sensory responses of an auditory area by means of provoked and spontaneous discharges issued from the contralateral homologous area and transmitted by

the corpus callosum (Bremer, 1952, 1953a); the facilitation of the same auditory responses which is associated with rhythmic discharges of the thalamic relay nucleus (Chang, 1950, 1951; Bremer and Bonnet, 1950); the functional depression of the thalamic nuclei of diffuse cortical projection following a homolateral decortication (Morison *et al.*, 1943, Magoun, 1950); the psychomotor akinesia of Parkinson's syndrome (Terzuolo and Stoupel, 1952).

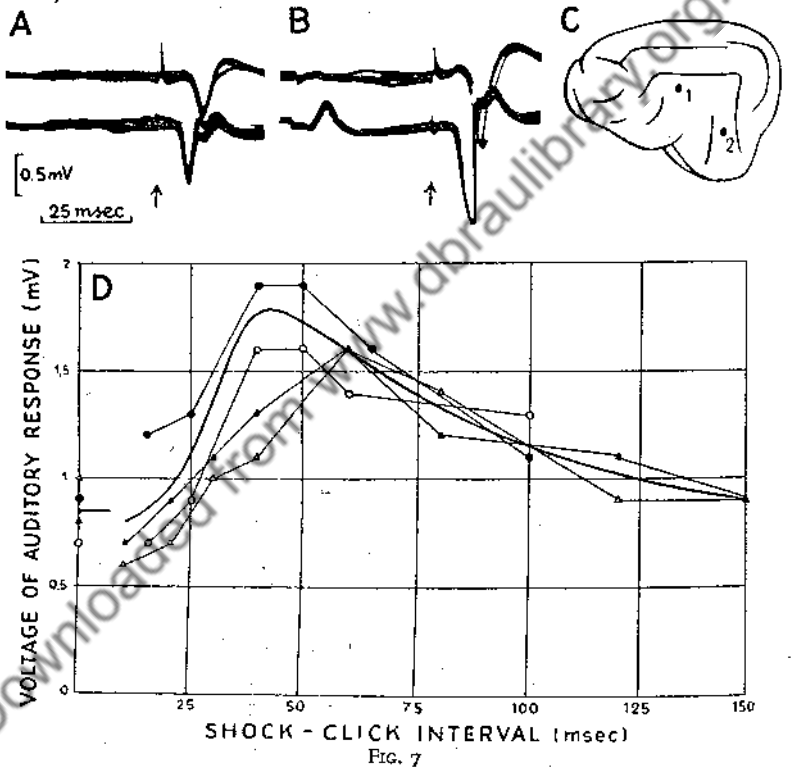


FIG. 7

Inter-cortical (callosal) facilitation of a sensory response.
Cat, *encéphale isolé*; monopolar leads on the lower part of the posterior ectosylvian gyrus (Ades's secondary auditory area) and on the primary auditory area (lower tracing); superposition of sweeps eliminating chance variations. A, response to a click; B, facilitation of the same response by the precession of a callosal volley shock applied on the contralateral auditory area I, symetrically to point 1 on the figurine C; D, curve of facilitation drawn from all records of the experiment. Notice that, although the secondary area does not show a direct response to the callosal volley (as it could be expected from the homotypic distribution of callosal fibres), its response to the click participates to the facilitation. The last one disappeared entirely after the section of corpus callosum (Bremer, 1953).

Among these various facilitation phenomena those which can be demonstrated by the combination, at a definite time-interval, of a callosal volley and a sensory acoustic volley reaching the same patch of the primary acoustic area (Fig. 7) present a particular interest. They may perhaps illustrate the general mode of action, and also the functional significance, of dynamogenic afferents. One of the characteristics of the callosal facilitatory effect is its habitual predominance on the surface-negative phase of the cortical sensory response. As already mentioned, a similar electivity has been observed by Jasper and Ajmone-Marsan (1952) for the interaction of an unspecific thalamo-cortical volley and a sensory one in the visual area. It may perhaps be correlated with the mode of termination of the callosal and thalamo-cortical unspecific afferents in the superficial layers of the cortex, among the dendritic arborization of the pyramidal cells (Lorente de Nó, 1943; Chang, 1953a). Another feature of callosal facilitation is the long duration of the effect – it may exceed 150 msec.– and its sensitivity to barbituric narcosis. The existence of a continuous (tonic) callosal facilitation is indicated by the fact that in a non-narcotized animal the paralysis of the acoustic area on one side (following the local application of a depressant drug) may result in a significant reduction of the sensory response of the other side.

In the class of extended cortical activations not transmitted by the reticular formation, one could perhaps also mention the excitation of a vast cortical area behind the auditory area which is produced by rotary stimulation of the homolateral vestibular labyrinth (Gerebtzoff, 1940; Gernandt, 1950); and also the lowering of the threshold of excitation and EEG activation of the motor cortex resulting from faradic stimulation of the neo-cerebellum (Rossi, 1913; Walker, 1938), and which is apparently distinguished by this spatial limitation, from the diffuse activation provoked by anodal polarization of the anterior lobe (Mollica *et al.*, 1953).

The picture of the functioning of the brain in its fully waking state is beautifully evoked by Sherrington (1946) when he describes the glowing of the awakening brain as it would appear if the impulses running in all directions could be made luminous.

It is in this functional solidarity, in which all the cerebral neuronal agglomerations are closely associated, that we must doubtless seek the explanation of the ubiquity and of the funda-

mental similitude of the oscillographic manifestations of the waking and sleeping states in the whole diencephalon and telencephalon (Starz *et al.*, 1951b; Bremer, 1951; Hodes *et al.*, 1952; Hess *et al.*, 1953; Bernhaut *et al.*, 1953). Sleep, like peace, is indivisible.

THE PROCESS OF FALLING ASLEEP

This dynamic solidarity enables us to explain the process of normal falling asleep without having recourse to the hypothesis of an hypnogenic mechanism. A slackening of activity of any region of the brain must result in a lowering of excitatory state in areas or nuclei – including the reticular formation – with which the region in question has facilitating relationships, and so the whole of the synergic structures are gradually affected. Doubtless, the functional depression of the reticular formation, on account of the latter's central position in the homeostatic mechanism of arousal, plays a preponderant, if not always an initial, role in this process of cumulative 'de-facilitation'. And it is moreover plausible to suppose that the barbiturates owe their hypnogenic action to the particular depressive effect which they exercise on the tonic activity of the reticular apparatus. This selective depression, which has its counterpart in the special excitation of the same reticular formation by amphetamine and related drugs (Bradley and Elkes, 1953), does not necessarily imply a differential localization of these narcotics in the brain. It can be explained, without reference to this contested chemical affinity for the cells of the reticular formation, by the synaptic complexity of the latter and by the intensity of its tonic functioning, making it more vulnerable to narcosis by barbiturates. However this may be, the hypothesis of the elective sensitivity of the reticular formation can be based on experiments on barbiturate narcosis in which the resistance of its sensory response has been compared to that of an area of cortical projection (French *et al.*, 1952b; Arduini, 1953).

But although the barbiturates do not reduce – and even eventually do intensify – the primary response of a specific projection area to a single sensory volley, they considerably weaken, to the extent of suppressing it completely, the rapid after-discharge of this area (seen in Fig. 5, D), which is the manifestation of *local* and transient awakening following the primary response. They

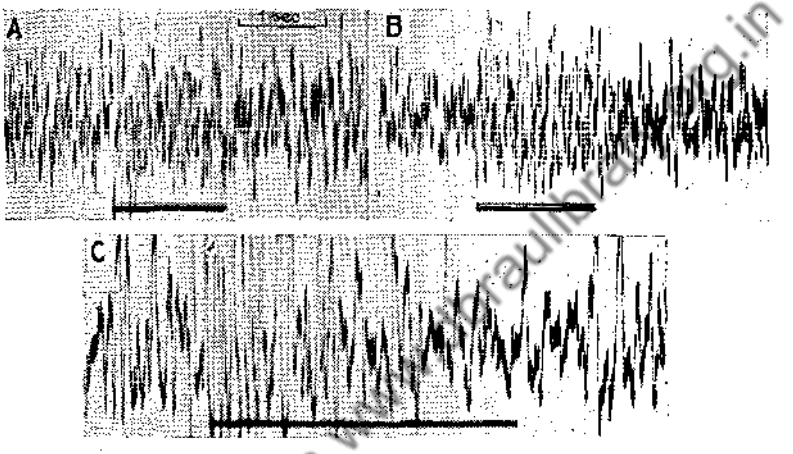


FIG. 8

Abolition of the response of the auditory area I to a whistle stimulus in barbituric narcosis. Persistence of the same response in ether narcosis.
Cat, *encéphale isolé*; bipolar lead on auditory area I; A, typical response to the whistle before any narcosis; B, persistence of the response during an ether narcosis which had abolished the corneal reflexe and markedly reduced the spontaneous cortical activity; C, its disappearance, except for an initial burst of alpha waves, following the i-v injection of 2 cg/Kg. *Dial*, made after the dissipation of the ether narcosis (Bremer, 1937).

affect in the same way, the reaction of the sensory area to a continuous stimulation (Bremer, 1936b, 1937). As Fig. 8, C shows, a barbituric narcosis of moderate depth abolishes completely (except for an initial burst of alpha loke waves) the response of the acoustic area to the whistle stimulus. The same response is much more resistant to ether narcosis (Fig. 8, B).

The process of de-activation *en avalanche* described above should normally be initiated by a neuronal fatigue (at cortical, diencephalic or reticular levels), and favoured (Ebbecke, 1926; Kleitman, 1939) by any reduction in the continuous exteroceptive and proprioceptive sensory afflux, whose importance for the cortical reactivity has been clearly demonstrated by Claes (1939a) and by Chang (1952) in the case of the visual area. In its extreme form, this synaptic fatigue may be of the nature of an intoxication (Piéron and Legendre, see Piéron, 1913, 1927). An important condition for wakefulness, particularly obvious in the sleep of hibernating Mammalia, is represented by the interaction of the endocrines and the thermoregulatory nervous mechanisms (see Kayser, 1953).

This spontaneous evolution of the phenomena does not exclude the possibility of the intervention of a precipitating mechanism of active inhibition. The plausibility of this hypothesis is admitted. It is founded upon the well-known experiments of W. R. Hess (1929-49) in the cat, later supported by observation of Nauta (1946) and Jorda (1948) in the rat (see also R. Hess *et al.*, 1953). The difficulties which it raises, have been discussed by us elsewhere (Bremer, 1951). We mention here merely that these difficulties and objections are of various kinds: the legitimacy of attributing the effects of hypnogenic electrical stimulation of the subthalamus or thalamus to the excitatory action of the currents employed, rather than to the electronic blockade of ascending arousal fibres, consequent on the polarity, duration, slope and voltage of the pulses (Marinesco *et al.*, 1929; Ranson and Magoun, 1939; Harrison, 1940b; see also Hunter and Jasper, 1949); the difficulty of a theory of hypnogenic inhibition resulting from the uncertainties which still exist concerning physiological inhibitory phenomena affecting directly cortical activities (the example of the Pavlovian inhibitions and of the suppressor bands is significant); the validity of oscillographic and behavioural criteria of

the 'sleeping states' provoked by electrical stimulation of subcortical structures (e.g. the caudate nucleus, Heath and Hodes, 1952; R. Hess *et al.*, 1953). It seems thus that the question must remain open until these difficulties will be cleared up.

GENERAL CONCLUSIONS

The waking state is, in Mammalia, the expression of a dynamic equilibrium between the activation of cerebral neuronal networks maintained by the incessant impact of innumerable ascendant and associative impulses, and the cumulative functional depression resulting from the very continuity of this state of excitation. A special mechanism, located in the reticular formation of the brain stem, integrates and multiplies the arousal ascendant impulses which, by sustaining the diencephalic and cortical excitatory state, are the immediate condition of waking activity. But the cerebral cortex participates actively in its own arousal and in the maintenance of its waking state by the corticofugal impulses which it sends to the brain stem reticular formation.

The physiological process of falling asleep may be explained, without necessary recourse to the hypothesis of a hypnogenic centre, by the cumulative de-activation (de-facilitation) of the encephalic neuronal networks resulting from synaptic fatigue and favoured by a reduction in the exteroceptive and proprioceptive sensory afflux. In this process of neuronal de-activation which culminates in sleep, the functional slackening of the brain stem reticular formation, by reason of the latter's central situation in the nervous apparatus of arousal, plays without doubt an essential role. The hypothesis of a hypnogenic centre cooperating with the waking apparatus in the regulation of sleep is a logical assumption, but one whose adoption still raises theoretical and technical difficulties.

GROUP DISCUSSION

MAGOUN: Some of the data presented by Dr. Bremer throw light on the question of the relations of the mesencephalic and the more caudal portion of the reticular areas to the diffusely projecting nuclei of the thalamus. We have discussed earlier the extent to which the diffuse

projecting nuclei of the thalamus represent the cephalic relay to the cortex for these more caudal structures. In Dr. Bremer's *cerveau isolé*, the animal is considered asleep, thus suggesting that the activity of the more caudal portion is essential for wakefulness and that the cephalic portion is unable by itself to maintain wakefulness. Therefore, there would appear to be a functional difference between these two portions. Dr. Bremer also showed that in an *encéphale isolé* asleep, the animal may be aroused by cortical stimulation. He suggested that this effect may be obtained through a pathway leading from cortex to subcortical structures and thence back to the cortex. I would like to know if cortical stimulation can induce EEG arousal in a *cerveau isolé*. I would also like to know for how long the *cerveau isolé* can be kept and if sleep is maintained indefinitely.

BREMER: It looks as if the cephalic portion of the reticular formation depends for its functioning on the lower portion which receives and relays the enormous contingent of afferent impulses transmitted to it by the spinal roots and by the bulbar cranial nerves.

I have no data as to what corticifugal impulses may do in *cerveau isolé* preparations, but I don't think that even maximal discharges of such impulses could overcome the deep fall of diencephalic and cortical tonus resulting from the mesencephalic transection.

Cerveau isolé preparations have been observed during three days without any change in their sleep behaviour (ocular and electrocorticographic), which suggest that this state of sleep would be maintained indefinitely.

JASPER: Dr. Magoun appears to oversimplify the reticular formation. There are alternatives between the thalamic recruiting systems and these portions of the reticular system below the collicular level. Many structures in the tegmental region, and hypothalamus, have been shown to have no part in the recruiting response but to be most capable of producing arousal, as well as other responses.

LIVINGSTON: Working on monkeys, Dr. French, Dr. Hernandez-Péon and I have confirmed Dr. Bremer's observations on cats, namely that cortical stimulation may arouse the animal. Yet, this observation of ours was infrequent. This may be due to the fact that we were using a curarized animal and not an *encephale isolé* preparation, or it may be a case of species difference. The projection of cortical cells to the reticular formation appears to be a property not of the whole cortex but of several separate islands of cortex in the monkey.

BREMER: I am glad that Dr. Livingston and his associates have been able to confirm on the monkey our experiments of arousal by cortical stimulation.

An animal under curare is perhaps not the optimal preparation to

study the phenomenon. The immobilization by curare does not result apparently in the labile functional state of the encephalic centres allowing the easy transition from sleep to a state of peaceful wakefulness, a transition which can be observed in the cat, after a high spinal section. Besides, curare has undoubtedly direct effect on neurones. This action may even be strychnine-like.

Our own data are not sufficiently numerous to allow an opinion concerning a possible specificity of the cortical areas the faradization of which can result in a general awakening of the brain in the cat.

JASPER: Dr. Marsan and I found that very light nembutal anaesthesia made a good preparation to study the awakening of the animal by cortical stimulation. We agree with Dr. Livingston that it is not all cortical areas which behave in this manner.

PENFIELD: It is interesting to inquire as to whether true arousal from sleep occurs in association with the arousal response. In human beings under local anaesthesia during craniotomies the patient often falls asleep spontaneously, yet, stimulation of most of the cortical areas will fail to arouse a subject, such is the case for the frontal lobe, the parietal lobe, the temporal lobe (if no hallucination is produced). It is only when specific sensory areas are stimulated that the patient can be aware of the stimulation. I would like to know if Dr. Bremer has stimulated any cortical areas other than auditory or visual.

BREMER: The whole cortex has not been investigated from that point of view. Yet, stimulation of the suprasylvian gyrus, which is not anything like a sensory area, will produce arousal. The best cortical area to produce arousal has appeared to us to be the frontal pole.

The apparent discrepancy between the observations on the animal and Dr. Penfield's observations on man, may depend (*a*) on the fact that the arousal effect, in the cat at least, requires an intensity of current which might cause convulsions in the epileptic human cortex, and (*b*) on the fact that a large surface, if related to the dimensions of the animal's brain, is embraced by the bipolar electrodes.

WALTER: Bradley (1953) has been working in Birmingham with cats with implanted electrodes. The animals have been kept for up to two years. Phlegmatic cats were chosen deliberately. He has studied particularly the relation between the EEG and thalamic activity and the behaviour of the animals during waking and sleeping states. He compared the effects of sensory arousal – auditory and visual – with those of pharmacological arousal as induced by amphetamine and lysergic acid, etc. The effects of amphetamine are easily seen and recorded and closely resemble the arousal induced by sensory stimulation. Smaller doses will lower the threshold of arousal by sensory stimulation and this same effect of amphetamine is seen in the *en-*

céphale isolé preparation. But with the *cerveau isolé* it is no longer true, that is neither amphetamine nor sensory stimulation will arouse the animal. The same author found it very difficult to arouse his preparations by cortical or cerebral stimulation unless the intensity of the stimulus was such as to produce movement. The same was true for the *encéphale isolé* preparation. But in the *cerveau isolé* he never got arousal.

KUBIE: Was Bradley sure that amphetamine got into the tissue of the *cerveau isolé*?

WALTER: The drug was injected by various ways, among others, intraventricularly and by intra-carotid injection.

ADRIAN: Dr. Magoun and Dr. Bremer have shown that if a click stimulus follows another type of sensory stimulus, after a certain critical interval, its electrical sign will be occluded in the reticular formation. Yet I would expect a conscious man thus stimulated to be aware of both stimuli. Does that mean that whether the signal excites the reticular formation or not this has no importance in relation to his awareness of both stimuli? Does that mean that the participation of the reticular formation is not essential for the signal to get into the mind?

BREMER: An occluded stimulus at the level of the reticular formation may not be occluded at higher levels. The reticular formation subserves a function of diffuse, dynamogenic mass effect, which helps the function of other regions of the brain, including those concerned with consciousness. This occlusion seen in the reticular formation is not unique. The same has been observed even at the cortical level, i.e. in auditory area III of Tunturi, where most diverse types of afferents not only converge, but may actually occlude each other.

This suggests a fundamental distinction between areas of the brain subserving an analytical and discrimination function, the sensory and psychosensory areas of the cerebral cortex, and central structures endowed with a tonic activity and a regulatory influence of a wide distribution, in which the sensory information is diluted and lost — e.g. the central core of the brain stem reticular formation, the diffuse thalamic projection system, auditory area III, and also the cerebellar cortex.

MORUZZI: With reference to Bradley's experiments, which have just been quoted by Dr. Walter, I should like to recall the results recently obtained by Bonvallet, Dell and Hiebel (1953). They were able to elicit EEG arousal with small doses of intravenous adrenaline (5 to 10 μg./Kg.) following pontine transection, but no result was obtained with the same injection following intercollicular transection. They have made many other experiments suggesting that the arousal elicited

by strong nociceptive stimulations is due to both neural and humoral (adrenaline and sympathin) activation of the reticular system.

As far as the mechanism of myosis in sleep is concerned, one can wonder about its nature. It could be an increase in the excitability of the Edinger-Westphal neurones. The following experiment by Rossi (1953) seems relevant: The acute or chronic section of both optic nerves leads to blindness and mydriasis. This is replaced by strong myosis following a lower midbrain transection (*cerveau isolé*). The same effect is elicited by barbiturates. Therefore, the myosis is not due to retinal impulses; it is either due to automatic activity of the Edinger-Westphal neurones or to excitation coming from somewhere else. Furthermore in a *cerveau isolé* preparation one cannot get mydriasis, i.e. behavioural arousal, with an olfactory stimulus, whereas the electrical picture of arousal may be elicited. Hence a dissociation between behavioural and EEG sleep can be obtained (Arduini and Moruzzi, 1953).

THE ACTION OF ANAESTHETICS ON THE NERVOUS SYSTEM

WITH SPECIAL REFERENCE TO THE BRAIN STEM RETICULAR SYSTEM*

By

MARY A. B. BRAZIER

Many excellent reviews[1] dealing with this subject have been published, but no comprehensive appraisal has been made since the revolutionary discovery that the specific afferent systems in the brain are not the only sensory route for inflow to the cortex. Within the last decade the existence of an ascending system from the reticular formation of the brain stem has been established beyond doubt. That this new knowledge needs to be incorporated in any modern theories of general anaesthesia is obvious, and hence no apology is offered for giving so much space in this paper to a review of its development during the last few years.

Before proceeding to an examination of these neurophysiological data there are some other facets of the action of anaesthetics that it might be well to review quite briefly.

Among the aspects of anaesthetics which should have some attention are, besides their pharmacology, their effect on cellular metabolism; on the propagation of the nerve impulse in axons; on isolated neuronal systems; and on the behaviour of the organism as a whole. It is clearly impossible to cover all the known anaesthetics and therefore most attention will be given to the barbiturates, bringing the others in as they illustrate contrasting or comparative effects.

Barbiturates have been chosen because so much of the animal work in neurophysiology has been done on animals under dial or nembutal and because so much electrocorticographic work has been done on patients under pentothal. Another reason is that

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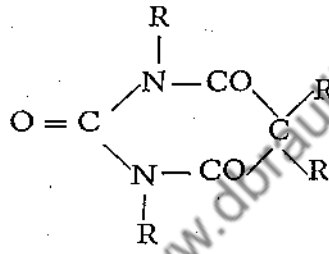
[1] Butler, 1950; Gerard, 1947; Henderson, 1930; Mécanisme de la Narcose, Paris, 1951; Toman and Davis, 1949; Winterstein, 1926.

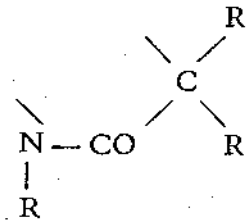
barbiturates are a common sedative and many observations on sleep induced by such drugs as seconal and nembutal have been made. If another reason for giving star billing to the barbiturates is needed, one may add that they are frequently used on the one hand as anti-convulsants in epilepsy, and on the other as activators of EEG abnormalities in temporal lobe epilepsy.

THE CHEMICAL STRUCTURE OF BARBITURATE DERIVATIVES

The barbiturate linkage is derived from urea by combination with malonic acid. The formula is:



with the structure of each radical, R, varying with the specific derivative. It may be remarked in passing that a part of this structure is common to several anti-convulsants and hence by inference is suspected by some of being the structure responsible for this specific action on the nervous system. The part of the structure referred to is:



This linkage is found to be common to the barbiturates, dilantin, tridione and phenurone. It does not necessarily follow that the mechanism of action by these drugs on nervous tissue is the same, and of course there are many substances with a depressant action on the nervous system from which this linkage is absent. There is no specific molecular group common to all anaesthetics. For this

reason no further description of chemical structure will be given here, although some chemical reactions will be discussed later in this paper. Nor will space be given to a survey of the physical properties of anaesthetics (e.g. lipid solubility,[1] water solubility (Collander, 1947), molecular weight (Beecher, 1940), thermodynamic properties (Brink and Posternak, 1948), etc.) since conflicting reports as to the relationship between physical properties and anaesthetic potency can be found in the literature. References to the classic papers on these hypotheses can be found in the bibliography listed here. To this author the old controversy as to whether the action of anaesthetics is a 'chemical' one or a 'physical' one has very largely lost its meaning in the light of modern science where physics and chemistry merge.

ACTION OF ANAESTHETICS ON CELL METABOLISM

In 1912 Verworn suggested that anaesthesia was in fact a form of asphyxia and that narcotics exerted their influence by interfering with cell oxidations. A very great deal of work along these lines has since been carried out *in vitro*, references to which will be found in the bibliography.[2]

This concept began to be more meaningful when it was realized that the action of the narcotic was probably on an enzyme step in the oxidation cycle, for this would explain the conflicting reports on brain metabolism. The major part of modern work along these lines stems from the studies of Quastel[3] on the oxygen consumption of brain slices and chopped brain tissue *in vitro*.

Restricting this discussion, for reasons of space, to the action of the barbiturates, it may be stated in summary that Quastel and his associates have been able to demonstrate that these narcotics inhibit the oxidation by brain tissue *in vitro* when the available substrate is glucose, lactate or pyruvate, but not when it is succinate. (This differential effect is, in fact, not restricted to the

[1] Behnke and Yarbrough, 1939; Lawrence *et al.*, 1946; Meyer, 1899; Meyer and Gottlieb-Billroth, 1920; Meyer and Hemmi, 1935; Meyer and Hopff, 1923.

[2] Field, 1947; Fisher, 1942; Fisher and Stern, 1942; Fuhrman and Field, 1943; Fuhrman and Field, 1948; Fuhrman *et al.*, 1941; Keilin, 1925; McElroy, 1947; Warburg, 1912; Warburg and Negelein, 1921; Zorn *et al.*, 1939.

[3] Johnson and Quastel, 1933; Jowett and Quastel, 1937; Michaelis and Quastel, 1941; Quastel, 1952; Quastel, 1939; Quastel and Wheatley, 1932a, b; Quastel and Wheatley, 1934.

barbiturates, for scopolamine, chlorotone and urethane also spare succinate metabolism.[1])

By process of exclusion the enzyme step in the oxidation chain most commonly suspected of being the vulnerable link is flavoprotein (Grieg, 1946a, b; Michaelis and Quastel, 1941) and it is thought that inactivation of this substance by a narcotic inhibits the interaction between dehydrogenase and cytochrome b. Succinate oxidation does not involve this step and hence such an hypothesis would explain the immunity of succinate to narcotic action (Quastel and Wheatley, 1932a).

Whether information of this kind about brain tissue respiration *in vitro* can be carried over directly into studies of general anaesthesia can be questioned. Several attempts have been made to do so, and conflicting reports have been published. Soskin and Taubenhaus suggested in 1943 that, by argument from Quastel's work succinate might be a useful antidote for barbiturate poisoning since it would supply the brain with a substrate whose oxidation would be impervious to the drug. They tested this hypothesis by studying in rats and dogs the length of recovery time from amytal and nembutal, and reported that they could shorten this recovery time in rats, but not dogs, by giving succinate. They also found it effective in a case of barbiturate poisoning in man. Attempts by others to confirm these findings have mostly failed (Corson *et al.*, 1945; Lardy *et al.*, 1944; Shack and Goldbaum, 1949), but some give partial support (Beyer and Latven, 1944; De Boer, 1946; Pinschmidt *et al.*, 1945). Paradoxical results with glucose were also found by some workers (Lamson *et al.*, 1950).

Enthusiastic reports on the ability of succinate to cut short recovery time from barbiturate anaesthesia in man have come from Barrett (1947, 1948), but as he used mostly clinical surgical cases no man in the series could be used as his own control. Conflicting reports have come from others (Zuckerbrod and Graef, 1950). In our experience variation in response to barbiturates from one individual to another is too great to permit the use of one person as the control for another.

In our laboratory we tested Soskin's hypothesis in man using

[1] Fuhrman and Field, 1943; Michaelis and Quastel, 1941; Quastel and Wheatley, 1932a; Quastel and Wheatley, 1934.

pentothal anaesthesia (Tucci *et al.*, 1949), and at first we thought we too had found a similar result, but were troubled by variations. In the course of making several control tests on the same subject with pentothal alone (before adding succinate) we found the probable explanation of the conflicting results. The mere repetition of the same dose of pentothal given to an individual in the same amounts and at the same rates of injection at intervals of a few days revealed a developing tolerance to the drug, evidenced in a reduction of the length of time before recovery. Recovery was assessed both clinically and electroencephalographically. Our conclusion is that some acclimatization to pentothal can occur, a finding which has clinical meaning in surgical procedures by stages requiring repeated anaesthesia. Some years ago Fulton (Fulton *et al.*, 1930) demonstrated a developing tolerance to dial in cats and some recent experiments have indicated that a similar tolerance to pentothal can be acquired by living mice (Hubbard and Goldbaum, 1949) but not by mouse brain *in vitro* as measured by oxygen consumption (Hubbard and Goldbaum, 1950).

The most recent work of Johnson and Quastel (1933) on the inhibition by narcotics of the oxidative synthesis of adenosine-triphosphate must await evaluation for the over-all problem of general anaesthesia until the controversy about the role of acetylcholine has been satisfactorily resolved. That the inhibition of respiration caused *in vitro* by narcotics has different characteristics from that observed *in vivo* has been stressed by Buchel and McIlwain (1950) in their studies of phosphate metabolism of the brain.

It would seem unjustifiable in the present state of our knowledge to make direct application of data from studies of tissue respiration of minced brain to the brain in living man.

THE EFFECT OF ANAESTHETICS ON THE RESPIRATION OF THE BRAIN IN LIVING MAN

Until recent years attempts to measure the respiration of the brain *in situ* had been centred around determinations of arteriovenous oxygen differences and calculations of cerebral blood flow. A great many first-rate studies (Himwich *et al.*, 1947) have

employed this method yet none could surmount the inherent physiological reasons for doubt as to the validity of such measurements (such as, for example, the assumption of a constant oxygen consumption (Kety, 1952)).

Outstanding in this context has been the work of Himwich (1952) and his associates who established that a decreased cerebral oxygen consumption followed surgical anaesthesia with pentothal. On the assumption that the venous drainage of the cortex and that of the subcortical areas was not evenly distributed between the two internal jugular veins (an assumption based on anatomical studies by Batson (1944) and by Gibbs (1934)) Himwich expressed the view that the activity of the cortex was depressed more and sooner than that of subcortical areas (Etsten and Himwich, 1946). Techniques developed since then (Kety and Schmidt, 1945, 1948) have shown this assumption of asymmetry of blood content to be unjustified (Wechsler *et al.*, 1951), although the differentiation between cortical and subcortical effects may receive support from other arguments. Himwich's finding of the decreased oxygen consumption at surgical levels of pentothal anaesthesia has been confirmed by Kety but has since been shown to be a secondary and not a primary effect of the anaesthesia (Kety, 1952). That pentothal might directly inhibit nerve function (as distinct from the metabolic effect) was suggested by Himwich (1952).

A great step forward was made when Kety and Schmidt (1945, 1948) developed their nitrous-oxide method for recording cerebral blood flow in man. To summarize their most recent conclusions, their data support the concept that surgical anaesthesia with pentothal suppresses neuronal activity and hence the oxygen demand by the neurones in their inactive state is lowered.

This hypothesis, covering as it does the activity of living neurones, inevitably seems more promising to the neurophysiologist than any hypothesis based on the chemical behaviour of minced tissue.

To the neurophysiologist, and to the electroencephalographer in particular, the postulate that the mechanism of action of anaesthetics on minced brain tissue *in vitro* can necessarily elucidate the effect anaesthetics have on functioning discharging neurones and on their interplay upon each other in the whole brain *in vivo*,

is one with little appeal. Information about interaction cannot be obtained from 'atomized' material. It should perhaps be remarked that the wheel has turned its full cycle and that Lillie's opinion (1923), expressed before the period of most intense work on the oxidation theory of narcosis had been done, may well be repeated today: 'Diminished oxidation is to be regarded rather as a secondary consequence than as a cause of narcosis.'

Kety's work has a further interest for electroencephalographers for we are all familiar with the difference between the electrical characteristics of sedated brains and of anaesthetized brains. The former evince considerable electrical activity, whereas the latter in deep anaesthesia show long periods of electrical silence.

It is interesting that Kety (Kety *et al.*, 1948) finds no measurable alteration in the rate of oxygen consumption by the brain during sedation.

This is perhaps the place to note that neurophysiology has now emerged from the era when the principal frame of reference was based on an energy system. Interest is now focused on the nervous system as a communication system and on the ability of nerve impulses to travel their normal routes. To draw a parallel from the vacuum tube, it is not the energy of the filament current that interests us but the 'message' on the grid.

The next logical step is to examine the effect of anaesthetics on the propagation of the nerve impulse and on its ability to cross synaptic junctions.

ACTION OF ANAESTHETICS ON THE CONDUCTION OF IMPULSES IN NERVE AXONS

The suggestion that anaesthetics produce nerve block by decreasing the irritability of the neurone was made in 1932 by Bishop, who gave evidence that depressants can cause block long before the sources of energy available to the nerve have been exhausted. Barbiturates were not among the agents used by Bishop, but pentobarbital as well as ether was used by Heinbecker and Bartley (1940) in their demonstration that either of these drugs will raise the excitation threshold of frog nerve, as well as lengthening its refractory period and slowing its conduction. In the main barbiturates have been little used in studies of peri-

pheral nerve. The outstanding work by Lorente de Nó (1947) (mostly on frog nerve) has not been with barbiturates either, and one hesitates to attempt an hypothesis suggesting a similar mode of action for all anaesthetics. Lorente de Nó has emphasized that in addition to rendering nerve fibres inexcitable, ether also profoundly affects the electrotonic potential, whereas cocaine has the first effect but not the second. Lorente de Nó assigns the effect of ether to a depolarization of the resting membrane potential (for excitability can be restored by an applied current). The same is true in asphyxia of the nerve (by anoxia), but is not true for cocaine (Bishop, 1932). These findings (i.e. of a difference in action of cocaine and of anoxia) are another ground for doubting that all anaesthetic action can be due to interference with oxidation processes. In the case of ether, even, the nerve can recover its membrane potential in the absence of oxygen and hence its blocking (depolarizing) effect must be by some mechanism other than that of asphyxia.

Barbiturates have been used by Larrabee and Posternak (1952) as blocking agents in a comparative study of the sensitivity of myelinated and unmyelinated nerves, and have been found to have no differential effect on fibre type. This lack of selectivity is shared by other anaesthetics (ether, chloroform, chlorotone). In fact, Larrabee (Larrabee, 1952; Larrabee and Bronk, 1952) from his extensive work with sympathetic neurones concludes that there is no unassailable evidence that anaesthetics exert their effects by modifying metabolism. From his work with chlorotone and azide, Brink (Brink *et al.*, 1952) postulates that a different oxidative pathway is concerned in maintenance of the resting metabolism of a nerve from that involved in its activity. That there might be a qualitative difference between resting metabolism of nerve and that during activity was suggested by Gerard and Meyerhof (Gerard and Meyerhof, 1927; also Holmes *et al.*, 1930) long ago; the latter process may well be dependent on oxidative phosphorylation (Eiler and McEwen, 1949; Gerard, 1932) and hence the action of the azide may be, not an interference with oxidation of the substrate in the resting axon, but an interference with the uptake of free phosphate.

Recent work along these lines gives us the explanation of the independence of oxygen uptake and energy utilization in the

axon (Doty and Gerard, 1950), and further points up the possibility that anaesthetics may impair nerve metabolism without concomitant changes in oxygen consumption. That the enzyme systems of mitochrondria (Brink *et al.*, 1952; Davies and Krebs, 1952; Potter and Recknagel, 1951) are involved in these phosphorylation processes in nerve has been stressed by several workers.

ACTION OF ANAESTHETICS ON SYNAPTIC TRANSMISSION

It has become one of the tenets of neurophysiology that anaesthetics (Sherrington, 1906) (and barbiturates in particular) have a selective blocking action on synaptic transmission. Direct evidence for some degree of selectivity comes from the work of Larrabee (Larrabee and Posternak, 1952) on the cat's perfused stellate ganglion, a simple monosynaptic preparation without interneurones. For anaesthetics the highest selective action, a relative one, was found to be that of sodium pentobarbital which blocked synaptic conduction at 1/10th of the strength necessary to block the preganglionic axons. Similar results were found with the rat's superior cervical ganglion. Some degree of selective action at synapses was also established by Larrabee for chlorotone, chloroform, ether, cocaine and n-octyl alcohol but not for urethane or ethyl alcohol. In fact if anything, the latter drug had a more depressing effect on axonal than on synaptic conduction. An important finding was that some substances which have no anaesthetic action (e.g. nicotine) can block synaptic transmission in the ganglion far more selectively than any known narcotic. Larrabee points out that his experiments do not determine whether the depressive action takes place at the fine presynaptic endings, the cell bodies or the dendrites, or whether at all three.

Another important finding for us who work in the brain is that the selective action of pentobarbital on the synapse is potentiated by repetitive activity, although the question must remain open as to how close a parallel we may legitimately draw between sympathetic ganglia and synapses in the central nervous system. Other work implicating the synapse as the weakest link during anaesthesia includes the observations made on ascending impulses in the medulla by Forbes (Forbes and Miller, 1922) and on spinal roots by Bremer, by Lloyd, and by Eccles.

The specific difference in spinal root behaviour that can be seen between the unanaesthetized (decapitated) cat and the cat under pentobarbital anaesthesia is in the long lasting electronic potential found in dorsal roots after one of them has carried an afferent stimulus. This has been called by Lloyd and McIntyre (1949) the D.R.V. deflection for it is the fifth discernible potential change seen in neighbouring dorsal roots after stimulation of one root by an afferent volley. It is this long-lasting negative deflection that shows the effect of pentobarbital – not in its rising phase but in the prolongation of its falling phase (Lloyd, 1952a). Lloyd has found this in the cat, and Eccles in the frog (Eccles and Malcolm, 1936). The negativity of D.R.V. interpreted originally by Barron and Matthews (1938) and later by Brooks and Fuortes (1952) as persisting negativity in the terminal fibres of the active dorsal-root axons, has been ascribed by Bremer (Bremer 1933; Bonnet and Bremer, 1952) to interneurones. Lloyd (1952a) also considers it to be post-synaptic in origin; Rudin and Eisenman (1953) have demonstrated that there is no concomitant change in the after-potential of the parent axons of the dorsal column fibres. These results are of interest in the problem of site of action of barbiturates since these drugs have such a marked effect on this component of the dorsal root potential.

As for the motor outflow from the cord, Bremer some years ago demonstrated that the ventral root fibre spike can be abolished in animals anaesthetized by this drug. Eccles's (1946) experiments led him to conclude that the principal action of pentobarbital was on the soma of the motorneurone since the 'synaptic' (non-propagated) potential survived anaesthesia.

Bremer's (Bremer and Bonnet, 1948) experiments and emphasis on the action of barbiturates on interneurones in the spinal cord are well known. His experiments on frog (Bonnet and Bremer, 1948) led him to disagree with Eccles's interpretation for they implicated a drop in synaptic potential as the cause of block by narcotics (e.g. a synaptic potential depressed by narcosis could be raised to threshold by summation with an appropriately timed second stimulus).

EFFECT OF ANAESTHESIA ON BRAIN POTENTIALS

There are two forms of brain potentials that need to be considered: the 'spontaneous' potentials and those evoked by stimulation of a receptor or afferent system.

The first really systematic study of the effects of anaesthetics on cortical potentials was that of Derbyshire, Rempel, Forbes and Lambert (1936). They recorded from aseptic electrodes placed on the dura of cats and left in place for several days. In this paper

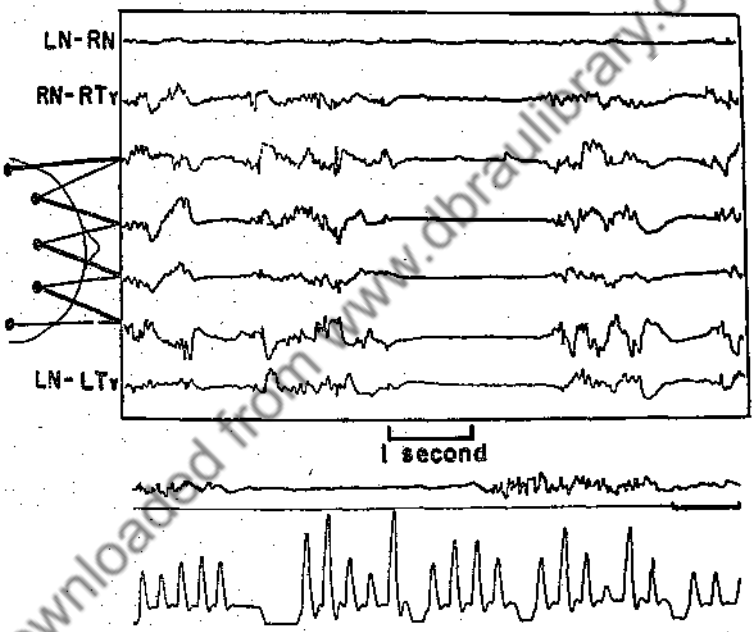


FIG. 1a

Recording from a patient in nembutal anaesthesia. The first channel is a bipolar recording from two naso-pharyngeal leads. These leads are evidently so close that no activity is recordable between them. The second channel records between the right naso-pharyngeal electrode and a tympanic lead in the right auditory canal. The seventh channel is recording between the left naso-pharyngeal and left tympanic electrodes and the remainder are from scalp placements as shown in the schema.

FIG. 1b

Automatic frequency analysis of burst activity in the EEG during deep barbiturate anaesthesia. The horizontal line on the far right just below the EEG tracing represents 1 second. The peaks in the histogram represent the activity at the following frequencies respectively (reading from left to right) 20.22.24.27.30 1·5.2.2·5·3·3·5· 4.5.6.7. 8.9.10. 11.12.13.14. 15.16.

these authors described the burst activity with intermittent periods of 'electrical silence' that are now so familiar to us in the human subject during deep anaesthesia (an example of which can be seen in Fig. 1).

They also described the fast activity seen in etherized cats and this we are now familiar with in human subjects. Some years ago (Brazier and Finesinger, 1945) we described how in the case of barbiturates the fast activity appeared first and was most prominent in the frontal regions. It may be remarked that the fast activity at this stage of ether anaesthesia is also more prominent in the frontal areas. The basal patterns of the EEG in etherized and barbiturized animals were described long ago by Bremer (1936b) and later by Beecher and McDonough (1939).

It was in the classic paper of Derbyshire and his colleagues (already quoted) that the observation was recorded that a rather deep stage of avertin or barbiturate anaesthesia (but not ether) favoured the recording of the cortical response to a peripheral stimulus. A surface positive cortical response to stimulation of the sciatic nerve had been recorded in dogs by Nemminski as long ago as 1913, but it is to Forbes that we owe our understanding of its importance. This is the surface positive response of long latency that was named by Forbes the 'secondary discharge'. Beecher's work demonstrated that low blood pressure and asphyxia also favoured the recording of this late response at the cortex (Beecher *et al.*, 1938), and extended our knowledge of the number of anaesthetic agents under which it could be recorded. More recently acquired knowledge will probably bring a rather different interpretation to these findings, as will be seen later.

In their detailed examination of the cortical response to sensory stimulation under barbiturate anaesthesia, Forbes and Morison (1939) showed the secondary discharge to be a diffuse response of the whole cortex and not (like the primary response) restricted to the appropriate specific projection area. The effect of giving ether to the barbiturized animal was to lengthen the latency of the secondary response and finally extinguish it (reversibly).

It was in this paper that Forbes and Morison (1939) made the suggestion that 'the afferent paths deliver the incoming volley not only to the sensory cortex, but also the thalamus or other sub-

cortical centres, and that from there impulses are distributed widely in the cerebral cortex'.

This suggestion of Forbes of dual ascending systems was followed up and tested on cats by Dempsey, Morison and Morison (1941) who concluded that on stimulation of a sciatic nerve, the primary response of short latency travelled by the medial lemniscus to the contralateral leg area of the sensori-motor cortex, whereas the secondary response of long latency travelled by both crossed and uncrossed pathways. Crossed pathways were shown to exist below the collicular level as well as in the anterior third of the corpus callosum. It was these investigators who established the independence of these two cortical responses; that their different latencies were not merely due to stimulation of different fibre types in the periphery; that the secondary responses did not travel by either sympathetic or cerebellar circuits; and that their spread was not by cortico-cortical connections. These workers later (Morison, Dempsey and Morison, 1941a, b) demonstrated that the secondary response could be obtained by stimulation of brain stem structures. Their discovery and study of the recruiting response to stimulation of intralaminar nuclei[1] led them to the suggestion (Morison and Dempsey, 1942a) that there might be a non-specific thalamo-cortical system with diffuse connections in addition to the classic specific projection system and that the recruiting response was identical with the 8-12 c/s. activity which occurred spontaneously in the EEG (Dempsey and Morison, 1942a) in the association cortex of a nembutalized animal. It is important to note that the parallel they suggested in this paper was with barbiturate bursts, although the distinction has sometimes been lost. Morison, Finley and Lothrop (1943a) concluded that intralaminar nuclei were indeed concerned with the production of these bursts for they recorded them from the region of the internal medullary lamina of the thalamus (and most markedly from the centre median) but never from any relay nuclei of the specific projection pathways (1943b). They also demonstrated that these bursts survived bilateral decortication (Morison and Bassett, 1945) and transection at the intercollicular level for as long as four days before degeneration of the nuclei finally abolished

[1] These authors included in this term the nucleus centralis lateralis, nucleus centralis medialis, nucleus paracentralis and the centromedian nucleus.

them. From stimulation experiments they concluded (Morison, Finley and Lothrop, 1943b; Dempsey and Morison, 1942a) that stimulation of 'medial thalamic' nuclei could inhibit barbiturate bursts. From Moruzzi's observations (Moruzzi *et al.*, 1950) it would appear as though the bursts were a sign of, rather than a mechanism for, waxing and waning of facilitation.

In 1947 Jasper and Droogleever Fortuyn reported control of these bursts in barbiturized cats by stimulation of the massa intermedia and moreover demonstrated that they could evoke a bilaterally synchronous wave-and-spike complex by stimulation at a rate of 3 per second, thereby simulating the electrical signs of *petit mal* epilepsy. Jasper later (1949) introduced the term 'thalamic reticular system' to describe the subcortical connections of what he envisaged as a diffuse thalamo-cortical projection system (i.e. inclusive of intralaminar nuclei and the true nuclei reticularis of the thalamus).

In this paper, Jasper (1949) described the controlling effect on 'spontaneous' activity of stimulation in the intralaminar region and noted maximal effect in the sensory-motor and frontal cortices of both hemispheres, and stated it to be identical with Morison and Dempsey's 'recruiting response'. He felt at that time that the 8–12 c/s. cortical bursts set up by single stimuli to the thalamic reticular system were analogous to the alpha rhythm of the human EEG. Their early appearance in the frontal areas of the unanaesthetized cat's brain (gyrus proreus and middle supra-sylvian) raises the question as to whether they might better be regarded as analogous to the bursts induced by sleep ('spindles'), which closely resemble those produced by barbiturates. They cannot be elicited in the truly wide-awake animal (Jasper). In other words the possibility of a common mechanism in thalamo-reticular stimulation (especially of the rostral and mesial parts of the system), barbiturate narcosis and sleep suggests itself. That the recruiting response may itself be a complex of afferent fibre discharge and cortical neurone response seems likely from the work of Arduini and Terzuolo (1951).

Primary cortical responses are unaffected by thalamo-reticular stimulation, but Forbes's secondary responses are abolished by it. The consideration of these many observations led Jasper to suggest a schema in which cell bodies in the reticular and intralaminar

regions would have direct projections to the cortex (Jasper, 1949; Jasper and Ajmone-Marsan, 1952). Some anatomists (McLardy, 1951; Rose and Woolsey, 1949) were reluctant to accept the postulate of such direct connections (except for the limbic cortex) since they conflicted with evidence from degeneration studies. However, the failure of nuclei to degenerate after decortication is not felt by Starzl and Magoun (1951) to be critical, for they hold that abundant collateralization could keep the cell bodies viable. The suggestion has however been made (McLardy, 1951; Rose, 1952) that an interconnecting system within the thalamus might be responsible for the diffuseness of the phenomena, and McLardy in 1951 pointed out that Dempsey and Morison's results do not exclude the participation by the non-sensory and association nuclei. However, more recent work by Hanbery and Jasper (1952) in which they demonstrated recruiting responses after destruction of the association nuclei would appear to rule them out. In any case it is clear that it is a multisynaptic pathway that is involved, for the latencies found by Jasper are quite long. In this context the finding of Droogleever-Fortuyn and Stefens (1951) that cells of the intralaminar system project not to the cortex but to the caudate nucleus is of the greatest importance. Connections are known to run from the caudate to the globus pallidus; this nucleus in its turn connects with the anterior ventral nucleus of the thalamus.

Although such a circuitous pathway could result in responses of only very long latency at the cortex, those who study the effect of anaesthetics on brain potentials will immediately recognize the cogency of this argument in relation to the phenomena they observe, for it is in the cortical projection areas of the anterior ventral thalamic nucleus (a non-sensory relay nucleus) that these events appear most prominently (i.e. in premotor Area 6, to use Brodmann's numbering). The slow wave type of response to sensory stimuli as recorded in man, whether under barbiturate anaesthesia or in natural sleep, is maximal in what appears to be Area 6.

The cells of the reticular complex of the thalamus, unlike those of the intralaminar region, were found by Rose (1952) to degenerate after removal of the cortex. The type and location of these degenerate changes suggested a widespread but specifically

topographical projection system to the cortex from the thalamic reticular nuclei; this forms an independent afferent system to the same cortical areas as are also served by specific afferents from the dorsal thalamic nuclei. Starzl and Magoun (1951) are however doubtful that any but the most cephalic parts of the thalamic reticular nuclei project to the cortex.

At a level below the thalamus but connecting rostrally with its mesial portion and with the hypothalamus is the ascending reticular system of the brain stem which has been investigated so extensively by Magoun, Moruzzi, Lindsley and others. They showed that stimulation of this ascending reticular activating system (which lies like a core containing many nuclei in a neuronal mesh in the brain stem stretching from the medulla up through the mesencephalon into the caudal end of the mesial thalamus) produces a generalized 'desynchronization' of the EEG potentials as recorded at the cortex, a response very similar in appearance to the familiar 'alpha blocking'. (It will also block the recruiting response of Dempsey and Morison.) This type of generalized response was found to be elicited most easily by low voltage, high frequency stimulation. The ascending effect is independent of the classical afferent lemnisci and the spino-thalamic tracts and survives their section at the midbrain; it relies for its sensory inflow on their collaterals (French, Verzeano and Magoun, 1952; Gerebtzoff, 1940; Starzl, Taylor and Magoun, 1951b), or possibly on independent fine fibres.

Stimulation of the mesencephalic reticular system has an arousing reaction (Moruzzi and Magoun, 1949) (both behaviourly and electroencephalographically) and in contrast, section of its ascending fibres induces a chronic sleep state. Bremer's (1935, 1936b) classic observation that his *cerveau isolé* preparation cannot be aroused from apparent sleep is now explicable on these grounds, rather than as the result of section of the specific sensory afferents. Bremer is however correct in using the term 'deafferentation' because afferent impulses are necessary to excite this system if it is to keep the animal awake. In fact the work of Lindsley and associates (1949, 1950) on acute and chronic lesions of the brain stem in the unanaesthetized cat and of French and Magoun (1952) in the monkey has confirmed this explanation beyond reasonable doubt. And in the context of anaesthesia, it may be

noted that repetitive stimulation of this system in the mesencephalon has been shown to wake a monkey from deep barbiturate anaesthesia.

The relationship of this ascending system in the brain stem to the thalamic reticular system has been explored by Starzl, Taylor and Magoun (1951a) who find two ascending routes for the impulses: one thalamic and one extrathalamic, the latter being identical with the pathway of Forbes's secondary response described above.

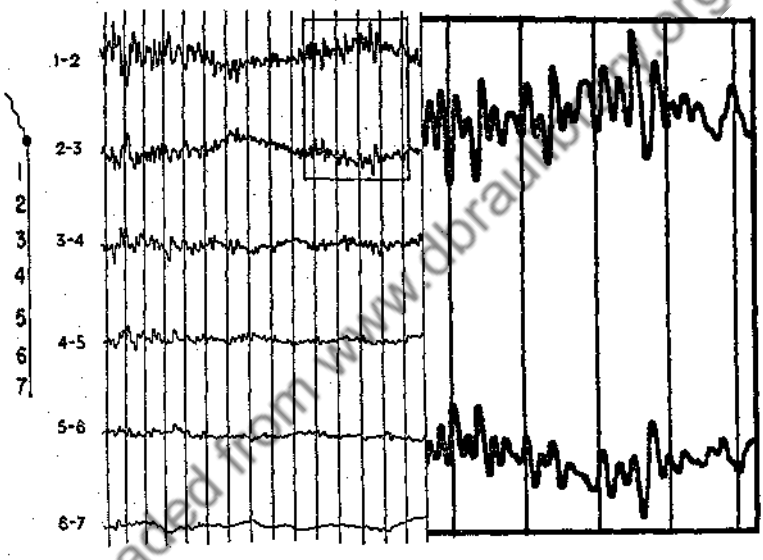


FIG. 2

Bipolar recordings from 7 points of an implanted needle electrode (Delgado technique) in the frontal lobe of a schizophrenic patient prior to therapeutic lobotomy.
The traces represent serial bipolar linkages from the most superficial recording points in the first trace down to the deepest pair in the lowest trace. Vertical lines represent $\frac{1}{5}$ second.
Inset on right is an enlargement of the framed section to illustrate reversal of fast activity at the second recording point from the surface.

AN EXAMINATION OF BARBITURATE ANAESTHESIA

From observation of both the EEG and the patient's behaviour it would appear that barbiturates act in rather clearly defined stages. In the first stage of pentothal anaesthesia, for example, the subject shows definitely disturbed behaviour but is not unconscious; eyeball movements are under voluntary control, corneal

reflexes are normal, pupils are normal and react to light and to pain (there is no analgesia). Electroencephalographers are very familiar with the brain potentials concomitant with this stage – they take the form of fast high voltage activity appearing first in the frontal regions (Brazier and Finesinger, 1945) and later spreading back over the head. The generators of this activity

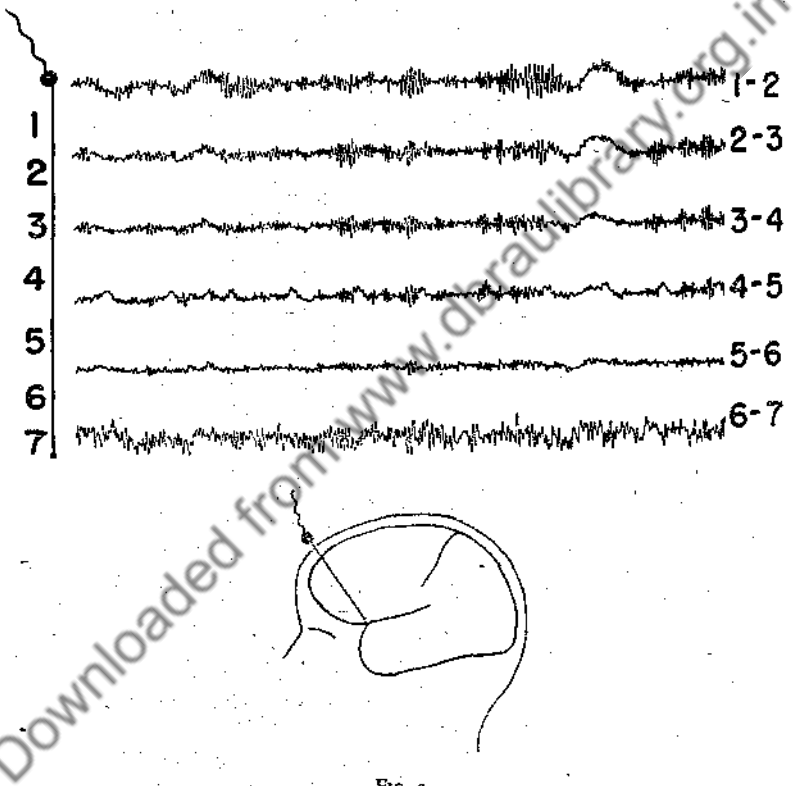


FIG. 3

Bipolar serial recordings from an implanted electrode reaching from the cortex of the convexity to that of the orbital surface of the frontal lobe. The schematic diagram underneath is intended only as an approximate indication of electrode placement.

appear to lie in the cortex itself and indeed the fast waves can be shown, by implanted electrodes, to reverse in the cortical layer.

In some work initiated by Delgado, Hamlin and Chapman, I have been given the opportunity to study the EEGs of psychotic

patients in whom Dr. Hamlin had implanted depth electrodes through burrholes made preparatory to therapeutic leucotomy. These electrodes were designed by Delgado and their description has been published (Delgado *et al.*, 1952). The falling gradient of voltage one records from deeper and deeper points of the needle is a consistent finding and all but the most superficial points of the needle appear to record only the field of the cortical potentials, as one would expect from white matter (see Fig. 2).

If one examines the traces from the bipolar linkages of the most superficial points of the needle (lying in the convexity of the frontal cortex) one sees that there is a reversal of sign between them. The framed section in this record has been enlarged in the inset in order to demonstrate this more clearly.

If the needle is implanted through the convexity of the frontal cortex so that it penetrates the underlying white matter as far as the orbital cortex the deepest point of the needle electrode now shows high voltage fast activity. An example of such a case is seen in Fig. 3.

The point to which attention is directed is that the fast waves of the orbital cortex appear to be independent of those of the cortex at the convexity. From evidence such as this it seems reasonable to deduce that the barbiturate *at this stage* is acting directly on the cortical cells and that the cortex is not being paced into any kind of synchrony from below, although the drug may well be having this same type of independent effect on neuronal groups subcortically.

A patient passes through this stage on the way to surgical anaesthesia and again when recovering from it. Only one further characteristic will be mentioned and that is that sensory stimuli do not at this level evoke a slow wave response from Area 6. Fig. 4 shows an example with scalp recordings from a patient in this stage. Shortly before this he had been in stage 2 of pentothal anaesthesia and on stimulation had given a clearly defined response, as is shown in Fig. 5.

The deeper stages of anaesthesia are also of interest in relation to the new knowledge of a parallel system of sensory relays to the cortex. Electroencephalographers are now familiar with the deep stages of barbiturate anaesthesia (Brazier, 1951; Kiersey *et al.*, 1951), and an example recorded from nasal and tympanic leads

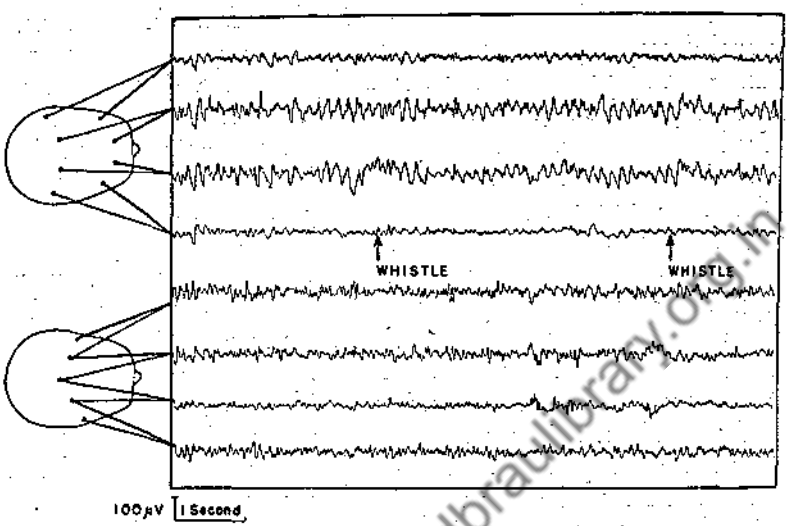


FIG. 4

Subject recovering from pentothal anaesthesia (now in stage 1). No pre-motor response to auditory stimulus.

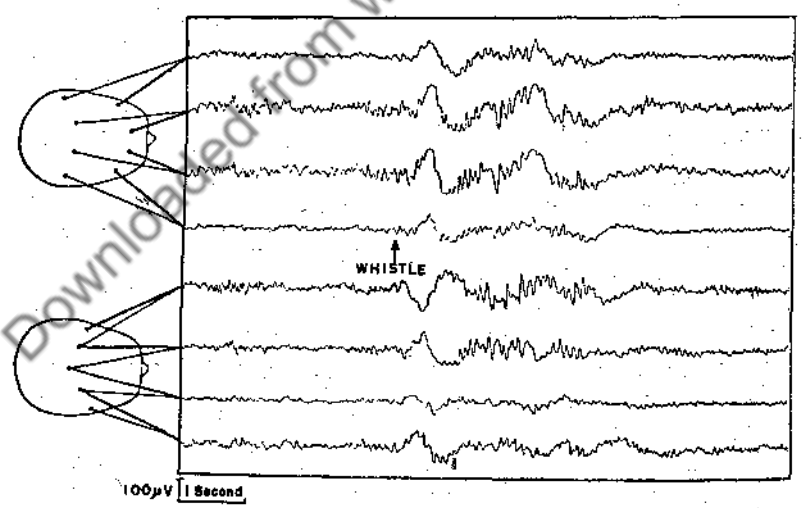


FIG. 5

Record from same subject as in Fig. 4, but taken while he was still in stage 2 of pentothal anaesthesia. Marked electroencephalographic response to an auditory stimulus, but no behavioural response detectable.

as well as from scalp electrodes has been illustrated in Fig. 1. The same stage is sometimes seen in barbiturate intoxication and is not necessarily a sign of a poor prognosis, for the process (as in anaesthesia) can be reversible. These are, of course, the familiar barbiturate bursts, so often referred to as 8–12 c/s. bursts, but they are in fact of mixed frequencies. There is very little periodic activity in these bursts and an automatic frequency analyser reports a mixture of frequencies (as can be seen in Fig. 1).

It is in a stage of barbiturate anaesthesia between that illustrated in Fig. 4 and that in Fig. 1 that the role of the non-specific ascending system is so great and it is here that the parallel between barbiturate effect and sleep becomes apparent. Bremer first drew our attention to this similarity by his classic experiments on the *cerveau isolé*. That barbiturates may exert their influence by producing a block at the reticular level has been suggested (Moruzzi and Magoun, 1949).

It would appear that even cranial nerve II, entering as it does above the level of the transection, has collaterals (or fine fibres) feeding into the alerting system of the brain stem, for photic stimulation of the optic pathway in a *cerveau isolé* preparation will not alert the animal.

Turning again to the ascending system for sensory stimuli, we have, besides the classic pathways carrying the primary evoked response through comparatively few synapses to the specific sensory cortical areas, Forbes's secondary response travelling by both thalamic and extrathalamic routes, the latter passing through the reticular formation in the brain stem and the mesial portion of the subthalamus and thalamus.

Since in anaesthesiology we are concerned with a problem centering in transmission through synapses it would seem essential in experimental controls to use a *physiological* sensory stimulus instead of the artificial volley of synchronous impulses that electrical stimulation evokes, for the simultaneous bombardment of a post-synaptic neurone by such a volley probably has no counterpart in nature. As mentioned above, the anaesthetic level that is of interest in this connection is one lower than that in which apparently the predominant effect is in the cortical cells. Hence comparisons need to be made between 'light' barbiturate anaesthesia and a 'deeper' level, in other words the control should

be, not an unanaesthetized animal, but one in light narcosis.

A study of the effect of deepening barbiturate anaesthesia on the response at a cat's visual cortex to a flash in its eye has been made. Unipolar recordings were made between a reference electrode and leads placed on the pia which had been covered with mineral oil before opening of the dura (as recommended by Marshall). Since there was a likelihood of the drug's having a depressant effect, it seemed wise to take precautions against cortical depression due to other factors (such as the spreading depression of Leão).

The cat's nictitating membranes were cut, the pupils fixed and a diffusing screen put between the light source (a Scophony stroboscope) and the cat's eyes to equalize illumination at the retinae. The flash duration was 35 microseconds.

Fig. 6 shows the response at the cortex to a single flash in the same cat at two levels of light nembutal anaesthesia. Difficulties of reproduction make it impossible to illustrate the whole of an experiment with the many exposures recorded. One typical experiment will therefore be described verbally.

In the lightest stage, so light that EEG potentials were interfering with the response, accuracy in measurement of latency was rather difficult to achieve. However, with these limitations, and from enlargement of the films the latency to the beginning of the first positive deflection for 9 consecutive exposures was found to be (in milliseconds) 11, 11, 11, 11, 12, 13, 12, 12, 11 (a mean of 12 milliseconds).

The secondary response[1] was seen to be extremely variable in amplitude (on calibration it is found to vary from 190 microvolts to 690), and its latency from the stimulus, with the limitations in accuracy mentioned above, lay between the extremes of 63 and 85 milliseconds with a mean of 74 milliseconds.

When the animal was given additional anaesthesia (in this case 30 mgm. nembutal) several effects could be noted. The most striking changes besides the well-known 'regularization' of

[1] Attention should be drawn to the question as to whether this response evoked by retinal stimulation is indeed the parallel to Forbes's secondary response from sciatic stimulation. Space limits a discussion here of its differentiation from a first wave of a slow after-discharge. Distinguishing characteristics include, of course, the diffuse cortical distribution of Forbes's secondary response and the discrete localization of slow after-discharge to the primary receiving area for the sensory modality involved.

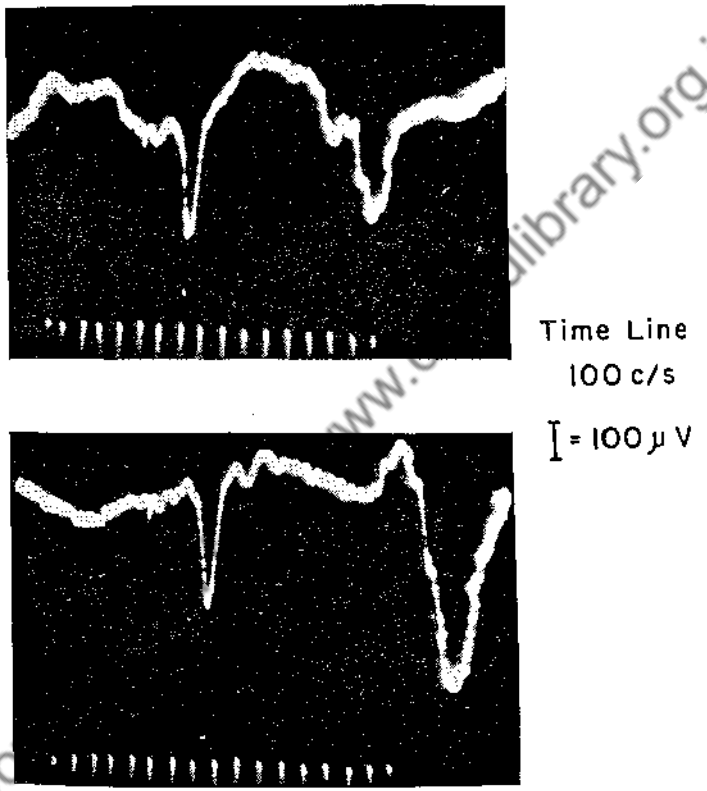


FIG. 6

Effect of deepening barbiturate on cortical response to a single flash of light 35 microseconds in duration. (cat)
Note: lengthening latencies and increase in amplitude of secondary response.
Relative negativity at the exploring electrode is recorded by an upward deflection.

TABLE I

	Primary Response				*Secondary Response*			
	Mean Latency to first positive deflection (msec.)	*Percentage increase due to drug*	*Mean Latency to peak of positivity (msec.)*	*Mean Amplitude of peak of positivity (μV.)*	*Mean Latency to second positive deflection (msec.)*	*Percentage increase due to drug*	*Mean Latency to peak of positivity (msec.)*	*Mean Amplitude of peak of positivity (μV.)*
Very light anaesthesia	12		22	358	74		100	353
After added nembutal (a) 1st 10 exposures	17	42%	27.5	312	110	49%	132	710
(b) next 10 exposures	19	58%	27.5	256	117	58%	136.5	699

responses were the great increase in amplitude of the second response (the smallest now was 590 MμV., the largest 800) and the increase in latency of response.

An examination of the latter in detail showed that in the first of the exposures taken 20 minutes after the intraperitoneal injection of added nembutal, the latency to the primary response had lengthened to 17 milliseconds, but even in the next 10 minutes represented by 20 exposures, taken 30 seconds apart, there was a tendency for the latency to continue lengthening (the serial figures for consecutive exposures in this experiment were: 17, 17, 17, 17, 17, 17, 17, 17, 18, 20, 17, 20, 18, 18, 18, 17, 20, 20, 20, 20 milliseconds). The mean of the first ten exposures is 17; that of the next ten is 19 milliseconds, the latter being a 58 per cent increase over the control figure of 12 milliseconds.

There was a striking increase in latency to the secondary response which was also still increasing; in the first ten post-nembutal exposures it averaged 110 milliseconds, in the next ten, 117 milliseconds, the latter being again a 58 per cent increase.

For easier comparison these figures are tabulated in Table I. Thus we have an increasing latency for both primary and secondary responses, a slight decrease in amplitude of the primary response and a very considerable increase in that of the secondary.

From all we know of the secondary response it can be said with some certainty that it has travelled through more synapses than has the primary. If the action of the barbiturate is to slow transmission through the synapses it appears to have done so by the same percentage for the synapses on the primary pathway as on the secondary. It has slowed the conduction *pro rata* but can it be said to have depressed the responses? In terms of amplitude there has been some depression of the primary (by 30 per cent) but there has been a very great augmentation of the secondary (by nearly 100 per cent).

The latter phenomenon suggests a 'release' effect as though *at this stage* of barbiturate anaesthesia some inhibitory system, possibly in the diffuse ascending system, had been put out of action by the drug, thereby releasing from control the responses carried rostrally from this system. Such a concept thus envisages that there would be in normal circumstances a condition of balance within the ascending system, a balance between inhibition

and activation, and that by increasing very gradually the depth of barbiturate anaesthesia the action of the one can be depressed before that of the other.

That a deeper level of anaesthesia can be reached at which this differential depression is lost, is, of course, indubitable. The effect of repetitive stimulation has not yet been studied by us, but others have published interesting results from repeated (non-physiological) volley stimuli (Jarcho, 1949; Marshall, 1941; Marshall *et al.*, 1941). That barbiturates prolong the recovery period has been shown by many workers.

It will be noticed that this would be an alternative explanation to the one usually proposed for the necessity for using barbiturate anaesthesia in order to record secondary responses. It would not be merely the suppression of the background EEG waves enabling the secondary response to be seen more clearly: it would be a true augmentation of this response.

Such an hypothesis would also suggest an explanation of the finding, so familiar to those who work on evoked responses, that these have an apparently more widely spread distribution in the anaesthetized animal than in the unanaesthetized one and that the distribution is variable with depth of anaesthesia. This could be an augmentation of previously invisible responses.

It is now of interest to examine the above postulate in relation to barbiturate anaesthesia in man, and to see whether any parallel demonstration of an apparent 'release' effect can be found.

One of the striking features of the EEG in barbiturate anaesthesia, to which our attention was drawn long ago by Bremer, is the similarity of one of its stages to that of sleep. This stage in each of these states is that at which a sensory stimulus will evoke a slow wave response from the premotor regions. It is suggested that this stage might perhaps be more accurately called 'barbiturate sleep' than barbiturate anaesthesia. The sensory response obtained at this stage has sometimes been called an arousal response, but the term seems unfortunate since its major feature is that it occurs *without* arousing the subject. Another reason for avoiding this term is that it has been used for the quite different phenomenon of generalized alerting that Magoun and his associates have shown to be due to activation of the ascending reticular system of the brain stem.

As is well known, the response first demonstrated in sleep by Davis and co-workers (1939) and since confirmed by too many to mention, is non-specific for sensory modality, although in man the auditory system gives the most easily elicitable response. The location of these slow responses, and of the spindles which so frequently accompany them, is (as far as we can tell in man with an intact skull) in premotor Area 6, by the Brodmann numbering. They are bilaterally synchronous (Brazier, 1949).

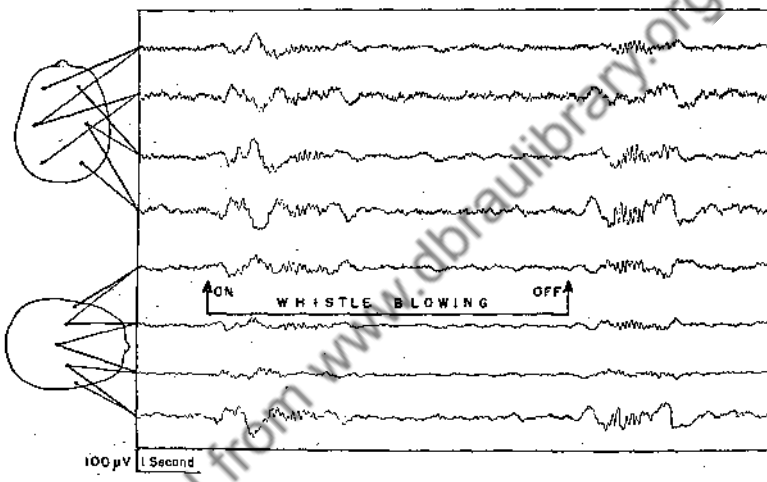


FIG. 7

'On' and 'Off' responses to an auditory stimulus in a patient under scopolamine and morphine. No observable behavioural response.

An example has already been shown in Fig. 5 of such a response in pentothal anaesthesia. It is not specific to the barbiturates, being, as is well known, readily obtainable with sedatives such as chloral hydrate, and I have found it in patients under operative premedication with combined scopolamine and morphine. In view of the strongly analgesic properties of morphine, it may be of interest to illustrate the arrival of sensory impulses at the cortex from a patient 'asleep' under this drug. Fig. 7 shows a response to a sound stimulus. What is of more interest, perhaps, is that one can sometimes get both an 'on' and an 'off' effect to a stimulus that is allowed to persist for some time. To illustrate for the record that this is not a specific auditory effect Fig. 8 shows the

same type of response evoked by the onset of a rather rapidly flickering light.

But to return to barbiturates, probably anyone who has studied sedation with these drugs would agree that in barbiturate-sedated sleep these responses are greatly facilitated. In some recent work in our laboratory, undertaken by Dr. Chafetz and Dr. Cadilhac, they inserted a needle into a vein of a normal person and then allowed him to fall into natural sleep when he felt like it. When

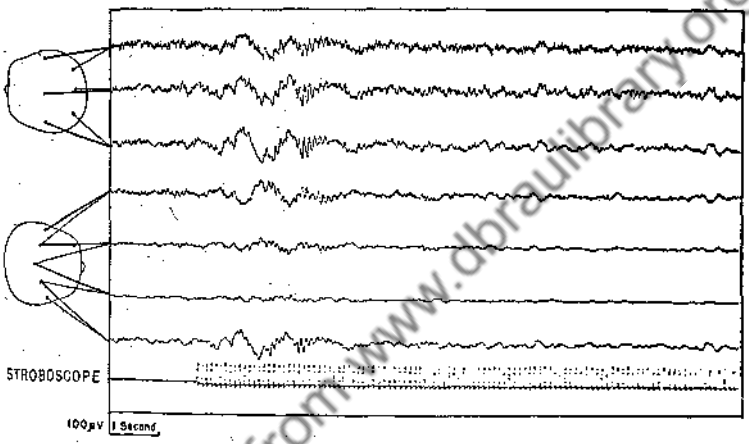


FIG. 8

EEG response to onset of photic stimulation in a patient under scopolamine and morphine. No observable behavioural response.

an adequate recording of the EEG in normal sleep had been obtained, pentothal was run into the vein through the previously inserted needle. Responses to sound were tested before and after introduction of the drug. An experimental design of this kind brings out very clearly the augmentation of response due to the drug. Again one has the impression that activity had been 'released' by the drug. The activity that now appears uninhibited would seem to be the parallel in man of Forbes's secondary response, as many workers have pointed out.

The hypothesis is offered as a starting point for discussion that, at this level of barbiturate action, a differential effect is taking place which has removed a subcortical inhibitory action, allowing the secondary sensory response to travel up unrestrained through

the mesial part of the thalamic reticular system to premotor Area 6 of the cortex. The long latency suggests that it has taken a circuitous route and, extending the hypothesis further, the cortical site (Area 6) suggests that the impulses may have travelled from the intralaminar system to the caudate nucleus (Droogleever-Fortuyn and Stefens, 1951), from there to the anterior ventral nucleus of the thalamus whose projections are to Area 6.

It would scarcely seem likely to be mere coincidence that the same premotor area of cortex in man should be the site of maximal electrical slow activity in each of the following circumstances: 'spontaneous' slow waves (or more probably, responses to inter-receptor stimulation) during sleep; non-specific sensory responses during sleep and anaesthesia; *petit mal* wave-and-spike complexes (Kaada, 1952); and the fact that all these conditions involve a state of impaired consciousness.

No account of the action of barbiturates would be complete without some mention of their effect on after-discharge. The work of Bremer and Bonnet (1950) has clearly demonstrated that the phenomenon of fast after-discharge can be seen only in the non-anaesthetized animal. The slow after-discharge (which looks like a repetition of the primary response) may be regarded as peculiar to a moderate degree of barbiturate anaesthesia. The distinction that Bremer makes between these two types of after-discharge has not always been clearly understood by others. The former he attributes to transitory intensification of 'spontaneous' cortical activity, whereas the latter he regards as of subcortical origin manifested only when barbiturate anaesthesia is at a level that depresses the autorhythmicity of the cortex. Slow thalamo-cortical discharges can be recorded in specific thalamic nuclei and survive removal of the cortex (Adrian, 1951; Bremer and Bonnet, 1950; Galambos *et al.*, 1952).

In summary, the following hypothesis is presented for discussion.

1. That the initial action of barbiturates is on neurones in the cortex.

2. That at a slightly deeper level of narcosis barbiturates appear to have a differential depressant action on a subcortical inhibitory system, the result being an augmentation of response in the non-specific sensory system that carries Forbes's secondary response.

3. That at a deeper level still, the differential action on inhibitory and activating systems is lost and the sole remaining activity is the barbiturate 'bursts' apparently carried by the same reticulocortical pathways that serve the recruiting system.

4. That a state of anaesthesia does not require that sensory impulses should be prevented from reaching the cortex. A disruption of balance between inhibition and activation at a subcortical level of integration would appear to determine whether incoming sensory impulses receive the elaboration necessary for 'awareness'.

ACKNOWLEDGMENTS

I would like to thank my many colleagues in the departments of Anaesthesia and of Electroencephalography for their help in making these recordings possible. I would especially like to thank Dr. John Loesch, now of the University of Illinois Medical School, for his skilled technical help in some of the experiments reported here. No one, however, but the author should be held responsible for the speculative opinions presented in this paper.

GROUP DISCUSSION

MORISON: The secondary sensory response described by Forbes is a long latency phenomenon best seen in deeply anaesthetized preparations by nembutal. It is recordable all over the accessible cortex. During light anaesthesia this response was seen better in our preparations, in which very little of the thalamus on either side had been left, than in preparations with intact thalamus. This would fit well with Dr. Brazier's suggestion. When the subcortical structures are taken out less activity is seen in the anaesthetized cortex and presumably more cortical cells are available for the response just described, hence, the response is bigger. In other words, the lack of Forbes's secondary response in the waking animal may be due not to inhibition but to the fact that the cortical cells being busy doing something else cannot respond in any other fashion, while during sleep the decrease of the spontaneous activity leaves them free to become recruited in a new response. No experimental data are available to distinguish the latter interpretation from one of inhibition.

In systematic explorations of the diencephalon with respect to Forbes's secondary response, it was found that its latency was still

surprisingly long, suggesting that the long latency is due to events further rostral. A tract stimulation which produced the response was traced under the thalamus and forward to the junction of the ventromedial angle of the internal capsule, globus pallidus and amygdaloid. Ablation experiments also suggested that there was a concentration of fibres in this area which spread out in some unknown fashion over the entire neocortex.

In other animals in which the cortex of one hemisphere had been removed 2 to 3 weeks previously a few secondary responses have been recorded in the caudate or putamen after sciatic stimulation. This again suggests the presence of a tract going below the thalamus to somewhere near or in the striatum or amygdala and hence to the cortex.

In deep anaesthesia or in animals without thalamus the characteristic activity of the cortex is a series of waves at 2 to 3/sec. which looks like Forbes's secondary response. By timing the stimulus appropriately one can trip off this 2 to 3/sec. activity. This suggested the possibility that the fibres mediating the secondary response of Forbes fed into a system which was capable of spontaneous activity which you could only see in either deep anaesthesia or after removal of the thalamus. Hence we could describe three sorts of activity: (*a*) the normal rapid activity, (*b*) the spindle bursts, (*c*) the activity previously described as seen in deep anaesthesia.

WALTER: We can confirm Dr. Brazier's suggestion for the localization of the fast activity in the cortex during pentothal anaesthesia and by our experiments during seconal induced sleep. The fast activity has a wide distribution over the cortex and is independent in various areas, i.e. no statiscally significant phase relations could be observed. Thus we have evidence of breaking up, of disintegration in some fashion, which is different from the activity observed during arousal.

The phenomenon of the K-complex is obscure. Its geometry in seconal induced sleep or in natural sleep is more complex than suggested by Dr. Brazier. One could visualize it as a fountain spreading over the cortex. It would appear to us to squirt out of the temporal lobe and spread out to the pre-motor zone, which is quite a unique feature. Now the K-complex is not accompanied by arousal. Yet the sleeping man can eventually be aroused by successive loud claps or by calling his name in a loud voice. The arousal thus produced is not accompanied by K-complex. Hence, our impression of the latter as a sort of preventive reaction.

PENFIELD: The observations of Dr. Bremer, Dr. Walter, Dr. Brazier, are consistent with the concept of these cortical areas as way-stations between periphery and the co-ordinating and integrating centren-

cephalic system. During the consciousness produced by anaesthesia or sleep the centrencephalic system is inactive. Yet, the cortical areas are even more easily activated as shown by these electrical measurements.

GASTAUT: I should like to ask Dr. Brazier whether she identifies the K-complex with Forbes's secondary response? It is a fact that the K-complex first appears as a sharp wave localized at the vertex. In 25 per cent of subjects in the waking state, characterized psychologically by hyper-emotivity, upon stimulation by noise or light, my wife has observed a sharp negative wave in the vertex after about 50 m.sec. latency. As the first stage of sleep sets in the same response appears but with increasing latency and amplitude. As deeper sleep is reached the response is followed by slow waves, spreading to the frontal regions showing all the characteristics of the K-complex. On account of these topographical differences, I would personally tend to differentiate entirely the K-complex mechanism, initially localized at the vertex, from the mechanism of Forbes's secondary response, which is diffuse from the outset.

HESS: I agree with Dr. Gastaut about the localization of the K-complex. The localization is the same for the spontaneous slow wave in man and it is also true in the cat, even though the underlying cortex is functionally different. Therefore, these waves do not bear any relation to the functional significance of that cortex. Also, observations have shown that the activity of the caudate nucleus is different to that of other regions during barbiturate narcosis. This may be relevant to Dr. Brazier's hypothesis.

KUBIE: Clinical observations must be included in our data. Using very dilute solutions of pentothal, slowly injected intravenously, any given individual will on one occasion slowly drop off to sleep, and on another occasion, when in a different emotional state, the subject will go through an initial phase of excitement before going to sleep. Critical changes in the response to a fixed dose of barbiturates will occur when the patient goes through a critical change in his emotional state. This is evidence that a number of phenomena interact in the pharmacology of narcosis.

BREMER: Multiplicity of factors are involved in narcosis: (*a*) There may be selectivity of action of drugs, either on account of a differential neuronic sensitivity, or as a consequence of a special physico-chemical affinity of the narcotic for central structures; (*b*) the possibility of a disruption of the balance between excitatory and inhibitory phenomena, i.e. a release phenomenon; (c) different narcotics may have quite different effects on the period of recovery of neurones; (*d*) the reduction of a background activity may result in an increase of the response

to a synchronized volley, a pseudo excitatory effect which seems to be particularly important in barbituric narcosis of the brain; (*c*) some narcotics at a certain stage of their action may have a true direct excitatory effect.

As an example, we can study the difference of action of chloralose and veronal on the ventral-root potential and associated discharge in a spinal frog. In an unanaesthetized preparation this V.R.P. is recorded as a slow wave, superimposed by fast spike activity. When two successive stimuli are given, the second V.R.P. is facilitated and this is more apparent in the spike components. In chloralose narcosis a single stimulus produces a smooth V.R.P. of sub-threshold intensity since it is not superimposed by spikes. Yet when two successive stimuli are applied, the second synaptic potential, being superimposed on the summit or on the decaying phase of the first one, reaches threshold value, as shown by a discharge of spikes. Therefore, in chloralose anaesthesia, the postreactional subnormality effect is very slight on spinal neurones.

If a dose of veronal is given one sees an increase in the voltage of both the V.R.P. and the superimposed spikes. But a second volley is almost without effect. And with more veronal given there is a still greater increase in the response to the first volley as contrasted with the complete suppression of the response to the second volley. We have in this case an example of the double effect of barbituric narcosis: apparent or true excitation, if one considers only the response to a single synchronized volley; strong depression, resulting from the increase in depth and duration of the post-reactional subnormality, if one judges from the response to a repetitive discharge of afferent impulses, which is the normal feature of natural sensory stimulations.

The same difference between barbiturics and other narcotics (specially the volatile ones) is observed in the acoustic cortex of the cat. A whistle stimulus which continues to activate it strongly in other narcosis is without effect (save for an eventual initial wave) during a barbituric narcosis of the same depth. At that time, the primary responses to clicks may remain of normal amplitude and may even be increased. But they are lacking the fast afterdischarges which characterize the reaction of the unanaesthetized brain.

We know from W. H. Marshall's work (1941) that this blocking of repetitive corticipetal impulses as a consequence of intensified post-reactional depression and resulting Wedensky effect is produced mainly at the thalamic level. The acoustic cortex in barbituric narcosis, being unresponsive to tones and to noises, is thus practically de-afferented, much more than in an ether narcosis of the same depth. The same conclusion applies for the somatic sensory cortex if one con-

siders its response to a continuous tactile pressure. These distinctive characteristics of barbituric narcosis, on which I have drawn attention in the past on account of their interest for the problem of sleep, have often been misunderstood.

JASPER: Studying unitary discharge in the cortex by means of micro-electrodes, we noticed that the very first effects of barbiturate narcosis was to increase the discharges in individual units. Shortly after, there appeared a cessation of unit discharges. This was seen even before reaching deep anaesthetic doses of barbiturate and before any real depression of surface slow waves was apparent. Is this a direct action upon the cortical cells or an indirect one? It would seem that cortical discharge is blocked early in the course of anaesthesia, before the surface positive evoked potentials are diminished. So that it may be necessary to be cautious in the interpretation of anaesthetic action based upon effects upon evoked potentials alone.

KUBIE: In evaluating the observation that excitation may antedate depression at the onset of narcosis, one might well bear in mind a difference between human and most lower animals. The activity of conscious human beings is almost never completely free and spontaneous. It is guided, restrained, limited by conventions, prejudices, fears, etc. and psychic pain always is associated with breaking through these barriers. If the first effect of an anaesthetic were to 'anaesthetize' this emotional pain, then activity would increase automatically. This, however, would be a release effect, and not an excitatory action.

BRAZIER: I would like to ask Dr. Jasper what he means by increase in unitary discharge. Is he speaking of amplitude or frequency or number?

JASPER: I was referring to increase in frequency and to the number of units discharging. These are 'all or none' spikes. With respect to Dr. Brazier's suggestion that the barbiturate effect is primarily a cortical phenomenon, it should be pointed out that this activity has been seen in isolated cortex of man by Scoville and Henry. As far as the apparent increase in the cortical response to sensory stimulation is concerned, it has been suggested that this may be due to the suppression by the narcotic of the pre-existing activity in the waking animal; partially occluding the response. It is striking that in certain epileptics the electrical paroxysms appear mostly or only during sleep.

BREMER: It is true that central response is increased in certain stages of barbiturate narcosis. But this applies only to single stimuli. For if a continuous stimulus is being used, there is only an initial increase of the response followed by extinction of this response.

BRAZIER: Dr. Bremer's suggestion would be in keeping with the notion that barbiturates act on the recovery process of the neurones.

JASPER: This points to the necessity of studying both early and later effects of sensory impulses to the cortex in narcosis. These late effects may be more important to the brain.

JUNG: I am very much in favour of a conception of balance between excitation and inhibition in the brain. Working with Toennies on electrical stimulation of the cortex (Jung and Toennies, 1950) we called the processes, acting against a maximal discharge, braking or restraining mechanism to avoid the somewhat equivocal word inhibition, which has so many different meanings. We were wondering why all normals are not epileptic. Why the enormous synaptic powder barrel we carry with us in our heads does not explode in a fit, although the potential energy for epileptic discharge certainly is present in the brain of all of us. It seems that the activity of the normal brain is always restrained by some mechanism. Partly this mechanism may be represented by the normal rhythms which hold the activity of the brain just at a happy mean level, restraining any abnormal epileptic discharge. This conception should also be considered when dealing with pharmacological experiments. Thus, in chloralose anaesthesia, the inhibitory or restraining mechanism as represented by the normal slow waves is absent. The cortex is rendered, so to say, 'reflex epileptic', as Dr. Adrian had shown long ago.

JASPER: Dr. Jung has correctly emphasized the interesting action of chloralose which produces an extreme facilitation of cortical responses and of synaptic transmission while still maintaining a type of anaesthesia.

ADRIAN: I have the impression that chloralose and morphia differ considerably from the barbiturates in their anaesthetic action. In certain stages the long refractory period, with practically no activity between each burst is something which recalls the action of strychnine, as opposed to the electrical pattern induced by barbiturates. Does not this suggest that these drugs produce anaesthesia in a different way?

BRAZIER: Morphia may produce excitation in man. A unitary hypothesis for the action of these various drugs is not possible at this stage of our knowledge.

JASPER: In view of the preceding observations and concepts presented by the speakers, is Dr. Bremer willing to admit that sleep is not only due to the decrease in the influence of the activating system.

BREMER: I am willing to accept the possibility of a release phenomenon as far as normal sleep is concerned. But with narcotics, the dual effect (excitatory and inhibitory) of all drugs is more likely to come into play. For instance in the spinal animal I find it difficult to visualize an effect of release when veronal is used. The augmentation seen is more likely to be purely excitatory.

GASTAUT: I have measured, in man and animals, the cycle of cortical excitability, using the technique of paired stimuli separated by variable intervals of time. I have subsequently investigated, with my colleagues, the variations of this cycle under the effect of various substances. I observed a considerable lengthening of the cycle of excitability under the effect of barbiturates and, in general, of all drugs producing anaesthetic sleep.

I found the same effect with chloralose but curiously associated with an increase in the amplitude of the cycle of excitability, similar to that produced by convulsive substances (e.g. metrazol). In 1951 I wrote a paper on this double and apparently paradoxical effect of chloralose on cerebral excitability.

I have also had the opportunity of measuring with Dr. Benoit and Dr. Vigoureux, the cycle of excitability during normal spontaneous sleep and sleep produced by hypnotics. Under these conditions the length of the cycle was not in the least modified in relation to its value as characterized by the waking state.

MORUZZI: About the excitatory influence of chloralose I should like to point out first that this effect is not seen in pigeons, in which only quiet sleep is induced (Moruzzi, 1946, 1947; Zanchetti, 1946); second, that the excitatory effect of chloralose is abolished by decerebration in mammals. If subtetanic doses of strychnine (0.05 mg./kg.) are injected in a chloralose cat, generalized clonic convulsions may be produced. These are abolished by decerebration (Moruzzi, 1944-45). Therefore, it seems that the excitatory influence of chloralose is connected with the more cephalad portion of the brain.

MECHANISMS OF NERVOUS INTEGRATION AND CONSCIOUS EXPERIENCE

By

A. E. FESSARD

'Quel rapport y a-t-il entre la matière connue et le sentiment? Comment une idée se place-t-elle dans notre cervelle? Peut-on avoir une sensation sans avoir l'idée, la conscience, le témoignage interne qu'on éprouve cette sensation? . . . Enfin, pourquoi a-t-on l'existence? Pourquoi est-il quelque chose?

'Si après ces réflexions on ne sait pas douter, il faut qu'on soit bien fier.'

(VOLTAIRE, 1768, *Œuvres Complètes*, Physique.)

I—CONSCIOUSNESS AND INTEGRATION

It is difficult to resist speculating about the integrative processes of the brain because the whole of human achievement depends on them – E. D. ADRIAN (1949 b).

The most common introspective observation reveals both the multiplicity and the unity of our states of consciousness, that are experienced as 'wholes' as well as in their ever-changing diversity. Psychologists, although considerably interested in the discriminating and selective powers of the mind, are generally agreed that integration is the major feature of consciousness, the principle of the hierarchy of its levels, and perhaps even that of its arousal: 'Consciousness arises when unconscious processes are integrated', writes F. Schiller (1952) in summarizing his recent review entitled 'Consciousness reconsidered'. But what is consciousness?

Certainly, it is not an easy concept to deal with, nor simple to define. In a modern 'Vocabulary' of psychological terms (Piéron, 1951) one finds that consciousness '*n'est pas susceptible de définition en tant qu'elle désigne l'aspect subjectif et incommunicable de l'activité psychique, dont on ne peut connaître, en dehors de soi-même que les manifestations de comportement*'[1]; and most psy-

[1] . . . 'is not susceptible of definition in so far as it designates the incommunicable subjective aspect of psychical activity, of which except for one's self only behavioural manifestations can be known.'

chologists of today have perfectly succeeded in developing a coherent science based on behaviour, taking no account of consciousness. Is it not puzzling to encounter such negative attitudes at the time when neurosurgeons are beginning, so to speak, to 'experiment' on consciousness and raise the question of its localization within the brain? The recent multiplication of symposia devoted to problems of consciousness is an expression of our present need, for scientific purposes, of a better understanding of a phenomenon which is indeed the most mysterious in the whole universe. For these scientific purposes at least, we doubt that epistemological discussions and metaphysical hypotheses, which in this field cannot be easily avoided, can ever be of real utility. By their subtleties and intricacies of points of view, the fallacy of certain analogies, the mixture of facts with respectable but unverifiable beliefs, they have obscured, more often than clarified, the naive notion every normal man has of his own consciousness.

As a consequence, one should not be surprised that the word itself has acquired a multiplicity of meanings, a fact that often creates confusion. The only generally agreed statement about consciousness is that expressed by Hughlings Jackson when he declared: 'There is no such entity as consciousness', then adding: 'we are from moment to moment differently conscious' (1931). This simply means that consciousness must be considered as an aspect of life in action, not as an entity but as an event, taking place in certain complicated organisms, and whose essential characteristic is to be 'experienced'. Be it described – and thus better termed than in the substantive form – as a feeling, a knowing or a willing, it is always an *experience*. An expression like 'conscious experience' as is sometimes proposed, would usefully be remindful of this point of view, were it not a mere pleonasm.

As a matter of fact, this primary and most direct meaning is often lost sight of in the course of discussions. We can easily detect two main sources of confusion. The one is the identification of consciousness with mind, a term which is better used to designate a more general concept, corresponding to a class of relational activities we suppose to occur within the brain where they prepare, initiate and control the most complicated forms of behaviour, those we cannot explain in terms of reflexes or automatisms. We call them *mental*. 'William James, Bertrand

Russell and Carnap maintained that patterns of relations are all that can be called mind', to quote Stanley Cobb (1952), who in his turn emphasizes the role of integration when, summing up, he declares: 'It is the integration itself, the relationship of one functioning part to another, which is mind and which causes the phenomenon of consciousness.' This phenomenon we propose to call an 'experienced integration' or EI, in order to distinguish it from mental integrations in general, for most of these remain unconscious (unexperienced).

The second source of confusion is, in contradistinction to the first, one by which consciousness is often identified with one of its most elaborated appearances, the 'Self', the 'Ego' of the psychoanalysts, and at still higher levels of complication self-consciousness or super-ego. But shall we refuse consciousness (in the sense of EI) to the baby who has not yet discovered its own 'Self', as distinct from its environment, and who cannot yet be aware of its awareness, probably in about the same way as we remember ourselves when just emerging from a deep sleep? Even in normal adults, and except perhaps in professional psychologists, the conscious process applies itself more often to external events than to mental ones. In spite of a tenacious illusion, all EI cannot be identified with the 'Self', this being a particular organization in the field of consciousness of an adult in the waking state: in other words, one can be conscious without being conscious of one's self and the essentiality of EI can be assumed to be present in the most primitive forms of sensibility as well as in the highest levels of intellectual life.

The objection has often been made that in trying to deal with consciousness we may be trying to seize an unseizable phantom under the pretext that we are not only aware of our own awareness, but also of the awareness of our awareness, and so on indefinitely. This argument has well been refuted by P. Guillaume (1942): it is clear that this process never goes very far, except in the form of a vague feeling of indefinite extrapolation; when it really takes place, it comes soon to an end, its last step being necessarily an EI that apprehends the whole situation, the mental process ceasing then to be an object for actual introspective operations, but not for retrospective ones.

It is true that it is not always easy to get sufficiently meaningful

and reliable ways of expression and symbolic communication such as are required to make an EI accessible to scientific study; but a normal man in the waking state is able to give good evidence of his being conscious or of having been so at a certain moment in the past. Sometimes, the only criteria available are crude behavioural symptoms. Then, unreliability and dangers of misinterpretation can only be surmounted by multiplying the cases, submitting the data to careful comparisons and statistical treatment, and by greatly varying the conditions of observation, including those offered by mental abnormalities. Doing so, psychologists have described and classified the main dynamic structures of mental life, establishing that EI is not the fatal result of a certain type of mental operation, although it generally accompanies the most complicated and integrated ones. Apprehension of values and meanings probably represents the highest levels of integration and the most enigmatic property of EI. Symbolism and language, the subtle tools for its expression, are at the same time powerful agents of its own organization.

Mental organizations have been particularly investigated in the domains of sensory preception, logical thought and motivation. But our major problem here is not to explain these innumerable forms mental integrations can create and reveal in characteristic behaviours or verbal expressions. Our problem is that of integration itself, particularly when it concerns EI, that is the way in which EI can be both *one* and *multiple* in each of its instantaneous states, and orderly organized in its temporal sequences.

Now the problem, if it has ever to be treated scientifically, is one *par excellence* for the modern neurophysiologist, he who knows since Sherrington that 'integrative action' is the dominant way the central nervous system operates. More specifically, we should say that the brain is at the same time an organ for widespread distribution of impulses and for their integration in spatially and temporally organized wholes. This capacity it has to carry out two antagonistic operations on the same mass of nervous messages appears to me as its most characteristic property, one we cannot fail to parallel with the main features of EI. 'But indeed, what right have we to conjoin mental experience with physiological?' To this question of his, which is also one I guess each of us has in mind, Sherrington (1934) makes a simple and direct

answer: 'No scientific right', he says, 'only the right of what Keats, with that superlative Shakespearian gift of his, dubbed "busy common sense".' Now to those who work on the nervous system, common sense speaks clearly enough, as it seems, for giving them the right to proceed without taking much care of the innumerable philosophical discussions that this question has raised in the past.

As a matter of fact, even those thinkers who do not accept a materialistic conception of Universe have little doubt that mental experience 'has a counterpart in a specific spatio-temporal pattern of neuronal activity' (J. C. Eccles, 1953). It will then be hardly disputable if as a convenient way of speaking we consider EI as a *property* of such a pattern, a property which some of us regard as intrinsic, i.e. as related to the matter and energy of the working system, while to some others it could be due to a sort of detecting power *vis-à-vis* the organization of an extra-physical world whose existence certain thinkers continue to postulate, for the dualistic hypothesis still receives support from eminent physiologists (cf. Sherrington, 1946). However this may be, our questions remain the same, viz.:

What neuronal activity is most likely to correspond to the existence of EI? How can we conceive of the integrative process that transforms an assembly of separately active neurone pools in the brain into a unified pattern? Where are all these processes likely to take place?

These questions present themselves as a challenge to the neurophysiologist of today: not that one could reasonably expect he would soon be able to offer satisfactory answers; but perhaps he could direct his experimental approaches more often towards elucidation of such fascinating problems, now that refined techniques, such as those of modern electrophysiology, have given him new means for collecting significant data. The three questions of course cannot be treated in complete separation; but that relating to localization is probably most accessible to discussion as having been the only one seriously and frequently debated in the past.

II—CONSCIOUSNESS WITHIN THE BRAIN

The mental action lies buried in the brain, and in that part most deeply recessed from outside world that is farthest from input and output — C. S. SHERRINGTON (1934).

Considerable disagreement is encountered as soon as one raises the question of a cerebral locus for consciousness.

To begin with, the remark of Herbert Spencer, noted by Penfield (1941), seems to be based on common sense: 'The seat of consciousness', he said, 'is that nervous centre to which mediately or immediately the most heterogeneous impressions are brought.' Clinicians and neurosurgeons, who have the merit of reasoning from concrete observations, do not hesitate at times to use the same expression of 'seat of consciousness'. For others, however, this has no meaning: 'There can be no centre, there is no one seat of consciousness', says Stanley Cobb (1952); and Schiller (1952) writes: 'Consciousness can have no seat, any more than terms like circulation or contractility.' I believe that the causes for these conflicting views are two in number although of unequal importance. The less important one appears to be simply a misunderstanding concerning the term 'consciousness'; the other deserves more discussion; it consists in differences of conceptions about the nervous mechanisms involved.

As regards the misunderstanding, it seems at least partly to rest upon the confusions or ambiguities we have pointed out above between consciousness, mind, the 'Self', etc. Attributing a locus to abstract logical constructions, as are often understood such terms, is obviously shocking. But when one considers this most concrete of all concrete events that is the arousal of a perception, feeling or memory, quite apart from what further intellectual analysis may reveal of its content or organization, the question takes on meaning. To take a loose comparison in the world of objects: it appears unreasonable to attempt to localize the concept of redness, of cherries for instance, although to localize the red colour of a particular cherry in its skin, does not make nonsense, although colours are abstractions, as are all attributes or properties. Likewise physiological contractility is localizable in muscles, and blood circulation has its seat in the heart and vessels. Indeed, what would be nonsense would be to speculate about a property without trying to refer it to a substratum, i.e. to the bundle of all the

other properties with which the one considered maintains strong bonds: or in other words, to speculate about a property isolated from its physical correlates, just as, in the past, one conceived of soul as detachable from body. Finally, a general agreement could probably be reached if we were not to speak crudely of a locus for consciousness or EI but of a locus for those processes which in the brain appear to be essential, but not necessarily sufficient for the special kind of integration we have called EI. About the seat of these processes, the divergences are serious, but the discussion can proceed on firmer grounds.

No one today would deny that there is a nervous substratum for EI in the brain. The question is to know whether we should consider this substratum as concentrated or diffuse, as specific to a narrowly limited region of the brain or as capable of being identified with variously situated nervous structures. This distinguishes between three main divergent opinions:

The first opinion is that the brain works 'as a whole' and consciousness is a property of its total activity; according to the second opinion, what really counts for perceptive integrations is the dynamic ever-changing patternings that are supposed to organize themselves within an undifferentiated mass of neurones such as are distributed all over the cerebral cortex; and the third is that there is a specific region involved in 'experienced' integrations (EI), the other parts of the brain participating in them only in the form of unconscious operations: the bulk of modern data indicates that this role might be played by reticular systems of neurones in the brain stem and/or the diencephalon.

The first point of view is the opinion of those who feel it contradictory to consider the possibility of a mechanistic explanation for a phenomenon such as integration, which by nature should escape analysis. Indeed any mechanistic explanation involves the recognition of parts endowed with different properties, none of which can express the resultant property of the whole assembly. It would thus be fallacious to speak of a specific centre, and in a general way to pretend discovering the solution of the problem in processes of *centralization*, although these are a major feature of brain activity. This is a negative attitude, for it expresses a renouncement as concerns the possibility of a complete understanding of nervous integration. It nonetheless leaves open a way to a

scientific approach, that directed towards the study of what appears as an essential condition for integration, namely *interaction*: in the hierarchy of conditions that integration requires, interaction between all parts of the system comes first, not centralization as is often supposed. But centralization favours interaction, and brain is already a domain of concentration *vis-à-vis* the total nervous system of which it is a part, or *a fortiori vis-à-vis* the organism as a whole. Thus we have to decide – as far as EI is concerned – whether it is sufficient to stop at this level of centralization (brain) or whether we should turn to a more concentrated structure, whose activity should in its turn be considered 'as a whole'. Of course this procedure has to stop somewhere, for pushed to its extreme, it would lead to an untenable conception, that of a privileged integrating neurone, 'one ultimate pontifical cell' as Sherrington (1947) afterWilliam James puts it not without humour.

Brain being mainly a system of intercommunications, it seems to offer the proper conditions for integrative interactions. Those communications intervening within each area and between cortical areas are classically assumed to be the determinant factors of the organization of states of consciousness. Unfortunately, there is a great deal of data showing how unimportant is the part played by intracortical connections in such organization, as well as in those that control mental operations or sensori-motor performances. Dr. Lashley's experimental contributions in this field are considerable and too well known to need being recalled here. Diverse association areas can be removed, even in monkeys, without great impairment of their perceptive or learning abilities (see Lashley, 1950). Likewise, criss-cross striations with knife cuts throughout sensory-motor fields have negligible effects on motor co-ordination (Sperry, 1947). More recently, Evarts (1952) did not observe diminution of retention or of post-operative learning capacities (auditory-visual conditioning) after extensive ablation of the Area 18 in the monkey. The effects of interruption of interareal association pathways are more severe, but more or less complete recovery regularly occurs. In man, extensive mutilations can be inflicted to grey matter without abolishing consciousness or even lowering its level of alertness; and section of important associative white tracts such as corpus callosum does not seem

to affect mental performances. Other similar observations in man or animals are now accumulating in great number and variety.

These results are so disturbing that one may be tempted to admit the irrational statement that a heterogeneous system of activities in the nervous system could form a whole in the absence of any identified liaison. The 'brain as a whole' hypothesis readily leads to such a renouncement, in favour of metaphysical postulates which are often invoked in these matters where science seems to fail. According to the holistic conception of K. Goldstein (1939) the *organism* conceived as a whole explains the unity; since it is itself one single whole, a common factor of the physical and the psychical, the claimed relationship between these two thus no longer needs explaining. According to the philosopher F. Ruyer (1946) the living being contains 'forms within himself capable of an intrinsic property of subjectivity': thus, in the case of the brain, capable of knowing the external world, since the latter projects itself thereon. On the other hand, many physiologists remain faithful to the dualistic postulate. In Eccles's view (1953) certain dynamic configurations of the nervous system may have the capacity to detect purely psychical configurations whose nature it is to be one. Sherrington considers that time is the agent of synthesis: 'Pure conjunction in time without necessarily cerebral conjunction in space lies at the root of the solution of the problem of the unity of mind' (1906, ed. 1947). He even goes so far as to say, taking as an example the fusion of retinal images: 'Their contemporaneity fuses them. There is here no need of spatial coupling in the brain' (1946). These speculations, and others, contain perhaps the germ of future explanations, but for the time being they are rather sterile in that they do not offer operational suggestions, capable of inspiring new experimental approaches.

The second and the third conceptions bring us back to a more scientific attitude as concerns the fundamental problem of *interaction*, and propose for it different solutions which are not beyond our present possibilities of experimental testing. If an integrated behaviour with its probable conscious accompaniment is possible in spite of extensive cortical interruptions of associative pathways, it may be that we have to consider other possibilities of interaction than those interfered with in our destructive procedures. First, enough transcortical or inter-areal pathways may

have been left to sustain low-level integrations as those required in the frequently poor performances selected for testing. Secondly, pathways to and from subcortical nuclei may form an equivalent or even the principal inter-connecting system; thirdly, forces of dynamic interaction may act in the absence of anatomical liaison. The first possibility would require a careful and critical examination of each experimental case. Only the second and third ones will be recalled here, and the more complicated mechanisms of integration suggested by the most recent data will finally be examined.

According to Lashley (see Lashley, this symposium, and 1944, 1950), the seat of highest integrations is still in the cerebral cortex, and preservation of function in spite of moderate mutilations would be explained by 'equipotentiality' of grey matter. An undifferentiated mass of short interlacing neurones as are found everywhere within the cortical layers would provide a network of neuropile through which excitation could spread and form 'integrative patterns'. This network could be fine enough to allow excitation to go round the obstacles or cuts and inter-connect areas lying wide apart. Some support to this conception can be found in Burns (1951, 1953) who studied the prolongation and transfer of excitatory states through isolated slabs of mammalian cortex, and invokes the same kind of mechanism to interpret his results. Properties of such neural nets will be considered in Part III.

The existence of reciprocal connections between cortex and subcortical formations such as association and diffuse projection nuclei of the thalamus immediately suggests another possibility for distant cortical areas to communicate and interact by means of nerve messages. This is the topological situation represented in Fig. 1, II, as distinct from that in Fig. 1, I, which schematizes a purely cortical integration. However, the general organization of these nuclei and others of the brain stem with which they are in close relationship renders improbable that they ever work as simple relay centres do. The non-specific thalamic nuclei together with the neural mass of the reticular formation of the brain stem, subthalamic nuclei and some of the hypothalamic structures form a complicated integrating system which seems to be more fitted to transform and reshape the incoming messages than to transmit them almost unchanged from one cortical area to another. This

system cannot be regarded as a simple alternative route for all-or-none signals that would be emitted and received by the cortex while organizing the dynamical unity it has at each moment of the waking state. It is the system itself that can pretend to be regarded as the leader of the whole organization. One is already tempted to infer this from the exceptional strategic position it has at the centre of the encephalon, a position that justifies the term of 'Centrencephalic System' proposed by Dr. Penfield (1952a) to designate it as a whole. But this leadership has been rendered more and more obvious since the last few years when the functional properties of the system have been explicited with the help of refined electrophysiological methods. After the pioneer works of Dusser de Barenne and McCulloch (McCulloch, 1944) and of Morison and Dempsey (1942a, b), decisive results have been obtained, particularly from experiments by Jasper and his collaborators, Magoun and his school, and from the interpretations Dr. Penfield gave of his systematic observations on clinical and surgical cases. Following these results, it became evident to many neurophysiologists that subcortical structures should play an important if not predominant role in the integrative processes that organize states of consciousness; but in what way, here again divergences of opinion are encountered, and there are three main views that I shall now discuss.

The one aspect that could not have failed to pass unnoticed is that relating to the role of the so-called 'diffuse projection systems' originating either in the upper brain stem (Moruzzi and Magoun, 1949; Magoun, 1952) or in non-specific thalamic nuclei (Jasper, 1949; Jasper and Ajmone-Marsan, 1952; Starzl and Magoun, 1951; Starzl and Whitlock, 1952; Hanbery and Jasper, 1953). These systems exert on the cortex a general activating action and through this, and more selective ones, control definite modalities of normal or abnormal behaviour, and their corresponding levels of consciousness. The hypothalamus is assumed by some (Gellhorn, 1952; Bernhaut, Gellhorn and Rasmussen, 1953) to be the co-ordinating centre of the whole centrencephalic system and thus to be the primary regulator of cortical activity and consciousness. But we are not concerned here with particular hypotheses nor with a survey of previous work in this field, where as everybody knows that of W. R. Hess has opened the way. It is to the

general statement that such corticopetal projection systems would offer the key for an understanding of mental and conscious integrations that it seems useful to give some more consideration and perhaps oppose some argument.

The discovery of subcortical mechanisms capable of exerting a simultaneous control upon activities occurring in separate areas of the cortex represents of course a fundamental advance towards the solutions of our problem. It has provided us with a common basis to explain the dynamic unity of cerebral cortex at different levels of mental activity, and also with a notion of how attention can exert its directional facilitating action. But this is *control* – either diffuse or selective – not real integration, if by this term we designate the co-ordinating mechanism as it works at its starting point and not only its end-effects. By these effects, cortical activity may be said to be 'integrated' but not 'integrating', this task appearing now to be that of the centrencephalic system. The diffuse projecting pathways thus seem to serve only to transfer a certain amount of order and general excitation from the central regions to the cortical areas. The problems of how these configurations are organized and on what factors the selective activations depend are then far from being solved in this way.

The possibility that the decisive integrating processes might be dissociable from those underlying conscious experience is an implicit assumption among those who recognize the predominant role of subcortical structures in integration but still refuse to locate consciousness anywhere except at a cortical level. Schema III, Fig. 1, corresponds to this conception. EI here appears as an end-product of unconscious integrations, an induced event correlated to certain levels of nervous activity in specific regions rather than to processes of interaction between these regions as had been supposed formerly.

This last conception is compatible with well-established facts in psychology; but from the point of view of neurophysiology, it is clear that it requires too much of the poorly differentiated centrencephalic system and not enough of the highly differentiated cortical structures. Most probably, considerable improvement of our formal representation of the phenomena under discussion is to be expected from a better recognition given to the role of *corticofugal projections* towards thalamus (relay nuclei

and nuclei of the diffuse projecting system), hypothalamus, subthalamus, pretectal region and midbrain tegmentum. These have particularly been studied by Niemer and Jimenez-Castellanos (1950), by Jasper, Ajmone-Marsan and Stoll (1952), by Livingston, French and Hernandez-Peon (1953). Different interpretations have been given of their possible functional significance (see Jasper and Ajmone-Marsan, 1952): regulating feed-back effects within the limits of each sensory field have most often been assumed; but in addition one cannot overlook the dynamic possibilities that would be offered by the convergence of messages from widespread areas of the cerebral cortex. Jasper and his collaborators (1952) have emphasized the probable significance of such a centralizing process for a better understanding of the way integration occurs. They proved the existence of a real centralization by showing that the corticofugal pathways project towards central fields that greatly overlap. Bremer and Terzuolo (1952) have added the demonstration of occlusion effects when nervous signals of heterogeneous cortical origin meet within the midbrain reticular formation. Referring to this 'network of closely interconnected neurones in the upper brain stem (including the thalamus)' Jasper and co-workers (1952) express their opinion that 'This central reticular formation might, therefore, serve an overall intergative function for many specific cortical activities . . .'. Schema IV, Fig. 1, is a formal representation of this conception. It emphasizes the importance of *centralization*, an operation which obviously favours interaction and the formation in X of integrated patterns of activity. Completed with indications relative to the other kinds of connections (interrupted lines), this Schema probably offers the best structural diagram the present data can inspire to represent the gross organization of cerebral interconnections that are essential to the accomplishment of a conscious activity.[1] Now the question once more arises of what part, if any, of the system has to be held responsible for the evocation of an 'experience'.

The three conflicting views mentioned above now reappear in a more precise way and to choose between them becomes more

[1] Discussions are opened concerning the details of this organization (see the suggestions of Chang, 1949; Bishop, 1949; Verzeano, Lindsley and Magoun, 1953, etc.) A synthetic scheme has been proposed by Jasper and Marsan (1952).

difficult. It is nonetheless certain that with the discovery of corticofugal projections the conception of a specific centre for EI has increased its chances. However, the primacy generally attributed to the cortex in this matter is not so easily given up and Schema IV is most often considered as nothing else but a refinement and secondary complication of Schemas III or I. Projection of cortical patterns towards X would be useful only in directing

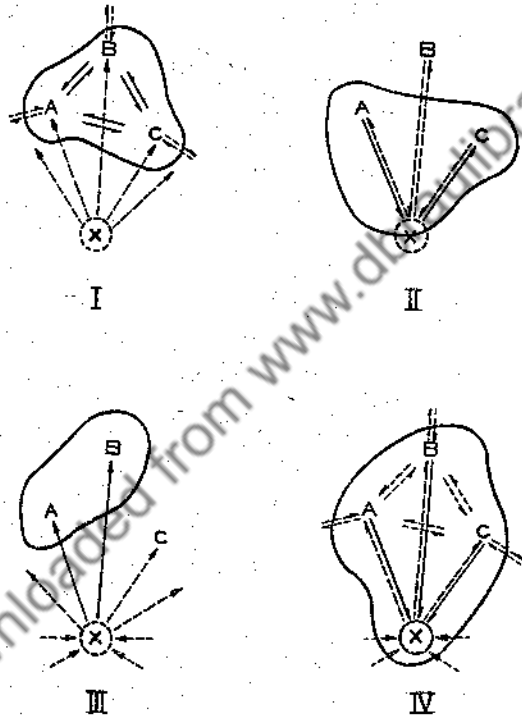


FIG. 1

Figuration, in a highly diagrammatic form, of different conceptions on the site of the nervous integrative processes that are assumed to be essential to the emergence of conscious experience. A, B, C: samples of cortical areas. X: the centrencephalic system. Connections that are supposed to be essential to EI at a certain instant are in solid lines, the other ones in stippled lines. Parts of the schematic brain that are assumed to participate 'as a whole' in a certain instantaneous 'experience' are enclosed within an irregular contour, supposedly of ever-changing aspect and location.

I. Purely cortical integration. II. Cortical integration by means of pathways through X. III. Cortical integration under the unconscious control of subcortical centres. IV. Two conceptions in a single diagram: either integration of the whole cortico-subcortical system, or pure centrencephalic integration (X).

subsequent facilitatory influences to the cortex through the non-specific corticopetal projecting pathways: an important factor of the selective activating process of attention would thus be explicited. Finally, the feeling that in the whole process centrifugal and centripetal communications are not to be really dissociated has inspired a semi-holistic view in which cortex plus centrencephalic structures are regarded as forming a unified dynamic system. 'In a very real sense, there is no "higher" and no "lower" in this system', declares Penfield (1952). 'The place of understanding is not walled up in a cell or in a centre of grey matter. It is to be sought in the perfect functioning of all these converging circuits.'

Be it as it may, the idea that EI could be specifically related to neural events occurring in a deep region of concentration is not to be rejected without serious examination. In the domain of facts, we could invoke psychiatric and neurosurgical observations that have since long supported the hypothesis of centralization of which Martin Reichardt (1928) was an early and eager proponent. Lesions restricted to the upper brain stem and regions in the vicinity of the 3rd ventricle are sometimes provocative of vivid hallucinations (Lhermitte, 1922; van Bogaert, 1927, etc.), and more often accompanied with loss or decline of consciousness: coma, hypersomnia, akinetic mutism, 'absence' in *petit mal* seizures, are the typical symptoms. A critical survey of the most reliable data now available can be found in the recent review of Cairns (1952) who declares in concluding that '. . . there are in the brain stem and thalamus mechanisms which are essential for the maintenance of crude consciousness. A healthy cerebral cortex cannot by itself maintain the conscious state'. Not less categorically, another neurosurgeon, Le Beau (1942) writes: '. . . *si elle est localisable, la conscience ne peut l'être que dans le tronc cérébral, et plus spécialement dans la région mésencéphalo-diencéphalique*'.[1] Observation of typical disturbances in behaviour and in EEG in animals (cats, monkeys) during local stimulations (Hunter and Jasper, 1949) or destruction (Obrador, 1943; Lindsley *et al.*, 1949; French and Magoun, 1952) of the same central regions have clearly confirmed their being highly critical with regard to the maintenance of wakefulness, i.e. of the con-

[1] '. . . inasmuch as it is localizable, consciousness could only be so localized in the brain stem and more specifically in the mesencephalo-diencephalic region.'

scious state, inasmuch as we can infer of it from overt behaviour.

The restriction just raised is a useful recall of the subjective nature of EI, a condition by which it seems highly improbable that despite the convincing appearance of so many favourable data a true scientific demonstration can ever be given of the reality of the postulated specific centre. This is a situation in which one has rather to judge and make a choice from theoretical reasons and doctrinal standpoint rather than to expect decisive experimental evidence; for it is fairly certain that many of the same known facts could be, and have been interpreted according to the needs of the other two theories. But it may not be vain to show that the theory of centralization is not absurd, has its logic, and perhaps its advantages.

The theory of centralization starts from the notion that a distinction should be established between the nervous specific processes that would be *essential* to the arousal of EI and those that would not, although being nonetheless necessary. Let us compare brain to a radio set, consciousness to melody: vibration of the moving coil in the loud-speaker could be called the 'essential' phenomenon, and it would not then seem absurd to speak of a locus – if not for music, at least for its basic material instrument. Other elements (valves, sources of energy, etc.) are necessary for the delivery of a good concert; but crude sounds can still be obtained in many ways from a poorly equipped loud-speaker. Likewise, the question arises as to the presence of a rudiment of consciousness (subjective experience) in living beings that are devoid of functional cortex (anencephalic monsters) or that have been experimentally deprived of it (decorticated animals). Some of these monsters can survive for years; they sleep and wake, react to sensory stimuli, express signs of pleasure and displeasure. Gross discriminative reactions are still elicitable in thalamic animals. Spontaneous movements occur. From these and other observations, one generally comes to the conclusion that a vague rudimentary awareness should exist (Cairns, 1952). This assumption cannot of course be proved; it is partly inspired by the feeling of continuity (development of consciousness in growing babies, maintenance of an unchanged waking state in human beings after ablations of different amounts of cortical structures, etc.). If the preceding statement be agreed, the two main conflicting views

under discussion may be formulated in the following way: Either subjective experience depends upon the activity of some central neuronal assembly endowed with specific properties; or it is indifferently evoked by the activity of a great number of other neural structures, particularly those within the cerebral cortex. In the first case, full consciousness would appear as a mere enrichment of crude consciousness, as a result of the projection of cortical patterns of activity down to the specific centre; in the second, full consciousness should imply a process of integration of all particular generators – so to speak – of subjective experience.

From the point of view of the neurophysiologist, it is obvious that integrative processes are more easily conceivable when interactions are known to occur within a limited space. My feeling even is that no rational basis for the identification of the nervous correlate of EI can be found in the functioning of those machine-like neural nets composed of well isolated pathways through which impulses propagate according to the 'all-or-none' principle. (The holistic and semi-holistic theories postulate emergence of EI from patterns of activity thus displayed in long-distance interconnecting nerve tracts.) Models, such as those proposed by Cybernetics, may provide in their performances good imitations of the most complicated *operations* by which behaviour reveals high-level mental activities, but they do not offer any dynamic correspondence to EI, for it appears unlikely that such a correspondence might ever be deduced from an assembly of impulses propagating along their separate pathways. This is in accordance with the common view that *consciousness seems to be linked with the preparation of action rather than with action actually taking place.* It is even probable that it is more often linked with deferred action, and that it therefore involves more inhibition than excitation. To quote Sherrington once again: 'It is possible enough that this signalling we seek to correlate with a mental event may enter in the brain a region of inhibition, there to die down and become in so far an end-effect in the brain' (1934, p. 26). This has to be kept in mind in view of the suggestions presented below (Part III).

A serious objection against the centralization hypothesis is the doubt that the converging pathways be in sufficient number and the space of projection wide enough to account for all the com-

plications and subtleties of conscious life. Considerable impoverishment of information is to be expected in this hypothetic transfer from wide cortical areas to the narrow and compact mass of poorly differentiated tissue of the centrencephalic system. However, the importance of this objection should not be exaggerated. Not only are we conscious *at every instant* of only a small part of all the information and memories available (experiments with the tachistoscope clearly show the small amount of information apprehended in the instantaneous content of the visual field) but also these data appear as a unified configuration or *Gestalt*, often simply in sketchy outlines. Projections towards an integrating centre would thus be carried out in these simplified forms, never using the total mosaic of primary projections, of which we are never totally aware in its detailed complexity. A great number of fibres would not be necessary, for only patterns seem to count in this operation and no longer point-to-point correspondence. The perceptive field is not the only one to be thus schematized; economy also exists in logical thought, that could not develop without abstractions and symbols; in voluntary command that can only lay claim to conscious control for one act at a time; and anyone has had experience of how intense pain or powerful affects completely invade the field of consciousness. In other words, there are in our conscious activity so many signs of simplification and indigence, of competition, occlusion and dominance, of complementarity between fineness and extent of operations, of dismissal to the unconscious and automaticity, that we may scarcely doubt that this is indeed the consequence of a lack of neural space, the price we pay for our capacity of integration.

Other difficulties remain, particularly that of the preservation of 'qualities' in spite of the poor differentiation of the central structures involved, but this feature has not to be so well taken for granted. Olszewski (this symposium) describes a number of nuclei of very different structure in the reticular formation and Nauta and Whitlock (this symposium) declare that 'patterns of topical organization' are likely to exist within reticular thalamic regions. On the functional side, the arousal value for a sleeping person of particular patterns of stimulation seems to reveal that the central activating system, as an acceptor of well-determined

complex messages, is itself capable of delicate dynamic differentiations. The selective process of attention also implies such a power; and we have more than one reason for relating awareness to attention, and attention to will and affectivity, whose determinant neural factors are known to operate at the basal levels of the brain.

The major question of how certain neuronal assemblies could be endowed with intrinsic properties that would specially favour integration processes is that which leads us to the next two Parts.

III—INTEGRATIVE MECHANISMS IN NEURAL NETWORKS

The integrative functions seem to be carried out as well without as with the main associative tracts. The major integrative functions must, therefore, be carried out by the network of cells of short axon — K. S. LASHLEY, 1951, in *The Hixon Symposium*, p. 133.

Whatever the way those neuronal activities related to EI control behavioural expressions of consciousness and their correlated EEG patterns, wherever it may seem adequate to locate these processes, within brain stem, thalamus or cerebral cortex, they have appeared to owe most of their dynamic features to intrinsic properties of *reticular* arrangements of neurones with short axons. Are these properties fundamentally different from those of other types of neuronal structurations? It is unlikely, except by virtue of possible but still unknown biochemical specificities of their neurones. But reticular systems may exhibit particular intrinsic properties simply on account of the special stress their internal configurations can give to certain general nervous processes. Microelectric explorations will provide us with direct data on this point, but for the time being we must be content to reason on the basis of analogies offered by the functioning of certain simpler experimental preparations or even by the formal properties of abstract schemas.

From the nature of their external relations, we can deduce that reticular systems have to perform three kinds of general operations, giving them about equivalent importance, whereas other ganglionic or nuclear centres are predominantly occupied with only one.

— They behave as a multiple transmitting system, by means of well-defined afferent and efferent pathways;

– they can receive messages without immediately sending off corresponding orders (input without output), working then as integrators;

– they exhibit spontaneous activities (output without corresponding input), generally in a rhythmic form, and exert actions as pacemakers.

For convenience, let us denote T (transmission), I (integration), A (autogenic activities) these three kinds of operations. They are performed according to intrinsic mechanisms that depend upon the geometrical as well as the dynamic characteristics of the component neurones of the system.

We have very little information concerning the arrangements these three-dimensional polysynaptic fields of short neurones actually form. We may imagine that they combine two extreme types of arrangements. The first corresponds to a non-systematically directional disposition of neurones: these may be either randomly distributed or more or less regularly connected to one another (this being more in accord with the way in which tissues grow during ontogenesis). The highly schematic figure reproduced here (Fig. 2) is that Eccles proposed (1953) while he tried to deduce some dynamic properties from the geometry of such systems. These of course must necessarily be rich in closed loops, and probabilistic reasonings have been used to render this clearer (Rapoport, 1948). The two-dimension diagram in Fig. 3A, as proposed by Burns (1951), renders this more apparent. The second type represents those neuronal connections that obey a directional tendency. It consists in neuronal chains with over-

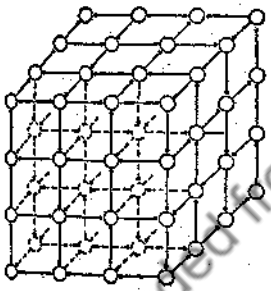


FIG. 2

A schematic representation of a simple type of neuronal network (reproduced from Eccles, 1953, Fig. 85 B). Owing to the complexity of the diagram, only the surface neurones of the deeper layers are shown, and the full connections between neurones are not all represented.

lapping fields of collaterals ending at synaptic barriers that present themselves in close succession. It has three main varieties, the linear type (Fig. 3B) that fits the T-operation, the converging type (Fig. 3C) corresponding to the I-operation, and the diverging type, not represented here.

Considerations of general neurophysiology will now be applied to the three prototypes of neural organization we have retained. We have sufficient knowledge to suspect what elementary mechanisms may underlie some dominant features of the T, I or A operations, not enough to make accurate deductions or even to be fully certain of our explanations. Before examining each operation separately, two general statements can be made which in my opinion are fundamental:

1. The reticular systems constitute fields of neural interactions in which the activity of each individual neurone can hardly be conceived in isolation; factors of interaction can be either those directed by the structural patterns of converging-diverging synaptic connections, or these same factors modified by continuous field influences of electric, osmotic or chemical origin. Dynamic properties of neurones *en masse* should predominate over a machine-like working as that exhibited in sets of well-isolated chains of neurones.

2. Due to the shortness of their axons, the component neurones of a reticular system must participate in the total activity much more by their somato-dendritic potentials than by their axonal spike. For technical reasons, physiologists have arbitrarily been accustomed to consider a neurone as essentially devoted to conduction of nerve impulses according to the 'all-or-none' principle. In neurones whose axons are thin, non-myelinated and often much shorter than the usual space constant of propagation, one may wonder whether true action potentials can really develop. Admitting that they do, a minimum velocity of a few metres per second with spike duration of 1 ms. or more would result in a wave length greatly exceeding the total length of the neurone, thus allowing only reduced potential gradients to appear externally. Local potentials on the contrary can give rise to important external gradients along the relatively large surfaces offered by the somas and dendrites where these slow variations take place. There is little doubt that these graduated potentials

are the predominant controlling agents of activity in these systems.

1. *The Reticular Systems as Transmitters*

In transmission of messages through successive synaptic barriers we ordinarily pay exclusive attention to the transformations the individual messages undergo at each step of their private lines.

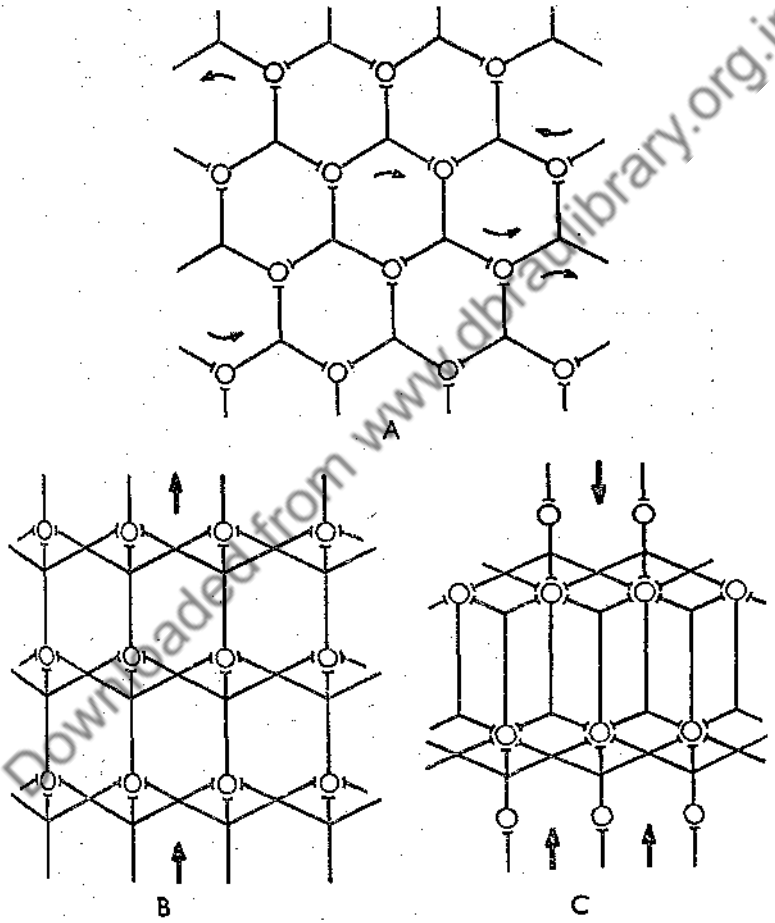


FIG. 3

A schematic representation of three fundamental forms of neuronal networks. (A) Modified figure, after Burns (1951) in order to illustrate the property he postulates that neurone rings (those containing an arrow) can be the site of a long-lasting circular activity. (B) A polysynaptic uni-directional transmission network. (C) Convergence and intrication of two opposite transmission networks.

These successive transformations, such as 'differentiation' or 'extension' (Grey Walter, 1953a) are the determinant factors of the operative properties of the neural chain considered.

In reticular systems, there are no private lines, axon collaterals form overlapping fields, and somato-dendritic surfaces are loci of converging impulses where each impulse loses its individuality. It is the number of neurones working *in parallel* that now becomes the important parameter (neurones *en masse*). Then an input-output curve of the type described in the studies of spinal monosynaptic transmissions (Lloyd, 1943; Rosenblueth *et al.*, 1949) can be applied, at least in the case of sufficiently grouped volleys of afferent impulses (Fig. 4A). In reticular systems a similar transformation exists at each set of synaptic barriers the nerve

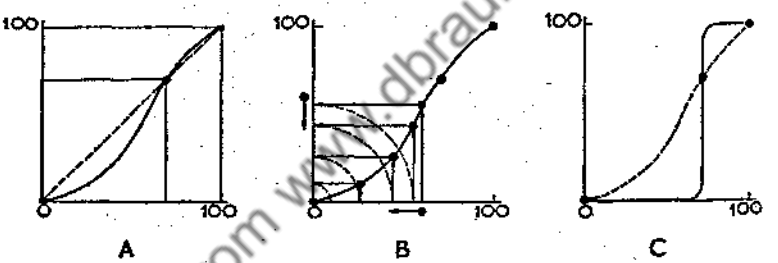


FIG. 4

This figure is intended to show how a typical input-output curve for a monosynaptic transmission of a synchronous volley (A), when applied several times in succession (B), finally results in a step-wise function (C). For details, see text.

impulses have to break through (Fig. 3B). For simplicity, let us utilize the same curve a certain number of times (Fig. 4B). Due to the sigmoid character of the curve, two different results can be distinguished. If the density of impulses exceeds a critical value (abscissa of the intersection of the curve with the bisector), the total mass of impulses will grow until it occupies completely the network available. But if the message is not too intense, it will gradually decrease until it stops somewhere within the network. The transmission curve for the whole activated region then tends towards an abrupt step-wise function, similar to the step-functions emphasized by Ashby (1952) in his 'Design for a brain' as playing an essential role in the maintenance of what he calls 'ultra-stability' (Fig. 4C). This may have something to do with the

total behaviour of the reticular systems. These at any moment are likely to appear as segregated into a number of transmitting sub-systems having each its proper step-function. A shift of the curves towards the left would correspond to an increase of the messages transmitted: this is the effect we can expect from repetition, and it could be the basis for the recruiting response.

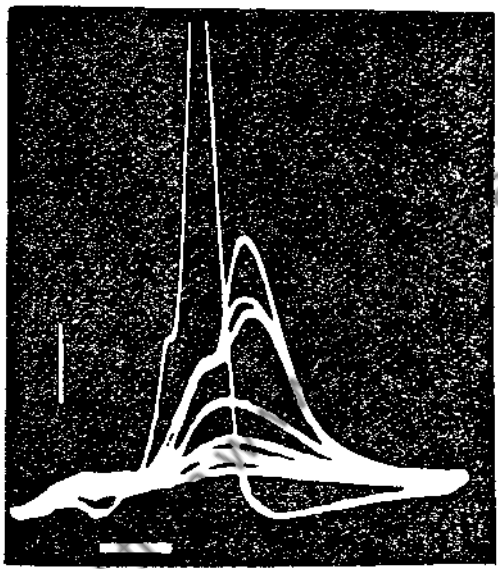


FIG. 5

Intra-cellular recording from the electric lobe of the fish *Torpedo* (cell diameter, 70-80μ; tip of the microelectrode <1μ).

Superimposed records showing responses of increasing amplitudes to a single afferent volley of increasing strength. (This increases the number of converging impulses.) All responses are non-propagated except the spike of highest amplitude.

Calibrations: Time, 2 ms; Voltage, 10 mV (from Albe-Fessard & Buser, 1952).

Experimentally, Starzl and Whitlock (1952) in their study of the diffuse thalamic projection system in monkeys have noted that the waves 'recorded at the various way-stations along their corticopetal route frequently undergo a damping as they ascend'. Such a damping effect must be even more marked in compact polysynaptic fields. Neural fields in receiving cortical areas do not always give evidence of an emission of efferent impulses in spite of well-developed slow potentials evoked in response to afferent

volleys. In a case in which this question was carefully investigated (tectum opticum of fishes, Buser, 1953), no detectable efferent effects could ever be found, except after strychnine. Although direct evidence is lacking, we may assume that in Mammals, messages from the cortex, as they converge down to the central reticular system, likewise stop somewhere, giving rise to local potentials in the somato-dendritic structures. At the cellular scale, these are the so-called 'synaptic potentials' of which an example is given here (Fig. 5) from an investigation by Albe-Fessard and Buser (1952) on the electric lobe of the fish Torpedo. This specialized centre can be taken as a model for testing the properties of synaptic fields. Record with an intra-cellular microelectrode reveals the somatic site of the local potential, and shows how it increases when the number of converging fibres to the same cell itself increases. Each local potential is thus the resultant effect of activities at different synaptic foci. Similarly, convergence of impulses on a single reticular neurone has been directly demonstrated (Moruzzi, this symposium).

2. *The Reticular Systems as Integrators*

What are the factors and modalities of integration in the poly-synaptic fields of reticular systems? Let us distinguish three cases.

1. The simplest integration process is that to be sought in the regions where well-grouped messages from a homogeneous population of afferents are arrested and have been transformed into local potentials. Gradients and currents due to these seem to be the main or the sole agents of interaction, each neurone being necessarily submitted to the electric field created by the total activity of its environing neighbours and consequently modified in some way through cat- or an-electrotonic actions. This assumption has been repeatedly made by some in the past and recently revived in interesting discussions (see *The Hixon Symposium*, 1951, discussion by P. Weiss, p. 90, R. W. Gerard, p. 108), but it has not been universally recognized, probably because no direct proof could be offered up to now of the physiological efficacy of these electric fields within the nervous centres.[1] In-

[1] Many demonstrations, however, have been given of the influence exerted on the excitability of a nerve fibre by the potential wave travelling through another one in close vicinity to it.

difference to gross experimental disturbances of the electric field in the brain is invoked against it (Lashley, this symposium), but this objection is raised against the Köhler's electric (macro-)field theory and may not be valid when one has to deal with micro-fields whose structure cannot be altered by superimposition of a *uniform* field (or regionally so).

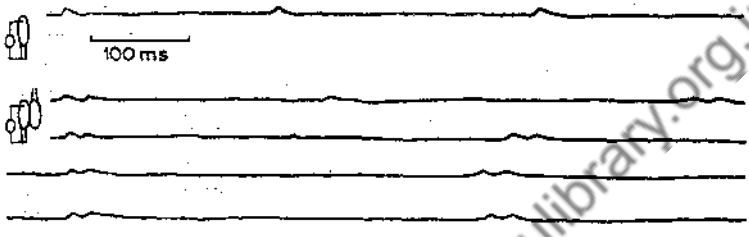


FIG. 6

First lines: autorhythmic activity of an isolated ganglionic cell from a visceral ganglion of *Aplysia*. Second and following lines: two similar cells, one active, the other passive, have been put in close contact. Note the driving effect exerted by the active cell upon the formerly inactive one (redrawn and simplified from Arvanitaki, 1942, Fig. 2).

At any rate, there exist experimental examples that bioelectric fields can exert an action — at least in certain favourable cases — on excitable elements and particularly on nerve cells. Driving and synchronization effects are eloquent manifestations of the field action of electric forces. Gerard and Libet (1940), Bremer (1941) presented striking examples, and I proposed (1942) an explanation of how two neighbouring spontaneously active elements may tend to synchronize their rhythms through the mutual electrotonic influences of their action potentials. During the same year, Arvanitaki (1942) succeeded in isolating giant nerve cells from a ganglion of Aplysia and in showing that somatic potentials from one active cell may be sufficient to stimulate a neighbouring passive one (Fig. 6). If the companion cell is also active and both rhythms are not too different, coincidences in phase are regularly more prolonged than would be expected (Fig. 7). Finally, from these experiments and also from a number of indirect observations it appears that synchronization of elementary activities in neurone pools is a very common aspect of the mass functioning of nerve centres, where it represents a gross form of integration.

2. Convergence of volleys from heterogeneous origins to-

wards a well-defined polysynaptic field is the complex activity that corresponds to the highest form of nervous integration. Fig. 3c above schematizes its simplest structural aspect, being understood

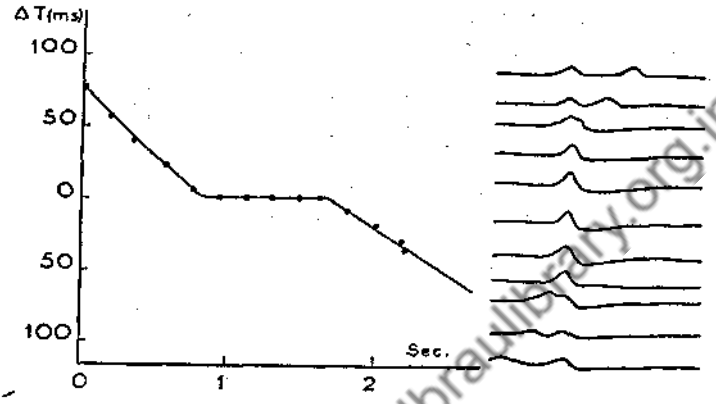


FIG. 7

Same experiment as in Fig. 6, except that each of the two cells now has its own rhythmic activity. On the right downwards, successive records showing the occurrence of the synchronized state and its maintenance in five traces. The same phenomenon has repeated itself several times.
On the left, a curve of the corresponding phase shifts ΔT.
(Redrawn and simplified from Arvanitaki, 1942, Fig. 6 and 5, respectively.)

that the reticular region is three-dimensional and can have much greater extension. A remarkable fact observable – at least in the reticular formation of the brain stem – is that one neurone taken at random can itself receive messages from various origins (Moruzzi, this symposium): this can only occur in such a finely fragmented field of neurones provided with rich collaterals as is a reticular system. This also lets us anticipate the most important dynamic feature of the total operation, viz., *competition* between different groups of afferent impulses for occupation of the same neural space.

There assuredly lies the essential mechanism to be analysed in order to explain integration within a space of centralization. According to the 'all-or-none' rule, competition can only result in the exclusion of those groups of impulses that arrive a little too late and find the lines 'busy': this is dominance of the first invader or 'occlusion', and has its behavioural expressions in unicity of

action. But this mechanism concerns only cases in which incident impulses can break through all synaptic obstacles. When the damping effect occurs and proceeds down to an arrest of all convergent groups of messages, what remains of these – after partial occlusions in marginal overlapping fields – obey another rule, that of co-operation and mutual adjustments. At the neuronal scale, the process is that of spatial summation of subthreshold excitations and inhibitions, and is now interpreted as due to electrotonic and possibly chemical spreading between the synaptic knobs ending on the same neurone. In a reticular system, mutual adjustments must mainly result – as far as we now know – from field interactions like those considered in the simplest case of homogeneous integrations (see above, paragraph 2(1)). Due to the diverse orientations of the feeding pathways, a great number of recurrent neurones must now be activated and this activation in the form of enduring circulations of impulses within reverberatory circuits is probably an important feature of the integrative mechanism. Whatever it may be, it is easy to understand that an infinite variety of transient patterns of excitation and inhibition can thus appear in a closed space: this evokes the appearance of a mosaic, the properties of a kaleidoscope or, to refer to a more modern analogy, the pictures which light up a television screen.

To what appears to be a sort of *representative function* of the receiving fields of neurones in contradistinction to their *operative* ones,[1] it is tempting to associate EI. 'I strongly suspect,' says Lashley (*The Hixon Symposium*, p. 133), 'that many phenomena of generalization, both sensory and conceptual, are products not of simple switching but of interaction of complex patterns of organization within such systems.' It would not be very difficult indeed to combine neural mechanisms of that sort whose resultant properties could be made formally equivalent to the outstanding characteristics of sensory perception (psychometric curve, figure-ground effects, contrast phenomena, etc.). However, it would be unwise, I believe, to give much credit to such 'explanations' until more is known about the intrinsic mechanisms and their specific relation to EI; for, on the one hand there are always a number of equivalent solutions for the same result, which means

[1] This representative function is finally operative in that it prepares facilitating patterns for future switchings.

that we have not enough to direct a choice; on the other, we lack a precise notion about what nervous intimate mechanism one has finally to correlate to the arousal of a conscious experience.

A necessary condition is a certain level of general excitation combined with a certain amount of selective inhibition (Jung, this symposium). Momentary distributions or patterns of subthreshold excitatory and inhibitory states in limited neural spaces, rather than the total aspect of propagating impulses through neural nets, has been proposed here as the basis for conscious experience; but what makes a pattern 'conscious' of its own patterning remains an irritating problem. In all probability, the phenomenon is related to the capacity for the elements of a pattern to acquire a great amount of mutual dependence, i.e. to integration. It has been advanced here that the interneuronal electric field could have a major role as a factor of patterning, and the poorly differentiated reticular systems have been shown to offer good conditions for these and other possible forces of interaction to play. But is there any parameter of a physico-chemical process, or a more or less complicated function of a certain number of parameters that we could pretend to correspond to levels and organization of conscious experience? Some go so far as to propose a relation of *isomorphism* between the gross resultant electric field configurations in the brain (or cortex) and the spatial characteristics of perception (Köhler, 1929, 1951). This bold conception of the early days of *Gestalt Theorie* cannot be said, in my opinion, to have many chances to survive. A *relational isomorphism*, rather than a purely geometric one seems to be a more adequate conception, but the notion of isomorphism itself, as applied to our problem, should be critically considered and more carefully discussed than can be done here.

To conclude, it is the concept of *patterns of excitatory states* that finally stands out, and it is significant that not only the spatial or temporal organizations of EI, but also its qualities – colours, tones, odours . . . – appear to depend on such excitatory patterns. This has been beautifully demonstrated recently by Dr. Adrian for odours. As for the integration process that would give rise to 'experience', not only to that of a perceptive *Gestalt*, but also of meaning or value, it might perhaps be sought in the *coaptation* of each instantaneous pattern to a pre-existent one,

present in the form of a memory trace. This is not a new idea. However vague it may seem in its present expression, it can be retained, I believe, as a promising concept.

3. There remains a case to be quickly examined, that in which a reticular system is activated in a diffuse way by incoming impulses (conditions of uniform stimulation, states of rest or sleep). Theoretically, it would not be difficult to show how the widespread and almost homogeneous activity then distributed throughout the network can only result in synchronized and periodic variations of potential. A regular rhythm is to be expected because inequalities, or even temporary absences in the afferent supply would be attenuated by the persistence of activity in the innumerable closed loops present within the system (see Figs. 2 and 3A). According to a recent and easily acceptable suggestion of Eccles (1953), the rhythm of these variations should be determined by the time characteristics of the recovery cycle of the component neurones, in parallel with the development of their positive after-potentials: the slowest rhythms would then correspond to the total duration of these, that is to around 10 a second or somewhat less. This is a striking coincidence with the order of magnitude of rhythms actually recorded from all these structures.

It is easy to understand why an arrival of sharply differentiated afferent messages can desynchronize the total cyclic pattern and conversely, why the regular cyclic condition of excitability as is found by the messages when coming in can influence the distribution and interaction of their local effects. Thus, the periodic activity is itself a factor in the integrative progress.

3. *The Reticular Systems as Autogenic Generators*

In a certain sense, rhythmic activity engendered by a mechanism similar to that just described may be called 'spontaneous', provided it is referred to the whole system, of which it is a mass manifestation. Other autogenic activities originate at cellular scale; these are the so-called 'auto-rhythmic' phenomena (such as those in Figs. 6–7). A great deal of micro-experimentation remains to be done in order to establish what part they play in functional integrations. As judged from investigations on models, they present two possible modalities: the one brings into play the recovery phase following an 'all-or-none' response, the other

does not require the emission of a spike and depends upon the auto-rhythmic forms of the local potential (Arvanitaki, 1943). Besides electrotonic influences, the factors controlling these rhythms would be mainly of a chemical nature (either of external or of intraneuronal origin).

Thus, there are many reasons why a reticular system can deliver rhythmic signals and act as a pace-maker for other regions of the nervous system. Conflicts or mutual adjustments may occur between pace-makers interconnected by long channels, for instance between a cortical and a subcortical one. All this concerns the story of their extrinsic relations. This role of pace-maker has been well-recognized in many instances, in which cortical rhythms are clearly under the control of a pace-maker situated in the centrencephalic system (cf. Gastaut, this Symposium). This is particularly striking in *petit mal* epileptic seizures, during which bilateral synchrony of the cortical EEG waves is observed.

IV—INTEGRATION AND TIME

Der Sinn des Daseins ist die Zeitlichkeit — HEIDEGGER, *Sein und Zeit* (quoted from Merleau-Ponty, 1945, p. 469).

Certainly the meaning of the sentence just quoted above is not perfectly clear; but it is an expression — among the many other proposed — of that obscure feeling one has that conscious experience and time might be related in an essential way.

Since the early days of philosophy, a great deal of speculation has been devoted to the problem, but scientifically we are not yet capable of making a precise statement about what this relationship may be. In the field of neurophysiology, the best way to do useful work in this matter is perhaps to multiply the investigations concerning the *kinetics* of nervous integration, particularly in cases showing clear correlations between cerebral activity and states of consciousness. Electrophysiological methods are well adapted to this kind of research, and striking correlations have already been obtained (Lindsley, 1952; Gastaut, 1951d; Walter, 1953a). But these results have remained sporadic and no general view about the *dynamics* of the process may be deduced with certainty. This is why only a few significant facts will be briefly presented below in

order to introduce some extrapolations whose speculative character is not to be ignored.

Attention must be given to the three main aspects of temporal organization of consciousness: EI in its instantaneous formation, the succession of conscious states, and the storage of these as memories; said more briefly, present, future and past. Let us say a few words on each of these points.

1. Whatever the mechanisms of interaction within neural fields may be, each new EI involves a process of reorganization that cannot be instantaneous: integration in time necessarily accompanies integration in space. Moreover, a small number of successive events, if not too far apart, can be perceived as a unified configuration or temporal *Gestalt*; if the intervals are too brief, less than .1-.05 sec., discrimination even becomes impossible and often new perceptive modalities appear. Some structure in the brain must constitute – so to speak – a time-binding mechanism. One finds reasons for this in elementary processes, where trace phenomena are often encountered; but the very fact that a quick succession of neural activities forms the basis for a single EI is no less an enigma than the fact of spatial integration.

It is interesting to note that a similar situation exists in microphysics where physicists are also up against the same difficulty, that of explaining the internal multiplicity of microphysical objects (atoms and molecules) and the fundamental unity of their behaviour. They did not hesitate to modify profoundly what had long appeared to be intangible concepts in order to give adequate formulations of the organization of energy at this level. Classical differential laws have been replaced by integral laws, continuity has been abandoned in favour of quantic discontinuities in exchange processes; and stationary states during which the passing of time has no meaning have proved to a be useful concept. The idea that this could serve as a lesson in other domains where similar difficulties were encountered has come to the mind of a French physicist (P. Auger, 1952) interested in psychophysiological questions. '*Pour faire apparaître cette unité, cette simultanéité qui permettrait un rapprochement avec les caractères des états de conscience*, he says, *il faudrait renoncer à l'analyse dans le temps physique . . . Il faudrait pour cela accorder à l'ensemble des cellules nerveuses qui sont en jeu, une période d'isolement qui leur*

permette de s'organiser en unité stationnaire . . .'[1] Speaking of this stationary system, he adds (p. 61): '*Il ne comportera pas d'événements, quoiqu'ayant une épaisseur de temps, il sera dynamique sans être cinétique. . . .*'[2]

Transient organizations of the conscious present do have a 'thickness in time', which cannot be neglected. One tenth of a second, or slightly more, is the common order of magnitude. Meanwhile, hundreds of dynamic interneuronal exchanges can take place in one single group of short neurones. During this time, do these integrating interactions remain unaffected by external perturbations? Relatively perhaps, if one may suppose that the screen of interposed multiple synaptic barriers yields only at moments, and then suddenly. A mechanism of transmission obeying the 'step-function' curve (cf. Fig. 4C) is just what we need. On the other hand, the rhythmic and synchronized form of intrinsic activity the reticular systems tend to take may correspond to an alternation between phases of exchange of signals (with other parts of the brain) and phases of relative isolation. Inasmuch as these systems control evocation of conscious experience, the latter should be better conceived as made of a succession of quasi-stationary states than compared to a 'stream' as it was so often proposed in the past.

Is it a mere coincidence that the most common period of the intrinsic rhythms elaborated in these systems be of the same order of magnitude as the duration of an elementary state of consciousness? Is it not striking that the spatial patterns these rhythmic activities form at each moment at the brain surface and that are revealed in toposcopic records (Grey Walter, 1953a) be capable of momentarily steady distributions, a condition without which a permanent blur would result?

It is not the place here for reviewing the facts that beyond doubt establish the existence of correlations between states of consciousness and EEG patterns. Correlations with *levels* of consciousness are particularly characteristic and are well known,

[1] 'To bring out this unity, this simultaneity which enables us to make a parallel with the nature of states of consciousness, we must renounce an analysis in physical time . . . For this we must grant to the totality of nerve cells which come into play a period of isolation allowing them to organize themselves into a stationary unit.'

[2] 'It will not include events although having a thickness in time, it will be dynamic without being kinetic.'

but it is no less important, I think, to emphasize the fact that striking exceptions have been observed, as Gastaut recalled it in offering typical examples (Gastaut, this symposium); for the discrepancies suggest that the significant relationship would not be between cortical waves and consciousness, but between the latter and a subcortical process that exerts a control which may be either strict or loose upon the cortical rhythms. The same remark applies to the association discovered between the moment of the onset of a *voluntary* movement and a certain phase of a cortical alpha rhythm (Boreham, Kibbler and Richter, 1949; Bates, 1951), for here too the correlation is not perfect, and this should cause no surprise as it is fairly certain that voluntary incitement is not a cortical affair.

The preceding observation, and many others on sensory aspects of consciousness such as the 'Brücke effect' (Bartley, 1941) and all the curious perceptive illusions due to flicker, show that most of the correlations discovered are between chronological characteristics. In relation to these, it is perhaps not without interest to recall here experiments performed long ago in Piéron's laboratory (François, 1928) that showed how the *sense of time* varies with body-temperature; for it varies according to the same law as chemical reactions do, and Hoagland, who had repeated the experiments of François, showed (1933) that the period of the alpha rhythm also obeyed the same law.

2. Time and EI appear in intimate relationship in another way: that in which the states of consciousness succeed one another. This process is an unconscious one, which delivers orderly sequences of these states according to rules that escape our present understanding: 'We are still very far from being able to form an explicit explanation of temporal structure,' says Lashley (1951), who has emphasized the importance of this problem, which he terms that of 'serial order in behaviour'. With regard to the present discussion, this process helps us to realize how we can be mistaken when in a retrospective judgment we try to appreciate the richness of content and power of action of any definite EI. These characters are most often greatly overestimated for we do not easily recognize the relative bareness of each *instantaneous* EI. Our judgment is itself the result of a temporal integration of successive experiences and of these with older memories; it is an

EI loaded with the vague feeling we have of the infinite variety of its possible states. It is the feeling of a rich property-owner who is conscious of the assets he has available at any given moment but of which he can only take advantage a little at a time. We feel also that with these assets, memory traces, logical schemas, plans of action, stored in reserve and elaborated in the appropriate cortical areas, it is possible for us to achieve a great variety of complex mental tasks; and, when contemplating some objective results, these appear in their whole complexity and multiplicity. But we too easily forget that they could not have been carried out except in innumerable steps delivered in a co-ordinated way: it is the coherence of the temporal sequences, much more than the complexity of instantaneous organizations of the conscious experience that is the dynamical basis for these performances.

3. Elucidation of the neural mechanisms that correspond to memory is undoubtedly a fundamental task for arriving at a better knowledge of the nature of the integrative processes that result in a conscious experience. The recent systematization Dr. Penfield has made, starting from his valuable observations on patients, is an important advance showing that these mechanisms begin to be accessible to scientific research, at least at the macroscopic scale of cerebral organization (Penfield, 1952b; and this symposium). But we can do very little except speculate as soon as we consider what may happen at the molecular level; and yet it is at this level that the critical contact – so to speak – establishes itself between the neural phenomenon essential to conscious experience and the forces and liaisons that exist within organized living matter, or rather within certain specific macromolecules of nervous proteins; for any conscious experience is at the beginning of a mnemonic recording, and any trace left by a conscious state is capable of engendering it anew; thus it seems difficult to suppose that the ultimate basis of 'experience' in the physical world could be of another nature than that generally admitted for the storage of memories, i.e. a more or less durable modification imprinted on a plastic ultra-structure of the neurone. The chemical specificities of the different neurones could then play a determinant role, and it must be recalled that this specificity is the property of macromolecules endowed with plasticity and hysteresis. These have the capacity of taking an almost infinite variety of metastable

states, and they may also be of this kind that is endowed with the power of self-reproduction (autosynthetic molecules). This is a view that has been recently expressed and developed by J. Katz and W. C. Halstead (1950); it may help to understand how a certain *transfer of order* could take place from the molecular domain to the neuronal populations whose activities control all the macroscopic operations of behaviour, including those of mental origin. This is the main difficulty such conceptions attempt to solve. Katz and Halstead (1950) state that: 'If a sufficient number of unorganized neurons are available, new networks may be established from templates which remain intact after cerebral injury or insult. It appears therefore that the present model is not incompatible with what appears experimentally to be anatomical non-localization of the memory traces.'

This would likewise apply to instantaneous conscious evocations, and although for these authors the responsible networks would be those within the cerebral cortex, one may wonder if less differentiated and better situated regions of the brain as are the subcortical reticular systems would not be better adapted to play this role of amplifiers of molecular forces. The real mission of interneuronal electric fields could then be that of a physical link between the infra-neuronal states of activity which determine their variations (by way of ionic changes) and the dynamic patterns of excitation they create within the neuronal fields of reticular systems. These patterns, inasmuch as they are also under the control of extrinsic factors (incoming impulses, hormonal changes, etc.) might induce re-arrangements within the same molecular structures, that would now act as 'acceptors'. This would represent an ultimate basis for the mechanism of nervous integration.

Excitability, this fundamental property of living matter which nervous structures possess to the highest degree, has long been known only by its functional consequences. It can now be expected that it may be explained in terms of molecular structures and forces. If consciousness be the most elaborate consequence of excitability, may it not be said that its deepest source likewise resides at molecular levels? Or may not consciousness be conceived as a pure product of complication?

These questions must remain unanswered at present: to this

day there is no scientific evidence which warrants a choice between two concepts which, under different guises, have been opposing each other throughout the preceding pages.

GROUP DISCUSSION

JASPER: We are all pleased that Dr. Fessard has brought us to grips with the major problem of the symposium. Although his recent work has been on the unitary elements in the electric fish, he has elaborated for us a theory which embraces the largest aspects of nervous function. The issues raised by Dr. Fessard are the very heart of our conference and should be fully discussed. However, since time is short and we have such a full programme to complete, we shall have to return to these problems later.

FESSARD: I suggest we might limit the discussion to the more elementary processes leaving the problem of 'consciousness' to be dealt with later.

JASPER: I can see the wisdom of waiting to get some more views before discussing the whole subject of Dr. Fessard's presentation, but I do hope that we won't skirt this problem for ever.

RIOCH: Just one comment on your quotation of Lorente de Nó. I accused him some years ago of supporting this idea of reverberating circuits. He denied this and pointed out that in a footnote to his chapter on the anatomy of the cortex in Fulton's book he says that the distribution of recurrent fibres is such that the probabilities of reverberating activity are vanishingly small. There are so few connections from any one cell to any given cell, that the only chance of getting reverberation is by complete organization. The 'feed-back' effects are to modify rather than to stimulate – otherwise we would be in convulsions all the time.

FESSARD: We must not forget the fact that Golgi preparations are far from giving a total picture of the neuronal distributions. It seems to me that there is a sort of geometrical necessity for a field of short neurones closely packed in a small volume, and with intermingling axons and collaterals distributed in every direction, to offer a non-negligible number of closed loops.

THE PHYSIOLOGICAL BASIS OF PERCEPTION

By

E. D. ADRIAN

Electrophysiological research on the brain has given us a new range of data to interpret in terms of cerebral activity, but until the last few years its most clear-cut result has been to confirm the findings of the neuroanatomists. Records of electrical activity have shown that the messages from the eye go to the striate area and from the tactile receptors to the post-central: they have added a great many details to the picture of cortical localization, but it is essentially the picture of projection and association areas sketched out by Flechsig, Campbell and their contemporaries fifty years ago.

The picture does not tell us how the brain deals with the messages which reach it, but it does suggest that the cerebrum has at its disposal a map of external events expressed by the spatial and temporal distribution of excitation in the receiving areas. At all events the signals from the body surface, the retina and the cochlea are all found to preserve the distribution of the excitation of the receptor surface. Such an arrangement is not surprising and may be no more than the natural anatomical grouping of nerve fibres. But if the information has to be displayed in this way for the brain to deal with it, we ought to find the same sort of arrangement for all the sense organs: we ought therefore to find that the signals from the olfactory organ are arranged to form a spatial and temporal pattern which will show the particular odour which has reached the nose.

During the past few years I have recorded the discharges from the mitral cell layer of the olfactory bulb with this question in view, but I cannot say that the results are completely decisive. There are certainly gross spatial and temporal differences in the excitation pattern corresponding to different odours, but there is also a considerable degree of specific sensitivity to different odours in neighbouring groups of receptors. I do not know how the

signals are distributed when they reach the cerebrum, but if the mitral cell arrangement is preserved it looks as though the quality of the smell may be signalled by the arrival of impulses in particular fibres which are scattered over most of the receiving area, although they may be more numerous in one part of the area than in another. It may be then that smells are distinguished by the fine detail of the receptor pattern as well as by its overall distribution. A similar uncertainty arises in connection with colour, for the general pattern of excitation could give a representation of the light and shade in the visual field, but the colour of each element of the pattern has to be signalled as well and at present we cannot say how this is done.

But before we reach the stage of having to decide the precise form in which information reaches the cortex there is a preliminary question to settle. The operations of the brain seem to be related to particular fields of sensory information which vary from moment to moment with the shift of our attention. The signals from the sense organs must be treated differently when we attend to them and when we do not and if we could decide where and how the divergence arises we should be nearer to understanding how the level of consciousness is reached.

On this question, fortunately, the last few years have given us a new directive. Thanks to the recent studies of the reticular system, we are beginning to learn something of the neural factors which decide what happens to the sensory messages, whether they find the brain fast asleep, or awake but preoccupied, or awake and ready to accept them. At all events we are in a much better position to consider the possible factors which make one sensory message pass unnoticed and give another the power of evoking sensation.

The question which I should like to hear discussed is one which may be already answered. It is the question whether the afferent messages which can evoke sensation are allowed at all times to reach the cerebral cortex or are sometimes blocked at a lower level. Clearly we can reduce the inflow from the sense organs as we do by closing the eyes and relaxing the muscles when we wish to sleep, and it is quite probable that the sensitivity of some of the sense organs can be directly influenced by the central nervous system. But even in deep sleep or coma there is no reason to

suppose that sensory messages no longer reach the central nervous system. At some stage therefore on their passage to consciousness the messages meet with barriers which are sometimes open and sometimes closed. Where are these barriers, in the cortex, the brain stem or elsewhere?

We know that in very deep anaesthesia sensory signals can still enter the cortical receiving areas. Marshall and Bard's localizing studies depend on this, and the block, as Bremer has pointed out, comes somewhere beyond the afferent endings in the cortex. Yet it is conceivable that the deep anaesthesia has suppressed an inhibitory activity which would check some or all of the signals at a lower level if it were operative.

The suggestion that the pathways may not be so freely open when the brain is nearer to the waking level arises partly from the greater difficulty of recording their cortical effect in light anaesthesia and partly from the fact that in normal waking life the picture which is presented to consciousness has many details left out. First one element of the pattern claims our attention and then another. At some stage the complete report from the sense organs must be subjected to an editing which emphasizes the important items and sets the unimportant aside.

There is clearly some such editing at work in most of the sensory pathways. It occurs in the nervous layers of the retina and probably in the olfactory bulb and it might be expected wherever the signals pass through a sheet of closely connected neurones. It might be expected in the reticular formation which provides a common meeting place for all kinds of signal, but there are the private pathways from each sense organ to the cortex and unless these are blocked at the brain stem level the signals from them should be able to reach the cortex, condensed and edited by their own relay apparatus but not by passage through any general editorial office.

We have therefore two possibilities which might be put forward. One is that the afferent signals from, e.g., the ear may be summarized on their way up the auditory pathway, but that the content of the message is allowed to reach the cortex whatever may be going on in the other sensory pathways. This means that at any moment the cortex would have at its disposal the complete pattern of the environment provided by the sense organs, but

that there is some controlling mechanism (of which the reticular formation may be a part) to decide that the auditory elements of the pattern should have priority and to make the auditory region of the cortex specially receptive and the other areas less receptive.

The other possibility is that the controlling mechanism operates at an earlier stage and that we attend to the sound and are unaware of contacts and pressures because the auditory signals are allowed to reach the cortex and the tactile signals are not.

We cannot expect to decide the point from EEG records made through the skull. In favourable conditions it can be seen that massive afferent volleys will produce a distinct cortical response, but the absence of response does not show that impulses cannot reach the cortex. The waves which we record from the surface of the brain or the skull seem to express the activity of cortical neurones rather than of afferent axons; indeed in barbiturate anaesthesia surface records from the sensory area of a cat's brain may show a complete lack of correspondence with records of the afferent discharges which reach it. But it should not be impossible to record the afferent discharges to the cortex in a conscious subject by the same technique. In the cat's brain all that is necessary is to pierce the cortex with a fine wire electrode nearly reaching the white matter. Axon spikes can then be detected without difficulty in the visual and somatic areas, though in the auditory area I have found them in the monkey but not in the cat. Whether the method would be feasible in the unanaesthetized human brain must be left for the neurosurgeons to decide, but it would certainly be interesting to look for afferent discharges and if they can be identified to see what happens to those from the tactile receptors when the subject transfers his attention from touches to sights or sounds.

We have, of course, a good deal of evidence about the effect of a transfer of attention on the surface potential waves, though much of it relates to potential waves from the association areas. Visual activity, looking, has the unique power of suppressing the alpha rhythm for long periods, but if the eyes are not in use the effect of a shift of attention is never more than a transitory interruption of the prevailing activity. There is a striking example of this in Jasper and Penfield's work on the motor area. They recorded the beta waves from the precentral region of the exposed

human brain and told the subject to clench his hands. The wave ceased, but returned again within a few seconds. When the subject was told to relax his grip there was again a brief cessation and return of the waves. In fact their disappearance seemed to be associated with the change in motor activity or the change of attention which is involved rather than with its continuance at one level or another.

Apart from vision in fact it seems to be a general rule that the rhythmic surface activity of the cortex is only disturbed for a short time by a shift of attention, although our sensations or motor efforts may continue after the cortex has reverted to its former behaviour. Thus the alpha rhythm may be suppressed for not more than a few seconds by a sound which we continue to hear for several minutes. A different but probably related phenomenon is shown in the response to flickering light, where directing the gaze to a circumscribed flickering area sets up the flicker rhythm in the corresponding occipital region for two or three seconds, yet we continue to see the flicker after the occipital rhythm has gone.

That our perceptions can outlast the alteration of surface electrical activity is not so remarkable when we remember how much can be going on in our minds when the only electrical sign of cortical activity is the regular alpha rhythm. In fact one is tempted to wonder whether the cortical structures which give these electrical waves are ever directly involved in the processes which lead to perception or intelligent action. Their continued action may be a necessary condition for the carrying on of these processes by deeper, or at any rate different, structures and the suppression of the rhythm may do no more than indicate that there has been some underlying disturbance great enough to disrupt the synchronized beat.

At all events in the unanaesthetized brain electrical records from the surface show little more than the appearance and disappearance of rhythmic potential waves and, although we can correlate their disappearance with a shift of attention, they tell us next to nothing about the complex activities on which the attention is engaged.

Now there is one example of such a rhythm which gives a little, though not much more, information, because the structures

concerned in it are more accessible and probably simpler than those in the brain proper. It is the rhythm from the surface of the rabbit's olfactory bulb. It can be recorded by an electrode led through a small hole in the skull over the bulb and brought out through the scalp incision. The frequency is high, 80–100 a second, and the waves continue as long as the animal is breathing quietly, but if it begins to sniff or if an odorous substance is brought near the nose, the rhythm disappears or gives place to the slower rhythm which occurs at each inspiration and is due to the olfactory discharge. Within a short time, 20 seconds or less, the rapid rhythm returns, although the olfactory stimulation continues; it builds up gradually in moderate anaesthesia and rapidly when the anaesthesia is lighter, but a change in the stimulus may suppress it again. In fact it shows the characteristic feature of the slower cortical rhythms in that the condition for its suppression seems to be a change in the pattern of activity rather than the maintenance of any particular level.

By leading with a wire electrode from the mitral cell layer in the olfactory bulb as well as from the surface one can try to see what effect the presence or absence of this rhythm has on the passage of signals from the olfactory region to the brain. It is seldom possible to distinguish what is happening in single units, but the general effect is that when the rhythm is present there is a continuous axon spike activity in the mitral layer; when the rhythm is suppressed by olfactory stimulation the continuous discharge gives place to one occurring only at each inspiration and obviously controlled by the stimulus.

In this case, therefore, the suppression of the rhythm involves a genuine suppression of activity, not merely a change from synchronous to asynchronous discharges in the units which gave the rhythm. This, I think, is to be expected in any collection of cells of varying degrees of instability, for once a synchronized beat begins in a small number of the most unstable cells it will produce a massive excitatory effect which will force hitherto inactive cells to join in, and similarly when the synchronized beat is broken up the more stable cells will come to rest again. At all events the development of the rapid rhythm produces continued activity and the true olfactory discharges can only be distinguished when it is kept in abeyance.

Here we are dealing with the signals from one sense organ, not with the entire range of sensory information, but the rhythmic activity of the bulb seems to provide a means for blocking the signals after a short time by keeping the lines continually occupied, for producing olfactory adaptation in fact. The organization of the olfactory pathways may be quite different from those for other forms of sensation, but it is natural to ask whether the rhythms which are found in the cerebral cortex may not operate in the same way, whether their function or part of it is not to block the further passage of afferent discharges when the information has served its purpose. The reticular formation might well be the decisive factor in the direction of attention, i.e. in the suppression of the rhythm in one region, for the signal arriving by the direct route to the cortex reinforced by one from the formation might disrupt the rhythm[1] and gain a clear path, whereas a signal not so reinforced would be unable to break the barrier.

It is easy to see difficulties ahead: the lower frequency of the cortical rhythms is a formidable obstacle and in any case it is difficult to accept the waste of energy involved in suppressing information by crowding it out with meaningless activity. Indeed the whole argument may be based on false analogy: its only purpose is to suggest experiments. Unfortunately it is only too easy to suggest experiments on the brain and it is usually far from easy to carry them out, but it should not be impossible to decide whether the appearance of a wave rhythm in the cortex does or does not involve increased activity in the cortical neurones. When we know this we shall be at least a step nearer to deciding the neural events which must occur to allow a sensory signal to reach consciousness.

GROUP DISCUSSION

JASPER: Dr. Adrian has given us a beautiful model in the olfactory bulb which may be closer to the brain mechanisms in which we are interested than might appear at first.

LASHLEY: It has never been certain whether the topological distribution of afferents to the cerebral cortex has functional significance or is

[1] It must be remembered that the disappearance of rhythmic waves may be due to other causes than desynchronization. Bremer has shown that the waves in the spinal cord under strychnine can be increased or brought to rest by electrotonic currents, and it is quite likely that the waves in the optic ganglion of Dytiscus are suppressed in the same way when the eye is illuminated.

only a product of the parallel growth of fibres during embryonic development. It seemed probable that the regeneration of fibres after section of an optic nerve would result in a random or non-topological connection between the retina and central nuclei and the presence or absence of pattern vision would then indicate the significance of topological projection in sensory systems. Dr. Sperry (1944) performed the experiments with Amphibia. The regenerating fibres became completely intermingled in the scar but, in spite of this, established their normal connections in the optic lobes. The test thus failed to give crucial evidence, but the fact that nature is at such pains to preserve the spatial arrangements in the nervous system argues for their functional importance. Study of the topology of other sensory systems reveals that only those concerned with orientation in space continue to the cortex the topological arrangement of the sensory surface. This fact must be considered in formulating any theory of brain functions.

A second question raised by Dr. Adrian concerns the place of blocking of sensory impulses, when attention is directed from them. The fact that we can attend to a part of the excitations coming from a sense organ without losing sensitivity to the remainder argues against a subcortical blocking. Thus at one point in Strauss's Don Quixote, the various instruments are singing more than twenty themes at once. The listener can follow one of these voices yet continues to hear the others as an harmonic background. All the effects of the complex sound wave reach the conscious level.

JASPER: Does the same mechanism apply to different sense modalities, for example, between visual and auditory, tactile and visual?

LASHLEY: Just now I am getting reception from my right great toe and Jasper simultaneously.

ADRIAN: There could be all sorts of degrees of the two; there may be more of your toe and less of Jasper, and *vice versa*.

KUBIE: There is a great deal of careful experimental work, dating back at least to Wundt, as well as much clinical data to prove that events of which one has been totally unaware, can register and be reproduced. Usually such events involve more than one sensory modality.

MORISON: Does anyone happen to know whether Dawson with his technique of recording incoming impulses in man notes any difference when the subject is devoting attention to incoming stimuli and when he is not.

ADRIAN: I am not at all certain. But I think he is stimulating at a very rapid rate and it is quite possible that it does not make any difference whether the subject is attending or not.

WALTER: In the visual system, attention makes all the difference to

the response; not so much in the direct projection region, but in the distribution of activity beyond the first projection; that is a function exclusively of attention.

HEBB: The problem of consciousness is not only a problem of integration, that is, the finding of an area or a system in which diverse things may be brought together, but also a problem of temporal order. As far as integration as such is concerned, you can find it in the flatworm, or in the spinal dog as Sherrington showed, but we cannot assume that this is consciousness. If we make a separation between an organism such as man, in which we are sure of consciousness, and lower forms in which consciousness is doubtful or negligible, we find that the greatest difference in behaviour is the complex temporal integration in the higher animal – implying a series of events going on in the cranium which are to some extent independent of the environment. There is intention, immediate memory, ideation or expectancy, involving processes which are not fully determined by concurrent external events. That is, I should like to raise the question, as Dr. Fessard has done, of providing not merely for the integration of present incoming sensory activities but also for activities which are not fully controlled by the present afferent input.

FESSARD: I quite agree that the problem of consciousness is not only one of integration of heterogeneous signals at each moment, but also one of temporal order. However, the ordering in itself is an unconscious process. But Dr. Hebb is right in emphasizing the role of temporal integration and of memory.

BREMER: I would like to cross swords with Dr. Fessard who has attempted to locate conscious integration in the reticular formation, and the dynamics of that integration. For the dynamics, I would fully agree that we should consider not only the all-or-none impulses, but all the subliminal phenomena and also field effects and of course memory traces. But one point on which I do not agree would be the location of that integration, if it has indeed a location, and for me it is very doubtful, because I consider integration as a dynamic abstraction and not localizable in space. However, I would certainly not have chosen the reticular formation for that location on account of the fact that information is lost there by reason of neuronic convergence and occlusion. Conscious integration excludes dilution and loss of information.

I would also like to comment on the fact that Dr. Adrian was deceived by not finding the pattern that he expected and that he located the olfactory analysis on a unitary cellular level. But after all, could not his two sets of observations be reconciled?

In the auditory system I think that Woolsey and Walz, Licklider and

Kryter, and Tunturi, have given us very strong evidence of tonal localization represented by octaves equally spaced. Given such spatial localization we are still faced with the question Dr. Adrian raised himself some years ago: if patterns arrive at the cortex, who reads the patterns?

At the time when I myself was sceptical of tonal localization I became convinced that there was a pattern and also something that was not a pattern, at least a macroscopic one: a point on a cat cortex would respond to a 1000 cycle-tone and, when after a few seconds that response was exhausted, a sudden shift, to an 800 cycle-tone for instance, evoked a response as strong as the first one. This showed that there are – as we knew from Helmholtz – separate cochleo-cortical lines, converging to the same cortical patch but not the same cortical neurones. Here the pattern, if any, should be on a microscopic scale. The ratio of the two tonal frequencies which could be so discriminated electrocortically by the observer corresponds to the ratio which a cat is able to discriminate from behavioural evidence (about a quarter-tone).

With regard to the function of the alpha rhythm I was intrigued by the suggestion that it could be a mechanism of attention. It seems more likely to me that these waves are what I called sometime *ondes de repos*, nothing else but the cells beating together because they have nothing else to do. However the waves could eventually be associated with fluctuations of cortical excitability. Experiments by Bates have shown that a voluntary movement could be triggered by alpha rhythm.

ADRIAN: I agree that there is a mixture of the pattern and detail in the olfactory mechanism. The receptors which are specifically related to acetone, etc., are more numerous in the front, whereas those for oily smells are usually found further back, but I doubt whether the distribution is anything like as well spread out as it is in the auditory system.

JUNG: Is there any relation between the rapid 50 to 100/sec. rhythm and the axonal discharge you can record in the olfactory bulb? The second question is to Dr. Fessard, concerning the relation between the slow rhythm in single cells and that of the spike discharge. Working with microelectrodes in the cortex we were very disappointed to see that there is not much connection between the spike discharge and the slow waves.

ADRIAN: The olfactory bulb shows very little relationship.

FESSARD: Our recent work with intracellular microelectrodes has indicated a close relationship between spikes and slow waves, but it is true that picking up outside the cells gives results that vary from one trial to another.

JUNG: I like Dr. Adrian's suggestion of the alpha rhythm wiping out what was going on because we have been thinking on a similar line. Toennies and I believe that the normal rhythms provide a homeostatic mechanism keeping the cortex at a happy mean level of activity, and preventing convulsions.

MAGOUN: Does Dr. Adrian recall the suggestion by Bishop and Bartley that the alpha rhythm keyed the excitability of the cortex so that in phases of it there was a facilitation of evoked potentials and some psychological phenomena that indicated more acute visual perception than in other phases of the alpha rhythm.

JASPER: This has been called the Bartley effect in visual perception. They found that brightness was increased subjectively when frequency of flickering light reached the frequency of the alpha rhythm. This was presumed to be due to the facilitation of the afferent volleys and alpha as they reached the visual cortex.

WHITLOCK: In a recent study conducted in collaboration with Dr. Arduini and Dr. Moruzzi, spontaneous all-or-none spike discharges were recorded from the pyramidal tract or from the corresponding motor cortex of unanaesthetized cat in which the mesencephalon had been transected except for the cerebral peduncles. The units selected for study were those which discharged only during and more or less synchronously with the spontaneous spindle activity in the cortex. These all-or-none units disappeared completely during arousal elicited either by electrical stimulation of the thalamus or by blowing a puff of air into the nose. When a 0.2 per cent solution of strychnine was applied locally to the motor cortex, the frequency of the spike discharge augmented. The same stimuli, however, were still effective in blocking their discharge. This tends to support Dr. Adrian's hypothesis that suppression of rhythm in the olfactory bulb involves a genuine suppression of the activity of some cells and not simply a change from synchronous to asynchronous activity.

FESSARD: May I add a few comments in reply to Dr. Bremer's serious objections towards some of the ideas I discussed here. I agree that assigning a limited sub-cortical region the power of integration that manifests itself in conscious processes is a bold hypothesis, of which — needless to say — I am neither the originator, nor the sole proponent here. But is it a bolder hypothesis than its alternative, which rests upon the assumption that consciousness might be a consequence of the total activity of the brain ('brain as a whole'), or at least of that of the whole cortex? Shall I repeat that we are pretty sure that only some parts of brain are involved in any instantaneous conscious experience, and that unless we believe in the possibility of an integration outside our world of matter and energy — which I do not — we have to conceive of a

way through which such parts can communicate and rapidly interact, in spite of their often being supported by structures that lie wide apart. Now, however cautious one may be as regards the interpretation and generalizations to be given to experiments and clinical observations that show the minor role played by transcortical connections, one cannot deny or overlook the striking contrast between the tolerance of the cortex to mutilation and the existence of regions in the brain stem that are highly critical regarding consciousness. Consequently, I maintain that the first hypothesis deserves a serious examination, and should not be rejected too quickly under the pretext that it could not easily fit with our present views on the fundamentals of central nervous activity.

Dr. Bremer has judiciously pointed to its main difficulty, that is, to the loss of information that would result from the simultaneous arrival of impulses from different origins upon the same neurone, as we now know that this happens in the reticular formation. I admit that this difficulty is not easily disposed of, but I do not agree with Dr. Bremer when he says that integration cannot go with a loss of information: psychologists would certainly support the idea that integration is only obtained at the cost of big losses of details, as when a perceptive Gestalt is apprehended as a whole, its components being totally ignored. On the other hand, as regards the neuronal mechanisms, it is true that multiple messages converging upon one single neurone result in a loss of most of their informative content as soon as one of the messages fires off the neurone, thereby occluding the others; but the situation is quite different at subliminal levels, when the structure of each message exerts its action independently and locally, at its own synaptic loci. This finally results in a micro-integration at the surface of the neurone, a process which is simultaneously present in the whole population of similar neurones that are activated by the same family of axon collaterals. This is still all classical, I suppose. The boldness appears only as soon as one considers that these infra-neuronal differentiations and structurations might have a functional significance, especially for the arousal of consciousness, and thus contribute to specific patternings within an otherwise undifferentiated pool of neurones.

As an excuse for this boldness, may I recall that one of the trends of our basic neurophysiology of today is to give more and more importance to subliminal processes and consider the neurone as a fractionable dynamic unit.

I would add that I do not want to commit myself in speaking of the reticular formation particularly; 'reticular systems' evoke the similar thalamic and sub-thalamic reticular structures as well.

THE BRAIN STEM AND CEREBRAL ELECTROGENESIS IN RELATION TO CONSCIOUSNESS

By

H. GASTAUT

This report is mainly concerned with an objective review of clinical electroencephalographic observations.

The evidence we propose to bring forward has been arranged in three sections, according to their relation to the possible existence of:

1. A non-specific system, diffusely projecting from subcortical structures to the cerebral cortex of man;
2. Several non-specific systems projecting to various parts of the cerebral cortex;
3. Relations between electroencephalographic manifestations of these two systems and variations in states of consciousness.

I—OBSERVATIONS INDICATING THE EXISTENCE OF A DIFFUSE NON-SPECIFIC SYSTEM OF PROJECTION TO THE CEREBRAL CORTEX OF MAN

The object of these observations is to show the existence of subcortical structures whose function is to regulate the fundamental electrogenesis of the cortex, i.e. to ensure bilateral integration and synchronization of its rhythms.[1]

Many authors accept as experimental proof of this regulation the fact that section of the corpus callosum does not suppress the synchronous bilateral expression of most of the spontaneous and provoked electrical activity of the cerebral cortex. Clinical electroencephalography is not lacking in such evidence; we have ourselves observed this in subjects with agenesia of the corpus callosum, verified radiologically and even anatomically. The records of these patients were taken from symmetrical points and

[1] We use the terms 'bilateral and synchronous activity' and 'bilateral rhythmic synchrony' in the electroencephalographic sense; that is to say, we have in mind those rhythmic activities most often in the form of fusiform bursts which occur simultaneously in corresponding regions of both hemispheres, with approximately equal frequency.

at high speed, in order to observe their phase relations; and it appears to us clearly established that spontaneous and provoked rhythms, both physiological and pathological, remained bilaterally synchronous in the absence of the corpus callosum. This is especially illustrated in the case of a patient (Fig. 1) in whom congenital absence of the corpus callosum was anatomically verified and in whom we observed the development, under the influence of a progressively fatal basal meningitis, of fusiform bursts of delta waves, bilaterally distributed, synchronous and symmetrical on the frontal regions.

Apart from this negative evidence, there are many points which demonstrate in a positive way the subcortical origin of bilateral synchrony in the EEG.

1. *Slow bilateral synchrony* may include three types:

Subalpha rhythm, 8 cycles/sec. continuously distributed over the posterior regions of the scalp.

Theta rhythm, 4 to 7 cycles/sec. more often in the middle regions, and tending to appear in bursts.

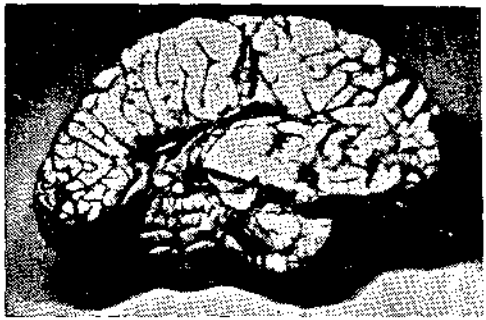
Delta rhythm, 2 to 3 cycles/sec., particularly in the anterior regions, and always in fusiform bursts.[1]

We have always attempted to demonstrate the subcortical origin of these slow, bi-synchronous rhythms, and in 1947 we presented a paper at the First International EEG Congress in London on 'Anatomical evidence of the subcortical origin of the theta rhythm'. Since then we have continued to take an interest in this question and we have been able to make about one hundred observations in this connection.

From these observations it appears that infiltrating and destructive lesions of the medulla oblongata and the pons do not appreciably modify cerebral electrogenesis, whereas those of the mesencephalon and the diencephalon produce slow bilateral synchronizations in fusiform bursts. In this connection we report the three following observations (Fig. 2, A, B and C):

A. A child showed a complex symptomatology suggesting polioencephalitis which became fatal without causing the slightest alteration in cerebral electrogenesis. Anatomical examination showed in reality an infiltrating glioma of the medulla and lower pons.

[1] These three types correspond, up to a point, with three degrees of increasing deterioration of cerebral electrogenesis.



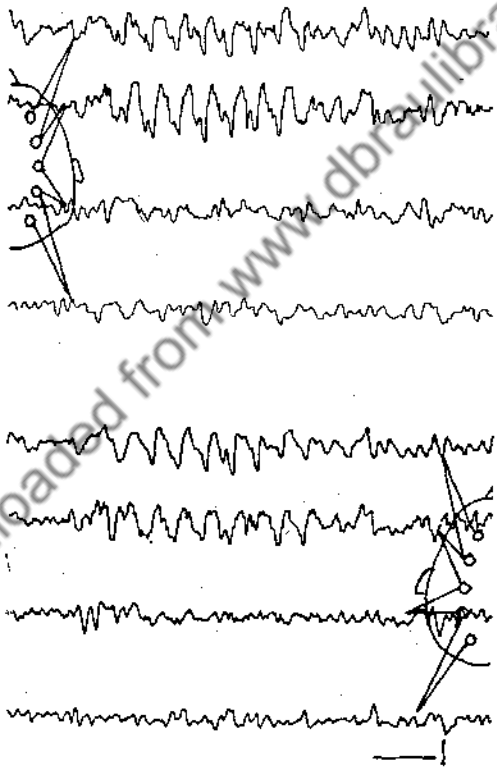


FIG. 1

Agenesis of the corpus collosum, diagnosed at Tel Aviv in 1944 by pneumoencephalography and confirmed at the Mayo Clinic in 1947. Post-mortem performed in 1950 at Marseilles. Death due to suppurative basal meningitis – EEG showed fusiform bursts of frontal delta waves typical of widespread basal pathological conditions – Note that bursts are bilateral, synchronous and symmetrical in spite of absence of corpus callosum.

B. A male patient showed a pedunculo-pontine syndrome, with involvement of the left 3rd cranial nerve, hemianaesthesia and right hemiplegia. His EEG was characterized by fusiform bursts of theta waves at 4 cycles/sec., bilateral, synchronous and symmetrical. Anatomical examination showed a small softening occupying the tegmentum of the midbrain and pons.

C. A female patient died in the course of progressive cachexia. Her EEG showed basic rhythms of 8 cycles/sec. with bisynchronous fusiform bursts of parieto-temporal theta waves and frontal delta

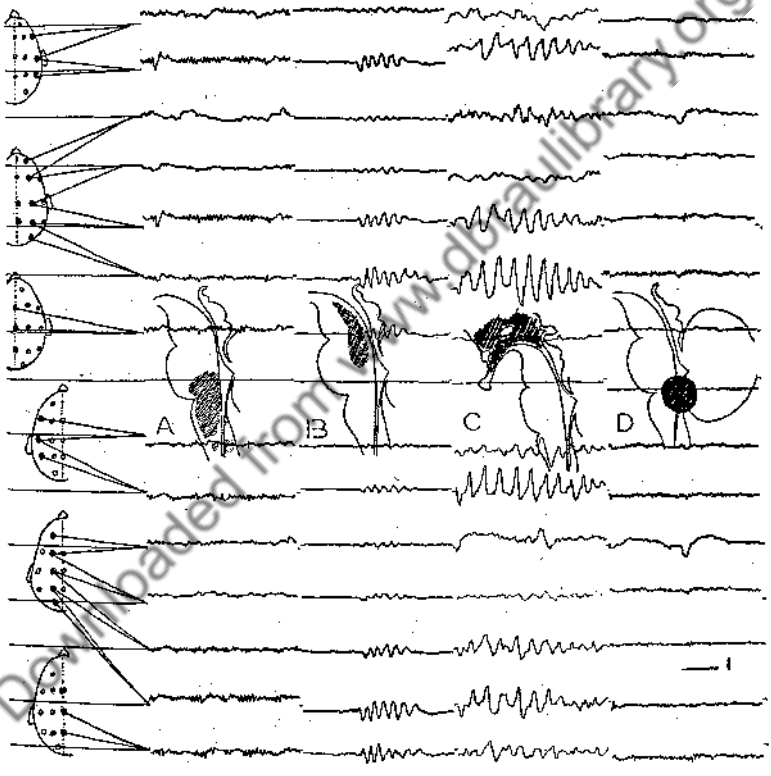


FIG. 2

Four records which illustrate the following rule:
(1) Destructive lesions of the cerebral axis do not alter the cortical electrogenesis when situated caudally (A = infiltrating glioma of medulla) whereas they provoke a slow hypersynchronization when situated rostrally (B = softening of tegmentum mesencephali; C = ependymoma of 3rd ventricle).
(2) Irritative lesions of cerebral axis provoke a desynchronization of cortical electrogenesis whatever their localization (D = Neurofibroma of the acoustic nerve).

waves. Anatomical examination revealed a systematized neoplasia of the ependymal lining of the third ventricle, covering the walls of the latter with a thin layer of neoplastic cells.

Apart from this anatomical evidence, there exists functional evidence from which we have selected a few cases of bilateral and synchronous delta rhythm appearing transitorily following operation in the supra-optic region. We distinguish these cases from others in which opening of the supra-optic lamina caused the same kind of rhythm to disappear by suppressing the ventricular hypertension which had provoked it.

2. *Rapid bilateral synchronizations* are exceptional apart from those encountered in cases of *grand mal* (epilepsy) during seizures or sleep. Their subcortical origin is generally admitted, and we will not mention here the ample clinical evidence for the diencephalic origin of *grand mal* epilepsy.

3. *Complex bilateral synchrony*, spike-wave complex (*petit mal*) and multiple-spike-wave complex are of subcortical origin; this is scarcely disputed. In this connection we quote the remarkable case of a young girl subject to typical electrographic and clinical *petit mal* lapses since the age of 6 years; the attacks began a few months after smallpox encephalitis which had resulted in an objective sequel of acromicria (the hands and feet of this adult girl have remained of the size of a six-year-old). We report also the case, already mentioned, of a systematized neoplasia of the ependymal lining of the third ventricle infiltrating both sides of the medial aspect of the thalamus. Under intermittent photic stimulation this patient showed complex bilateral synchronization of 3 cycles/sec. spike-wave type.

These epileptic hypersynchronizations are also interesting in that they are accompanied by motor phenomena which enable electro-clinical correlations to be observed. Comparison between motor phenomena and their accompanying cortical discharges shows that there is no causal relation between them, although they each depend upon a subcortical discharge (probably reticular) which is provoked by reticulopetal afferent impulses and which is responsible for the cortical complex by reticulo-(thalamo)-cortical projection, and for myoclonia by reticulo-spinal projection. This independence between cortical discharge and muscle twitch explains why one or the other may be lacking

in the electro-clinical picture (myoclonia without cortical discharge, as in sleep; cortical discharge without myoclonia, as in most inter-critical EEGs in generalized epilepsy). It also explains why one or the other may be asymmetrical (bilateral myoclonias more pronounced on one side of the body which may simulate somato-motor attack when they are rhythmic; or *petit mal* discharges more pronounced on one hemisphere; or *petit mal* attacks with conjugate deviation of head and eyes, etc.)

4. Finally we must consider bilateral activities commonly known as 'flat records' which seem to correspond to a process of 'desynchronization' of cortical electrogenesis, since intermittent photic stimulation is able to re-synchronize them in the occipital-parietal-temporal regions – (photic-driving). When recorded with suitably placed widely spaced electrodes, and with sufficiently high amplification, the records are seen to be made up of fast rhythms of low amplitude exactly corresponding to the 'activation pattern' of English and American neurophysiologists.

There is no doubt that the majority of these desynchronized records are related to the subject's mental state; for this reason they are frequently encountered in psychopathic cases and chiefly in anxiety states. For the same reason, they are usually observed in subjects experiencing intense and lasting anxiety-provoking sensations. These waves are characteristic of chronic tinnitus, whether of central or peripheral origin (Taury and Goubert, 1952); and they are usually observed in cases of psychosomatic affections – asthma (Panzani and Turner, 1952); eczema (Charpy *et al.*, 1952); arteritis (Taury and Audier, 1953).[1]

It is not less certain that the desynchronized records also accompany lesions which irritate the upper brain stem without infiltrating or destroying it, as in cases of acoustic neurofibromas. These lesions are too numerous to be all illustrated and we limit ourselves to indicating that desynchronized records are usual in cases of cranial trauma which have included comatose episodes and left a subjective syndrome (contusion of formations at the base of the brain resulting from *contrecoup*). We note also the semi-experimental observation of a case of a chromophobe adenoma of the pituitary which showed completely desynchronized waves and following operation recovered an alpha rhythm (Fig. 3).

[1] References are to work done in our laboratory.

Before closing this section, it is as well to mention that the organization of cortical electrogenesis does not depend exclusively on the subcortical regulating centres and their non-specific system of projection; specific afferent systems undoubtedly play a part in this connection. Here are two examples: on the one hand, the alpha rhythm—notable for its bilateral synchrony (each burst begins and ends on one hemisphere at the same time as on

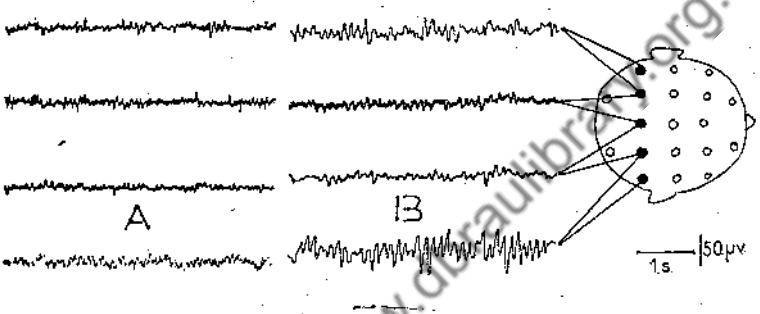


FIG. 3

Records taken from patient presenting a pituitary chromophobe adenoma.
A = before operation — alpha desynchronization.
B = after operation — distinct alpha rhythm.

the other)—occupies the occipito-parieto-temporal regions (which receive partially crossed sensory projections) and ceases on both sides at once when one eye only is opened; on the other hand, the beta rhythm—notable for its lack of bilateral synchronization (each burst occurring quite independently on the two hemispheres)—occupies the central region (which receives afferent impulses mainly crossed) and disappears on one side only when the opposite fist is clenched. It is therefore probable that the regulation of cerebral electrogenesis depends on specific as well as non-specific projection systems.

Conclusions

The above facts seem to indicate that in normal as well as in pathological conditions, the cortical electrogenesis of man is subject to the regulating influence of deep structures, among which the reticular substance of the brain stem plays a major role. This influence shows itself synchronously over the whole cortex

of both hemispheres, and must act through diffuse cortical projections which are still to be determined.

It seems probable that in clinical electroencephalography as in animal experiments (Moruzzi and Magoun, 1949; Lindsley, Bowden and Magoun, 1949) stimulation of the whole of the regulating structures of the brain stem provokes a diffuse desynchronization (activation pattern) whereas destruction of their rostral part leads to a slow synchronization in fusiform bursts. It is, however, certain that in both normal and pathological human beings, the coming into play of these regulating structures is more often functional than lesional, and that it occurs through reticulopetal afferents, a certain number of which consist of collaterals of sensory pathways. It is this mechanism which explains phenomena of desynchronization and resynchronization of peripheral origin which constitute many of the characteristic elements of 'functional' electroencephalography (transitory reactions of 'blocking' and 'arousal';[1] lasting desynchronization in painful permanent syndromes and tinnitus, etc.).

II – OBSERVATIONS SHOWING THE EXISTENCE OF SEVERAL NON-SPECIFIC SYSTEMS PROJECTING ON TO VARIOUS REGIONS OF THE CORTEX

We are personally convinced that most 'localized' EEG manifestations are of deep-seated origin and that they are projected to a point of the cortex from the corresponding subcortical structures; each system of projection thus delimited constitutes what may be termed a 'cortico-subcortical sector' (Gastaut, 1950, 1951c); we shall see later that it is more probably a question of cortico-thalamic or areo-thalamic sectors.

Madame Y. Gastaut (1951, 1952) has recently identified three localized varieties corresponding to this mechanism; namely the 'functional' spikes corresponding respectively to the occipital, central and vertex regions.

The occipital 'functional' spikes[2] (Fig. 4, TOd, TOg) exist only

[1] We will not deal with this important question, which has been the object of numerous clinical EEG studies, and has recently been taken up again by Li, Jasper and Henderson (1952).

[2] When Mme Gastaut described this EEG sign in 1951, she was unaware that C. C. Evans had already read a paper on the subject at the EEG Society of London in 1949.

when the eyes are open and when the recording is made in a well-lit room. They are bilateral and synchronous, though often asymmetrical; their topography, morphology and initial positivity enable them to be identified with potentials evoked in the same region by flashes of light, and for this reason Y. Gastaut considers that they are 'evoked by afferent impulses coming continuously from the illuminated retina when by chance a favourable tempor-

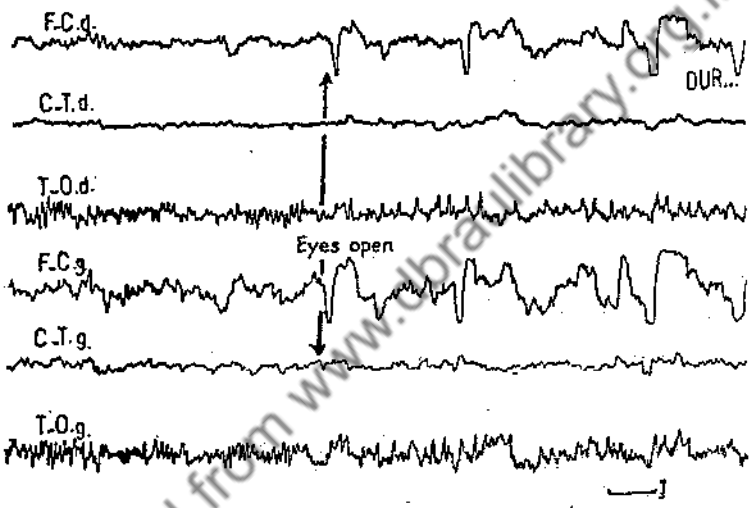


FIG. 4

Typical occipital spikes occurring when eyes are opened.
Channels = F.C. = Fronto-central; C-T = Centro-temporal.
T-O = Temporo-occipital (d = right; g = left).

ary summation enables them to make use of one of the phases of facilitation of the cycle of cortical excitability'. One should not be led to believe, however, that these occipital spikes are exclusively related to the conditions of lighting: they increase considerably when the subject is looking at a film although his retina is much less illuminated than when the lights are on. The spikes appear to be increased by the interest of the scene and the attention paid to it.

The central 'functional' spikes (Fig. 5) of the same polarity but of shorter duration than the preceding ones, are often asymmetrical when they come from both sides at once. They seem to

correspond to a hyperexcitability of the precentral cortex, in the same way as the spikes at the opening of the eyes correspond to a hyperexcitability of the occipital cortex. As the precentral projection system in man includes proprioceptive afferent volleys (G. Dawson, 1947; H. Gastaut, 1952c), Mme Gastaut relates the

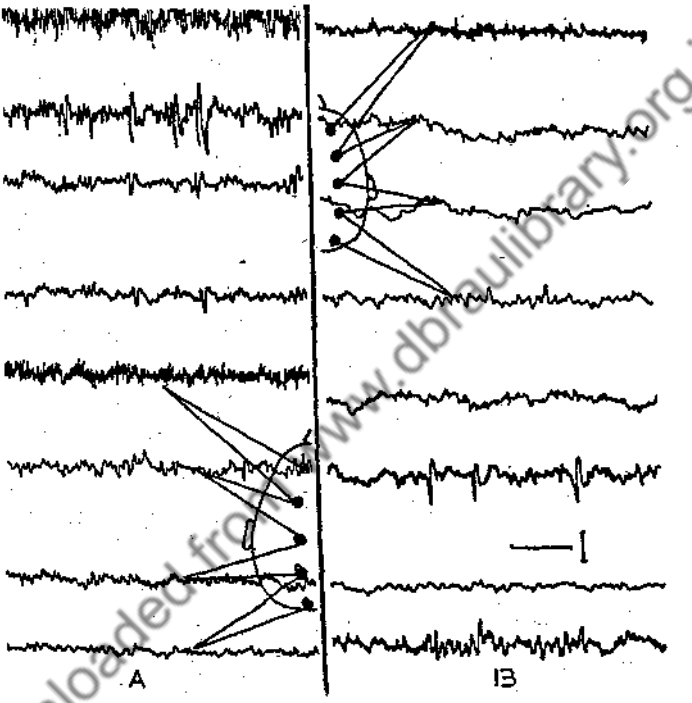


FIG. 5

Typical example of functional central spikes. The two records A and B belong to two different patients, both presenting a spastic diplegia. In A, hemiplegia more marked on the right side. In B, hemiplegia more marked on the left side.
Note that central spikes are localized on the same side as the hemiplegia.
Their functional nature explains their (paradoxical) localization.

functional spikes observed in this region to a local cortical 'tonus' condition, increased under the effect of a sustained bombardment of proprioceptive afferents (which explains why central spikes are observed particularly in dystonic muscular cases characterized by intense but variable spasticity or by paroxysmal recurrence of the tonus).

Unlike the above spikes, the 'functional' spikes taken from the vertex (Fig. 6) are initially negative. Their special characteristic is that only exceptionally do they occur spontaneously; they are provoked in 25 per cent of the subjects and with a latency of 50 to 100 milliseconds by auditory, tactile and (incidentally) visual

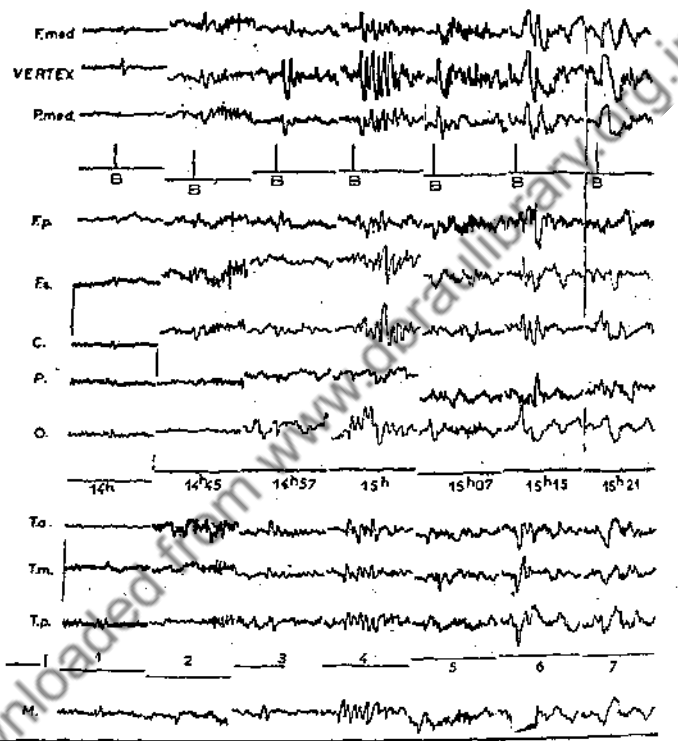


FIG. 6

Example of spikes from vertex.
Unipolar lead with contralateral occipital electrode.
F. med. = mid-frontal; P. Med. = mid-parietal; P. p. = frontal; F. s. = superior frontal; C = central; P = parietal; O = occipital; T.a = anterior temporal; T. m = mid-temporal; T. p = posterior temporal; M = mastoid.
In each segment, B indicates the noise provoking the spike at the vertex.
(1) Waking state: note the alpha blocking following spike at vertex (attention reaction).
(2) Drowsiness: note the reappearance of alpha rhythms after spike at vertex (arousal reaction).
(3) and (4) Light sleep: ample and numerous vertical spikes.
(5) Normal sleep: spike at vertex followed by spindle of 14 cycles/sec. rhythm in frontal regions.
(6) and (7) Deep sleep: spikes at vertex of great amplitude and duration, diffusing widely over head and taking on the appearance of 'K-complex'.

stimulation. The response is more marked as the stimulus is more intense and unexpected, which leads one to suppose that under optimum conditions all the subjects may respond.

The spikes obtained from the vertex are often accompanied by a brief cessation of the alpha rhythm in the parieto-occipital regions and by an electrodermal (psychogalvanic) response, sometimes so strong that it appears on the frontal derivations of the EEG.

If the subject goes to sleep, the spikes on the vertex become larger and tend to repeat themselves (multiple responses), at the same time occurring apparently spontaneously. Soon they are accompanied by small bursts at 14 cycles/sec. which also appear on the vertex region. Finally they become larger and spread out assuming all the characteristics of a 'K complex' (Fig. 6).

We presume that the spikes on the vertex represent in fact the potentials produced at the bottom of the medial aspect of the hemispheres, on the gyrus cinguli. This is in accordance with some electrocorticographic observations in man and with experimental data at present recorded in our laboratory (potentials produced in the cingular region of the cat by auditory, tactile and visual stimuli). If this is indeed the case, it would be necessary to admit the existence, on the medial aspect of the brain, of a region of convergence of all sensory routes.

Our hypothesis in our present work is that each specific message arriving at the cortex of the convexity (epicritic) may be accompanied by a non-specific 'duplicate' (protopathic) for the cingular region; a secondary message whose arrival is indicated by the spike on the vertex and which carries the affective charge of the information and determines the somatic and vegetative components of the 'startle reaction', psycho-galvanic response, etc. It is obvious that, according to this hypothesis, the increase in number and importance of the spikes on the vertex during the transition into sleep, followed by their transformation into K complex during sleep itself, would take on a considerable psycho-physiological importance. We would point out that Mme Gastaut, when describing the spikes on the vertex, was merely re-discovering a phenomenon already glimpsed by Pauline Davis at the very beginning of clinical electroencephalography. The latter admitted the existence of a non-specific response, comparable to the

secondary discharge of Forbes and Morison. This conception is untenable today as it is clear that response from the vertex is strictly localized whereas the secondary discharge of Forbes and Morison is characterized by its diffusivencss.

It is clear that the spikes from the vertex can only be caused by a non-specific projection system as they are provoked by auditory and visual stimuli which have no representation in that area. The existence of functional occipital and central 'spikes' does not demonstrate the existence of non-specific projections on the corresponding regions of the cortex. Everything leads us to believe, however, that specific projections are insufficient to explain the functional spikes referred to above; firstly because these spikes occupy a much wider area than the corresponding specific area, and secondly, even more important, because the occipital spikes, taken as an example may be observed on the opposite hemisphere to a homonymous lateral hemianopsia. This observation corresponds moreover to that made by R. Naquet and Y. Gastaut, according to which a cortical lesion destroying electively Area 17 does not suppress the alpha 'driving' by intermittent photic stimulation – it even increases it sometimes – whereas this 'driving' is suppressed in the case of a lesion destroying most of the occipital cortex without provoking hemianopsia. It is therefore necessary to assume the existence of non-specific systems projecting on to the specific regions and able to be activated by corresponding sensory messages (collateral branches).

We will now make use of pathological examples to illustrate the existence of non-specific areo-thalamic projections. For this purpose we will consider subcortical localized epilepsies whose electrical climaxes manifest themselves over a more or less wide region of one side of the cortex.

We have first individualized (Roger, Gastaut and Chatrian, 1953), a variety of epilepsy whose electric discharge affects one hemisphere to the exclusion of the other. It therefore does not correspond exactly to a partial epilepsy developed on a single areo-thalamic sector, but rather to a semi-generalized epilepsy affecting all the sectors on one side (or, what amounts to the same thing, the diffuse system of projection of one single hemisphere). From the electrical as well as from the clinical point of

view, it is a case of a partial *grand mal*, i.e. the characteristic discharge of rhythmic spikes affects only one side of the head, while the other side of the body presents a perfectly characterized tonic and clonic seizure. As the contraction is unilateral the head is deviated towards the affected side; and as the discharge is not generalized, consciousness and memory are partially retained. This explains the fact that such attacks are usually misinterpreted as adversive focal or somato-motor attacks.[1]

We have already carried out several investigations of attacks developed in a single areo-thalamic sector (or in a small number of such sectors, or in a part of one sector) (Gastaut, 1950, 1951c, 1953). We limit ourselves here to the mention of two characteristic examples:

1. A young male patient, each of whose attacks began with nystagmus of increasing amplitude, terminating in a complete blocking of vision to the right. At the same time the head turned slightly to the right, and the subject experienced complex visual hallucinations. The episodes lasted a little less than one minute, during which time the subject was completely conscious. Electrically, the attacks were characterized by a rhythmic discharge of progressively decreasing frequency occupying the left temporo-occipital region. From the pneumoencephalographic point of view, there was no sign of any cortical lesion; neurological examination was completely normal. Inter-critical EEG was also normal, showing no sign of focal deterioration. Diagnosis of subcortical epilepsy projecting to the left occipital region seemed clearly indicated. However, the attacks becoming more and more frequent and unresponsive to treatment an operation was performed, revealing a parieto-temporo-occipital cortex anatomically and electrically normal, with no pathological response to electrical stimulation.

2. The second case (Fig. 7) concerns a patient with left temporal interseizure discharges; cardiazol activation increased

[1] It is advisable to mention the existence of non-epileptic discharges affecting directly the whole of one hemisphere to the exclusion of the other. This is notably the case for bursts of slow sinusoidal waves of 2 to 3 c/s which occupy the unaffected hemisphere in cases of thrombosis of the carotid artery, when for a few seconds the free carotid is compressed. As these bursts disappear after two or three successive compressions, it is logical to suppose that they are due to the low resistance to ischaemia of the unaffected hemisphere. These may be considered as 'semi-syncopes' during which the subject, although stupefied, does not completely lose consciousness.

temporal discharges, followed by a completely typical electrical and clinical attack: bilateral synchronous discharge of slow waves lasting 40 seconds, during which the subject was completely unconscious, and showed rhythmic chewing movements. Exactly two minutes after the end of the attack, there appeared in the

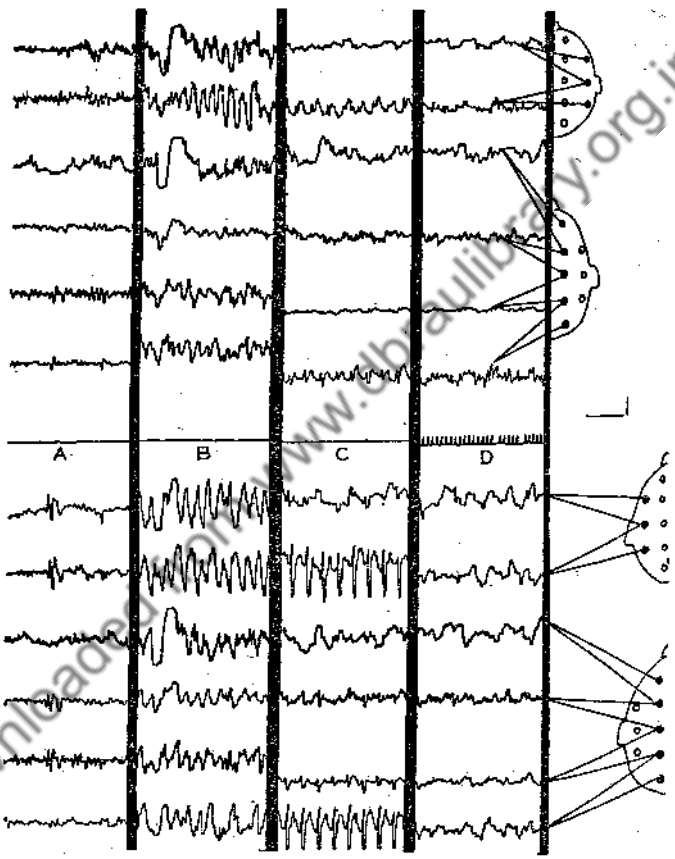


FIG. 7

Double cortical discharge in epileptic without demonstrable cortical lesion:
A — Left mid-temporal intercritical discharge.
B — First critical discharge constituted by diffuse slow waves dominating in left mid-temporal region and accompanied by typical psychomotor attack.
C — Second critical discharge constituted by rhythmic temporal spikes in left postero-occipital regions accompanied by visual attack.
D — Post-critical phase characterized by slow waves on the left, predominating in the temporo-occipital region — Intermittent photic driving nil on the left but exists on the right. (The patient presents at that instant a right lateral homonymous hemianopsia.)

left occipital region a rhythmic spike discharge, 2 cycles/sec., persisting for 6 minutes, during which time the subject at first showed no particular symptoms, then indicated spots of light filling his whole field of vision. Immediately following the attack, and for 20 minutes afterwards, the subject showed a complete right homonymous lateral hemianopsia and responded only on the right hemisphere to intermittent photic stimulation.

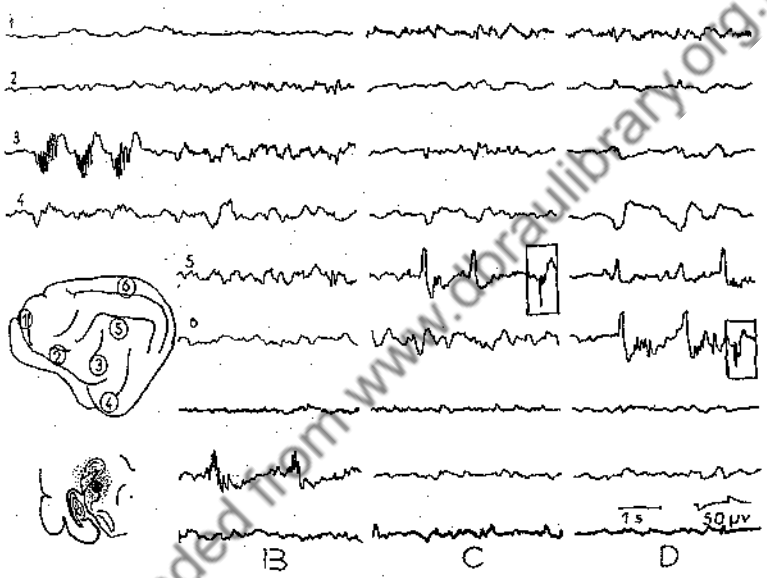


FIG. 8

Electrocorticogram of cat with single left postero-lateral thalamic lesion.
Note the multiplicity of intercritical cortical discharges situated in:
– homolateral insular area (A3)
– contralateral insular area (B 3')
– homolateral auditory area (C 5)
– homolateral visual area (D 6)
Note the auditory and visual evoked potentials, different from intercritical epileptic discharges from same area.

All further investigations in both this and the preceding case showed that there were no cortical lesions. We must therefore assume that in this patient a subcortical lesion was responsible either for a temporal discharge or an occipital discharge or for both subsequently to either one of them. These multiple cortical discharges provoked by a subcortical lesion are not exceptional

and we have recently devoted a full report to them. (Gastaut and Ricci, 1953.)

It will not perhaps take us far from the clinical field if we describe as a comparison, the following observation – one of a series – culled from the paper read before the Societé d'EEG de langue française (Gastaut, 1953).

Cat 'Ralu XIX' – Description of attacks (spontaneous and provoked by cardiazol injection). Attitude suddenly anxious, furtive flight, cowers under a piece of furniture and there chews and salivates abundantly. Subsequently remains confused for several minutes.

ECoG observations (Fig. 8). (a) Intercritical discharges of sporadic spikes on the left hemisphere; either auditory region (middle gyrus ectosylvius) or visual region (gyrus lateralis) or gyrus sylvius (doubtless corresponding to the insular and peri-insular regions); or sometimes all three. (b) Critical discharges of slow waves beginning in the left lower insular region and subsequently spreading to the auditory area on the same side, then to the prefrontal region (gyrus proreus) on both sides.

Anatomical study. The whole cortex of the left hemisphere is microscopically and macroscopically normal, notably the gyri sylvius, ectosylvius and lateralis. The lesion, constituted by alumina cream injected six months previously, occupies the dorso-lateral part of the left medial geniculate body; the glial reaction extends to the rest of the medial geniculate body, to the lateral geniculate body, to the suprageniculate nucleus, and to the lateral part of the thalamic reticular nucleus, which covers the two geniculate bodies.

Conclusions

The conclusion to be drawn from this second section is that there exist in man non-specific systems projecting to the different cortical areas; systems which may be independent of, or a part of, the diffuse system referred to in the first section. In the latter case, one must conclude that the diffuse system does not project directly on the whole of the cortex from a given point of the brain stem, but that it projects through intermediate stages in which a cortical representation takes shape progressively. In other words, we must suppose that there exists in the brain stem a structure controlling the whole of the electrogenesis of the cortex through the intermediary of a complex subcortical formation

connected region-to-region (if not point-to-point) with the various specific and non-specific cortical areas.

The work of Jasper (1949), and incidentally our own work (Terzian, Roger, Badier and Gastaut, 1952; Gastaut, 1953), indicates that the intermediate stage in question is represented by the reticular nucleus of the thalamus receiving ascending fibres from the reticular formation of the brain stem by way of the non-specific thalamic nuclei.

According to this hypothesis, each areo-thalamic sector includes specific fibres coming from afferent systems (primary or secondary) and elaborative systems of the thalamus, and from non-specific fibres coming from the intralaminary nuclei and the reticular nucleus of this organ. Taking as an example the 'medial geniculate body – supratemporal cortex' sector, connections of the first type would be represented by geniculo-temporal and temporo-geniculate fibres, whilst those of the second type would be represented by fibres connecting the auditory cortex and its neighbourhood with the supra-geniculate nucleus and the part of the reticular nucleus adjacent to the geniculate body.[1]

Histological observations by Minkowski (1951) Ubedda Purkiss (1952) and Chow (1952) confirm the soundness of the physiological point of view and assign to the reticular nucleus of the thalamus the probable function of a relay.

OBSERVATIONS LEADING TO AN EVALUATION OF THE RELATIONS WHICH MAY EXIST BETWEEN ELECTROENCEPHALOGRAPHIC MANIFESTATIONS OF NON-SPECIFIC SYSTEMS OF CORTICAL PROJECTION AND STATES OF CONSCIOUSNESS

It does not appear that the non-specific fibres of each thalamo-cortical sector, taken separately, play an important part in the organization of different levels of consciousness. For example, an epileptic discharge developed in one of these sectors does not appreciably modify the state of consciousness, whereas a much briefer discharge bringing into play the diffuse system of projection, causes a profound loss of consciousness. In this connection

[1] This would also explain the observation of Terzian, Roger, Badier and Gastaut (1952) that stimulation of the medial geniculate body, the supra-geniculate nucleus and the adjacent portion of the reticular nucleus, produces ectosylvian responses whose latency is between 8 msec. (specific response) and 35 msec. (normal recruiting response).

we cite again the case of the patient who showed, at two-minute intervals, a generalized discharge of 40 seconds with total loss of consciousness, and another localized occipital discharge of six minutes, without change in the state of consciousness.

This same example shows, however, that non-specific localized systems of projection play a considerable part in the regulation of the excitability of the region on to which they project. Thus the occipital discharge mentioned above had no clinical manifestation during the first two minutes, whereas at the end of that time it had sufficiently increased local excitability to cause hallucinatory perceptions in the subject. At the end of the discharge, moreover, the occipital region was sufficiently exhausted to cause a durable homonymous lateral hemianopsia.

In any case, when too many areo-thalamic sectors are brought into play, the proportion of the cerebral cortex whose normal functions are disturbed is too great to leave consciousness intact. This is what occurs, for example, when all the areo-thalamic sectors of one hemisphere are brought into play, as is the case in the 'semi-generalized epileptic fits' previously described. One of our patients, subject to such attacks, did not completely lose consciousness, since she remembered all the sounds which had been made near her during her paroxysms; but in spite of this, she was sufficiently stupefied to be unable to remember complex instructions which had been given to her at the same time.

With regard to the non-specific system of cortical projection considered in its totality, as a diffuse system, it regulates not only the form and frequency of the fundamental electrical activity of the cortex, but also the state of excitability, local or general, of the cortex; i.e. it controls the amount of information received by the cortical analysers, to be transformed into ideas or actions, or stored in the memory. These facts have two consequences:

1. The diffuse system of projection must play a major role in the organization of states of consciousness, or better of awareness.
2. There must exist close correlations between these states and the fundamental electroencephalographic rhythms.

These correlations we must now consider; they are well known to all encephalographers, at least so far as extreme conditions of the state of awareness are concerned. Everyone is aware in fact, that physiological as well as pathological losses of consciousness

(sleep, syncope, lapses, coma) are associated with a diminution in frequency and an increase in amplitude of the cortical rhythms, whilst states of attentiveness, anxiety and fear are associated with an increase in frequency and a diminution in amplitude.[1]

With regard to intermediate states of awareness, their relation to cortical rhythms is less well known. We have attempted (Gastaut, Gastaut, Roger, Corriol and Naquet, 1951) to touch on this problem in seeking first the correlations which may exist between spontaneous activity of the cortex and its cycle of excitability investigated by the method of paired stimuli at variable intervals (evaluation of the response characteristics of a so-called 'test' stimulus at a variable interval following a 'conditioning' stimulus). We conclude from such investigations that in man and animals in the waking state rapid and feeble background rhythms correspond in general to short, low-amplitude cycles of excitability, and correspond also to an aptitude on the part of the neurone system concerned to respond quickly and fully to excitations following closely on one another; whereas slow, strong background rhythms correspond to long, high amplitude cycles of excitability and to systems unsuited to the transmission of rapid signals.

These observations have led us to elaborate a theory of transmission of signals in the central nervous system. We presented this theory at the Conservatoire National des Arts et Métiers during a series of lectures on Cybernetics (Gastaut, 1952b). According to this theory, the neurone systems are able to reorganize nervous messages in the light of the following processes:

1. Post-reactional variations of each neurone's excitability (cutting out of signals arriving during the absolute refractory period; damping down of signals arriving during the relative refractory period or during the phenomena of post-reactional subnormality; amplification of signals arriving during phenomena of post-reactional surnormality).

2. Splitting up of the neuronal population into functional groups kept out of phase. (Such a condition would occur if a pacemaker existed which would bring into play, with constant

[1] In connection with the habitual accompaniment of comas with slow and wide amplitude EEG rhythms, it would be scarcely possible to cite better correlations than those obtained by Cairns (1952), who succeeded in causing a regression of both phenomena by emptying the cranio-pharyngeal cyst which provoked them.

phase relationship, groups of neurones of variable sizes to which would correspond the frequencies of the EEG rhythms.)

It is evident that, if this theory is valid, the regulation of the two factors by means of which the nervous system maintains its 'coding' under optimum conditions (i.e. by means of which it ensures the transmission of information with adequate continuity and amplitude) must represent one of the essential tasks of the organism. In fact, any slowing down or speeding up in transmission would lead to a lack or excess of information, whilst any diminution or increase in the amplitude of the transmitted signals would lead to an insufficiency or an excess of the transformation of these signals into sensations, ideas, or actions.

This is doubtless why the alpha rhythm is so strictly regulated at 10 cycles/sec. A subject with more rapid rhythms, having more functional groups at his disposal, must have more information transmitted; conversely, a subject with slower rhythms must have a lower rate of transmission. The former will not be *better* informed, for an excess of information is itself a fault; the subject will indeed be quickly disturbed by the excess of information. As for the latter, the undesirability of being insufficiently informed needs no comment.

On these considerations we have based the description of the three electroencephalographic syndromes of hyperexcitability, hypoexcitability and cortical instability.

The first of these is characterized by the existence of rapid, feeble background rhythms (alpha 11–13 cycles/sec. in the posterior regions and beta 15–20 cycles/sec. in the middle regions) coming in short bursts, in the intervals of which the records are completely desynchronized. Intermittent photic stimulation produces a high-amplitude result, sometimes accompanied by palpebral myoclonic responses. This syndrome of cortical hyperexcitability we believe to correspond to the existence of: (1) a very brief recovery period of the excitable elements, with a tendency to arrangement in numerous small groups of functionally synchronous elements (hence the rapid rhythms, feeble, irregular and desynchronized); (2) a very considerable recruitment, explaining the high-amplitude potentials produced by intermittent photic stimulation.

The syndrome of hypoexcitability is characterized by rather

slow strong background rhythms (alpha 8-9 cycles/sec. without beta), continuously distributed, without intervals of desynchronization and sometimes even without any tendency to amplitude modulation. We believe this syndrome corresponds to: (1) a rather long recovery period of neurone excitability after each stimulation, and a tendency of the elements excited to unite in large groups of functionally synchronous elements (hence the slow, strong, regular rhythms, well synchronized); (2) a slight tendency to recruitment, hence the lack of response to intermittent photic stimulation.

With regard to the syndrome of instability (lability or versatility), less well defined than the preceding syndromes, it includes the association of low frequencies (especially in the theta band) and high frequencies (especially beta) on a background of alpha rhythms 9-11 cycles/sec. The whole is of very variable amplitude from one moment to the next, and subject to almost instantaneous modulation in amplitude. The effect of intermittent photic stimulation is also variable from one moment to the next, but usually slight, whilst the hyperpnoea test causes a slowing which may result in a hypersynchronous theta, or even delta. We believe the mechanism of this syndrome corresponds to a lack of stability in the regulation of cortical excitability, which may oscillate continually between the two extremes of hyperexcitability and hypoexcitability.

These three syndromes are obviously insufficient to explain fully the complexity of cerebral electrogenesis and we have already seen that there exist apart from them, syndromes of regional or local hyperexcitability (occipital hyperexcitability, expressed by posterior spikes on opening the eyes; central hyperexcitability with high amplitude beta rhythms, dedoubled beta rhythm, *rythme en arceau*, prerolandic functional spikes blocked by clenching of the fists, etc.) They do, however, correspond to particular types of psychomatic behaviour, which are themselves related to appreciably differing states of awareness. For example, subjects showing a syndrome of cortical hyperexcitability are hyperactive types with exaggerated perceptive functions, whilst subjects showing a syndrome of hypoexcitability are calmer and slower in their perceptions. Subjects showing a syndrome of cortical instability are especially remarkable for their psychomotor

versatility and the paroxysmal liveliness of their reactions. We are not alone in having established correlations between behaviour and electroencephalographic records. We have grouped in a table the psychological characteristics attributed by various authors to subjects whose EEG records differ very little from those which have served as basis for our classification.

We are nevertheless convinced that this attempt at psychological classification of cerebral rhythms is very imperfect, and consider it as a working hypothesis at present on trial. It has so

TABLE I

Characteristics of Records	*Characteristics of Personality*	*Authors*
1. *Hyperexcitability syndrome*		
Rare and rapid alpha rhythms of small amplitude, grouped in short bursts on desynchronized activity.	Unstable, dynamic, enthusiastic and creative personality	Saul, Davis and Davis (1937)
	Active, independent personality; tendency towards leadership	Saul, Davis and Davis (1949)
Intermittent photic driving.	Hypersensitive, hyperemotional, hyperactive, nervous	Gastaut *et al.* (1951)
Uneffectiveness of hyperpnoea	Sharp, impulsive, unstable, strongly reacting	Mundy-Castle (1953)
	Nervous, sympathetic dominance	Ichinose (1940)
	Tendency towards anxiety state	Ulett *et al.* (1953)
2. *Hypoexcitability syndrome*		
Frequent alpha rhythms, continuous large amplitude, no desynchronized intervals.	Methodical, slow, dependent, cautious personality	Saul, Davis and Davis (1937)
	Passive, dependent, submissive, tending to shy away from effort, danger and responsibility	Saul, Davis and Davis (1949)
No intermittent photic driving.	Obedient, no aggressive tendencies, conformist, shying away from danger and responsibility	Palmer and Rock (1953)
Slowing after hyperpnoea.	Slow, even temper, calm	Gastaut *et al.* (1951)
	Slow, wary, firm, uniform temper, persevering	Mundy-Castle (1953)
	Slow, parasympathetic dominance	Ichinose (1947)
3. *Lability syndrome*		Saul, Davis and Davis (1949)
Alpha rhythm rare-associated with slower or more rapid waves or with both	Impatient, aggressive, hostile	
	Calm and not anxious but susceptible to rapid and violent reactions, grumbler affective lability	Gastaut *et al.* (1951)
Intermittent photic driving		
Slowing after hyperpnoea	Violent, aggressive, intolerant, egotist	
	Impatient and suspicious	Walter (1953)

far given quite satisfactory results; for example, in a group of adults who had chosen one of the most dangerous careers imaginable, that of naval air pilot[1] we encountered (Ciamin, 1953) no syndrome of cortical hypoexcitability or hyperexcitability but only syndromes of versatility, corresponding exactly to the extraverted and enthusiastic, but unstable and immature characters of these men who 'live dangerously'.

The relations existing between the type of cortical rhythms and the behaviour or the state of awareness are sometimes so close that it is possible to vary both factors in the same direction and at the same time under the effect of a common cause. We achieved this result in the case of 12 psychically and electroencephalographically normal subjects, who ingested 60 gamma d-lysergic diethylamide (LSD 25 Sandoz). After about one hour, 9 of them showed parallel modifications in their EEG and in their psychic aspect; e.g. (1) from the EEG viewpoint they developed a characteristic syndrome of hyperexcitability (acceleration of the occipito-parietal alpha rhythm from 0.5 to 4 cycles/sec., appearance of reinforcement of beta rhythm, increase in response to intermittent photic stimulation, and appearance of palpebral myocloniae); (2) from the psychic viewpoint there appeared an exaggeration of the perceptive functions and of overall activity, with affective instability in the direction of euphoria or anxiety and a lowering of the capacity for attention, abstraction and synthesis.

From the results reported above, taken as a whole, it should not be concluded that the evolution of states of awareness is indissolubly linked with that of electroencephalographic rhythms, and that the one may not be varied without the other. Nothing could be more false or more dangerous, for all the relationships which we have just established constitute nothing more than general rules, with many exceptions, and these exceptions we will now mention.

In *syncopes*, loss of consciousness is accompanied by slow waves; this is particularly true of vaso-vagal attacks, of which we have recorded many cases provoked by ocular or sino-carotid

[1] Pilots based on aircraft-carriers, who are catapulted off and must subsequently land on deck in conditions of zero visibility; a career made even more dangerous in view of active service conditions which have existed since 1939.

compression. This is, however, not an absolute rule, for there exists a type of syncope, provoked by injection of small quantities of cardiazol in predisposed subjects, which is characterized by a flattening of the records, preceded and followed by a few slow waves. Loss of consciousness, with accompanying slight generalized hypertonia, occurs during the flattening phase.

Petit mal attacks are always accompanied by slow waves, 3 cycles/sec. each preceded by a brief spike discharge; there do not

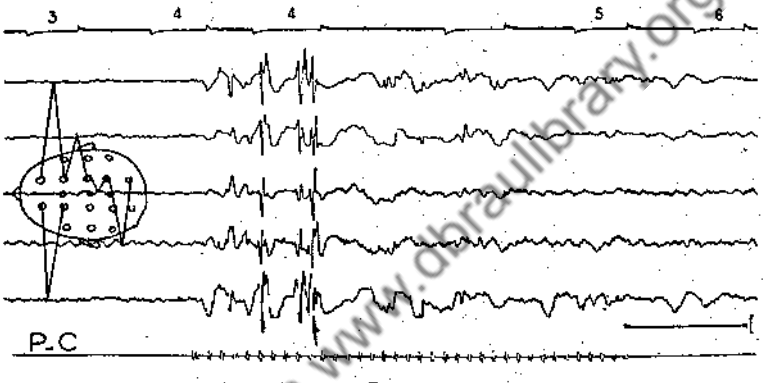


FIG. 9

Multiple spike evoked by intermittent photic stimulation in *petit mal* recorded while patient rhythmically presses on Morse key and counts from one to a hundred.
(The last line shows the flashes registered by a photoelectric cell. The first line shows the contacts of the Morse key and the number spoken by the patient.)
During the discharge the patient maintains his automatic activity (presses on the key) although his rhythm is altered. Speech is perturbed: he repeats 'four' during the multiple spike and forgets to say 'five' during the period of slow waves which follows.

appear to be any exceptions to this rule, but the converse is not true, and spike and wave discharges are frequently observed in the absence of *petit mal* attacks. It has been claimed that these subclinical discharges are different from clinical discharges; this assertion is true in certain cases but not in others, and the most characteristic *petit mal* discharge may occur without the least impairment in the state of consciousness.

We have personally investigated consciousness during *petit mal* seizures. With regard to myoclonias, we utilized a variable-delay electronic system operated by the peak of each spike recorded on the cortex, which enabled us to make a signal coincide with any phase of the paroxysm. Subjects always responded with a normal

reaction time, which indicates that awareness is intact during the paroxysm. With regard to lapses we employed more complex tests, to observe the perceptive faculties of the subject, his reaction time, and his automatic and voluntary mobility. Our observations show that, for identical electrical discharges, different subjects may present widely differing states of awareness, ranging from full consciousness to complete unconsciousness, including stages of dissociation in which perceptive functions and automatic activity are conserved, while cognitive functions and voluntary activity are diminished (Fig. 9).[1]

The independence between the clinical and electrical manifestations of *petit mal* is even more marked for provoked than spontaneous phenomena.

For example in certain 'photogenic' epileptic cases, intermittent photic stimulation at 3 cycles/sec. provokes after a quite characteristic period of recruitment a bilateral spike and wave discharge which repeats itself at the same frequency and is indistinguishable from a spontaneous electrical lapse (Fig. 10); this discharge is not accompanied by any clinical manifestation, and may be prolonged as long as is desired. Contrary to statements in our previous publications, we have not succeeded in provoking identical spike and wave discharges in non-epileptic subjects; the phenomena which we recorded at that time were of palpebral, not cerebral origin.

Brief temporal attacks, characterized simply by a lowering of the level of consciousness with or without 'automatism' are usually accompanied by a generalized discharge of slow waves. Such a discharge is however observed only in two-thirds of the cases; in the remaining third, on the contrary, rapid rhythmic discharges or desynchronization are observed, and even localized discharges in the temporal region of one hemisphere. It appears to us that 10 per cent of these psycho-motor attacks occur without apparent

[1] An interesting detail worth mentioning is the relative opposition existing between the subject's mental activity and the development of a lapse. For example in subjects presenting many attacks under the effect of intermittent photic stimulation or hyperpnoea, the mere act of counting from 1 to 100 may prevent the development of loss of consciousness which occurs immediately after the last figure is enunciated. A still more curious fact is that certain 'infraclinical' spike and wave discharges develop normally, whilst the subject is at rest, but are immediately interrupted if the subject makes any sort of mental effort or if he replies to a question put to him. This cessation of the spike and wave rhythm is completely analogous to the cessation of the alpha rhythm on opening the eyes.

modification of the records and it is well known that post-critical confused states, which often follow such attacks, continue after the wave forms have returned to their pre-critical state (Gastaut, 1953).

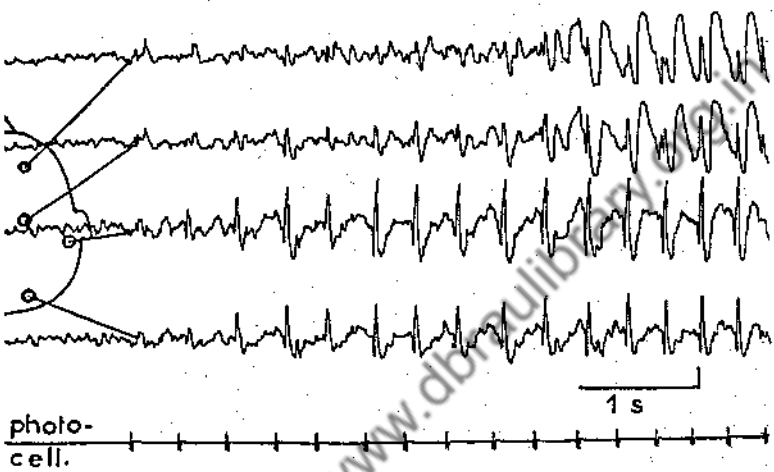


FIG. 10

Rhythmical spike and wave evoked by intermittent photic stimulation (3 cycles/sec.) in epileptic presenting *petit mal* lapses.

Up to the present we have considered only brief losses of consciousness, but discordances are just as numerous in the case of losses of consciousness of long duration. We will not dwell upon the questions of sleep and anaesthesia, which are to be discussed by other contributors; in these conditions rapid rhythms are often associated with states of unconsciousness as deep as those accompanying surgical anaesthesia.

With regard to *comas*, all authors who have investigated comas of hypoglycaemic origin are aware how frequently the slowest rhythms coincide with the most superficial comas. As for anaesthetic (anoxic) accidents (Fig. 11, A), they are generally characterized by very rapid and desynchronized rhythms when the subject is in extreme coma. But the most surprising discordances are observed in cases of artificial hibernation.

With this technique the characteristics of the background rhythms depend upon the substances used to produce the 'neuro-

vegetative blocking' and upon the degree of hypothermia provoked; nevertheless rapid and desynchronized rhythms are frequently observed to coincide with deep loss of consciousness (Fig. 11, B). This 'activation pattern' appears to depend especially on temperature, and occurs below 35° C.; we have observed it at temperatures as low as 31° C., at which there obviously no longer exists a 'vigil reaction'.

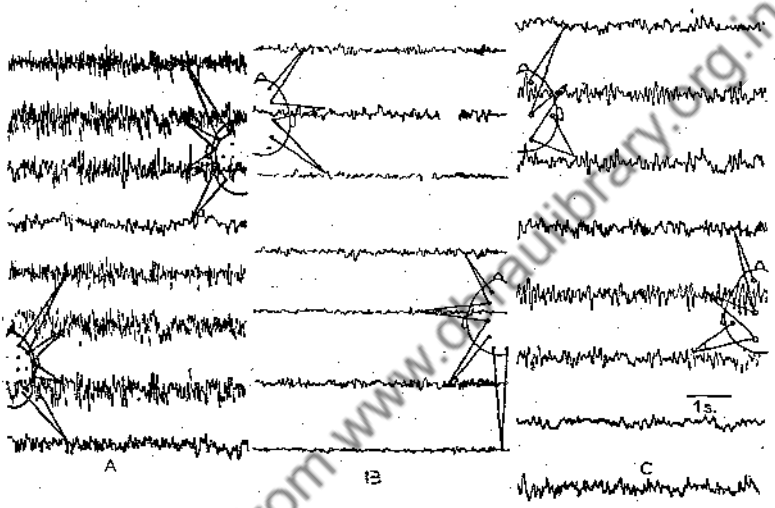


FIG. 11

Records of three cases of deep coma.
A – Severe complication of anaesthesia (record communicated by Dr. Schneider of Colmar).
B – Psychopath in state of artificial hibernation (31° C.) – (Record communicated by Drs. Ey and Berrard of Bonneval).
C – Patient presenting an intra-ventricular haemorrhage (Record communicated by Dr. Loeb of Genoa.)

The paradox is even more marked in the case of hibernation of an already comatose subject; one then observes the slow initial dysrhythmia gradually accelerate and give place to rapid, feeble rhythms, whilst the subject remains in a deep coma with total muscular relaxation, pupillary areflexia, paralytic mydriasis and superficial respiration at 6 r.p.m.

However it must not be imagined that in the absence of slow rhythm, rapid rhythms necessarily accompany coma. Perfectly normal waves sometimes exist. Dr. Loeb recently observed such a case during a haemorrhage of the tegmentum of the cerebral

peduncle opening into the 4th ventricle (Fig. 11, C). We have ourselves observed several cases secondary to haemorrhage into the 3rd ventricle.

We have stressed the fact that there may be loss of consciousness without associated slow waves – a fact of which many electroencephalographists still seem to be unaware. It has not, however, seemed necessary to mention the converse case in which slow waves occur without loss of consciousness, for this is a matter of common knowledge. In this connection we limit ourselves to the mention of a case of a young girl who, following a head injury of some consequence, suffered a coma of long duration, subsequent to which normal rhythms were not re-established. For the past three years she has shown without interruption a background rhythm of 3 cycles/sec., whilst her psychic state is quite normal. Her powers of abstraction and attention are even well developed and she has a remarkable gift for mathematics.

In point of fact, the relationship between the EEG and consciousness is not very close when one considers the highest functions of consciousness such as those which determine 'understanding' and which we call 'intelligence'. It is well known that cretins have slow rhythms which become faster as their intellect develops under treatment with thyroid extracts; but outside these exceptional cases there only exist negative correlations or correlations which do not appear significant. We have just seen that head injury may cause permanent slow rhythm to appear without impairing intelligence. Conversely certain acute infantile encephalopathies characterized by a myoclonic syndrome and a 'major electroencephalographic dysrhythmia' (Gastaut and Rémond, 1952; Gastaut and Roger, 1953) may impair permanently intellectual development without preventing the recovery of normal cerebral electrical activity. (This last point is very significant as it explains the high number of normal records in mental defectives.)

Conclusion

There is no doubt that the diffuse system of projection regulates local and general cortical excitability, and that consequently it regulates the state of consciousness; since it regulates also cortical

electrogenesis, it is logical to admit that a relation exists between cortical electrogenesis and the state of consciousness.

This relation is evident in the extreme cases of loss of consciousness and heightened consciousness, but much less evident in intermediate states of consciousness, which, however, appear to be related to certain characteristics of the cortical rhythms.

There are, however, numerous exceptions to these rules, which lead to the conclusion that if the diffuse system of projection plays a part in the regulation of cortical electrogenesis and the level of consciousness, these two factors are not directly dependent on each other and may evolve independently.

GROUP DISCUSSION

JASPER: I am sure we are getting a little closer to our problem and can see it more clearly. In passing I would like to confirm the complexity of these clinical conditions and, as Dr. Hebb and Dr. Lashley will no doubt point out with regard to loss of consciousness, differences may well exist in the physiological and psychological points of view. Studies like this may serve to bring order out of chaos in the comparison between clinical conditions and the EEG record.

BREMER: I would like to ask more details about the unresponsive patient with a lesion in the medulla who showed normal EEG activity. Was the spacing of the alpha waves normal? Was the activity continuous or were they spaced in regular spindles? If the alpha rhythm was normal or continuous it would be very difficult to correlate this with the lack of consciousness.

GASTAUT: In this patient, a girl, the rhythm was 10/sec., well modulated and with only a few slower components. I have seen other cases of lesions in the lower pons, medulla, or with haemorrhage in the third ventricle with a perfectly normal EEG. Dr. Loeb has published a case like this.

JASPER: Dr. Loeb's case was that of a lesion in the medullary pontine region. The patient was completely unresponsive until death but the EEG during this period was within normal limits.

WALTER: I discussed this case with Dr. Loeb while in Italy and saw all the records. Although no part of the record showed any abnormality it was abnormal as a whole because it showed no signs of any response to stimuli.

HEBB: There is little difficulty in detecting complete loss of consciousness; that there is no impairment of consciousness is much more difficult

to establish. Some changes are not detectable without psychological test methods. Thus it may be relatively easy to show that intellectual defect accompanies a 'normal' EEG; the converse is very difficult, that is to show that an abnormal record accompanies unimpaired function.

JASPER: Dr. Courtois has been following this line of work and confirms that with appropriate methods in most of these cases it is possible to detect some loss of function and that those losses occur in very interesting ways.

GASTAUT: In answer to Dr. Hebb, I shall choose a specific example: that of the slow rhythms which follow certain cranial injuries. Such an eventuality is indeed extremely rare, for most local cerebral contusions lead to focal electroencephalographic anomalies, whilst most cerebral commotions involving loss of consciousness leave in their train a desynchronization of the EEG. There are cases, however, in which for several years (perhaps permanently) there occurs and persists a considerable slowing down of the background rhythms whose frequency is reduced to a half, a third or a quarter of the normal frequency — i.e. 5, 3 or 2 c.p.s. in the occipito-parieto-temporal regions.

In such cases I have often observed visceral disturbances, mainly genital (persistent amenorrhœa) and subjective symptoms such as headaches, vertigo, or changes in character. On the other hand, thorough psychological examinations and psychometric tests carried out by specialized psychologists in my laboratory have never revealed the slightest disurbances in consciousness. Intelligence still appears normal, and you will remember that the little girl whose case I described in my paper, who had slow rhythms of 3 c.p.s. for years, was the brightest pupil in her class, and satisfactorily passed numerous psychometric tests.

KUBIE: I was particularly interested in those aspects of Dr. Gastaut's paper which dealt with emotion and personality and their relationship to the EEG record. The term 'consciousness' when rendered as *conscience* in French has a connotation which includes emotions and personality as a whole. This connotation, strictly speaking, is not in the English concept of 'consciousness'.

JASPER: Would you care to comment on this, Dr. Gastaut?

GASTAUT: I find it too difficult to express myself in English to engage in a discussion with Dr. Kubie in the field of psychological vocabulary, especially in connection with the word 'conscience', which has several meanings in French.

However, I would like to confirm Dr. Kubie's impression concerning the possible relations existing between the EEG and personality. These relations are close and numerous, although the problem has been

approached very differently by various authors, depending on whether the psychological conceptions of, for example, Kretschmer, Freud or Heymans were utilized. In spite of this, most authors have arrived at relatively similar conclusions, which agree moreover with the results of my work in 1951, in which I described the three syndromes of hyperexcitability, hypoexcitability, and cortical lability.

I would like to point out again that my conception of a cortical hyperexcitability corresponding to rapid rhythms or to desynchronized records, and of a cortical hypoexcitability corresponding to alpha or sub-alpha synchronization, is in very close agreement with the hypothesis formulated by the Russian authors who have investigated the electroencephalography of conditioned reflexes (quoted in the two recent articles of Maioztchnik and Spirine, 1951, and Tchougounov, 1951). According to this hypothesis, alpha synchronization corresponds to Pavlov's process of internal inhibition, whilst desynchronization corresponds to his process of cortical excitation.

FESSARD: Dr. Gastaut rightly insisted on the fact that these relationships are only correlations, far from showing strict dependencies between cortical activities and mental states. The same is true, apparently, with the association recently discovered by Bates and others, between a certain phase of the cortical alpha rhythm and the moment of the onset of a voluntary movement. Consciousness and will are closely united as mental events. The rather loose dependency that exists between such mental events and EEG patterns could be best explained, so I believe, by their both being under the control of certain subcortical structures.

GASTAUT: I would like particularly to thank Dr. Fessard for his remarks, which express my point of view perfectly. In fact, I consider that the state of psychic activity and that of the EEG are independent of each other, but that they both depend upon a third factor: their subcortical control. This is why they generally develop in the same direction while at times they may show marked discrepancies.

LASHLEY: I am a little lost among the EEG waves, but feel that there may be no justification for assuming that some particular form is an index of consciousness. How are the EEG waves related to patterns of neuronal activity? Are similar waves certainly due to the same activity? Conscious states may represent a high degree of neural organization. This organization might be abolished either by termination of activity, by excessive, disrupting activity, or by loss of specific components, such as the perseverating activity which is implied by immediate memory. Thus loss of consciousness might occur with quite different EEG patterns.

HESS: Even if we could propose that the conventional EEG-pattern

was related to consciousness, discrepancies of the type reported by Dr. Gastaut are only to be expected since the EEG represents only an incomplete sample of the total activity of the cortex.

BREMER: I think that each case must be analysed separately to be properly understood and that generalizations are dangerous. Anoxia is usually associated with a slowing of the EEG and disturbances of consciousness. In one of your cases Dr. Gastaut, you found a fast rhythm in anoxia and I would like to ask whether this could be a post-anoxic recovery which might still be accompanied by unconsciousness. Carbon dioxide may also be a narcotic but causes an acceleration of the EEG.

GASTAUT: I will reply first to Dr. Bremer, for the question which he puts to me shows that on account of my language difficulty I did not clearly explain the case which he recalls. It was not, in fact, a case of anoxia, but a very serious anaesthetic accident in which the coma corresponded to irreversible cerebral lesions which were themselves the result of anoxia.

With regard to anoxia itself, it is indeed accompanied by an electroencephalographic slowing which generally precedes the first manifestations of disorders of consciousness. This is at least the conclusion to be drawn from the remarkable work done in this field by Noel and Chinn in 1949 at the U.S.A.F. School of Aviation Medicine.

Concerning Dr. Hess's remark, I am in complete agreement with him. The EEG represents only a small part of cerebral electrical events, and only a small part of those which occur in the cortex. I have, for example, observed in an epileptic patient during an operation a paroxysmal loss of consciousness with consecutive amnesia, without any modification of electrogenesis on the convexity of the hemispheres, whereas there existed an electrical discharge of considerable amplitude in the region of the uncus. I have moreover often stressed the fact that many of the psychic modifications occurring in psychomotor epileptics, quite apart from any electroencephalographic modifications, must correspond to deep epileptic discharges which are not accessible with the means at our disposal. I will even go further in speaking of the relative value of such data, and recall that the total activity encompassed between two electrodes placed on the scalp is often quite different from the activity revealed by fine electrodes applied to the immediately subjacent cortex.

I also find very much to the point Dr. Lashley's remark, which brings out a point of view which I myself strongly hold and which I have stressed in my paper.

HEBB: I would like to return to Dr. Lashley's question which seems to me to be quite fundamental. What is the relationship between the

activity of the cells or cell groups and the EEG? Can we not have a discussion of this at some point during the conference?

JASPER: Perhaps Dr. Jung, in his communication at the end of the morning session will discuss this matter.

JUNG: I am not prepared to speak about neuronal discharge in this paper but perhaps we can cover the subject tomorrow.

JASPER: In that case perhaps we can bring it up tomorrow. Don't be too hopeful, Dr. Hebb, that you will get a very satisfactory answer.

STUDIES OF THE CEREBRAL CORTEX OF MAN. A REVIEW AND AN INTERPRETATION*[1]

By

WILDER PENFIELD

On one of my last visits to Sir Charles Sherrington, I found him confined by his great age and infirmity to an upper room in a nursing home at the seaside. But his mind still ranged abroad on excursions of inquiry and reflection. He asked me about the results of stimulating the temporal lobe. Then with the half smile and the twinkle in his eyes that I had known so well he said: 'It must be great fun to put a question to "the preparation" and have it answer!' Then he chuckled, recalling his own mammalian preparations.

MATERIAL

These observations have to do with men, conscious intelligent men, during cranial operations under local anaesthesia and at other times during periods of hospital study.[2] It was the curse of focal epilepsy that brought these patients to the operating table. Our approach to the study of brain function and states of consciousness is of necessity that of clinician, as well as psychologist and physiologist. But the methods used may seem unorthodox to workers in each of these disciplines.

In epilepsy there is an area of grey matter which is the source of recurring and often continuous spontaneous discharges that may be measured electrically. In the cerebral cortex, the surrounding grey matter seems to become hyper-reactive or conditioned by the long-continued epileptic state, so that electrical stimulation, when it is applied, may reveal the true function of the

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[1] The author's Discussion that appears elsewhere in this volume, page 489, should be considered part of the interpretation of the material presented here.

[2] For detailed study of this material see Penfield and Rasmussen (1950) and Penfield and Jasper (1954).

cortex in areas from which no response would be expected if the patients were not subject to seizures.

Although the cortical abnormality may seem to be large, and the area of electrical and functional hyper-activity still larger, the evidence of discharge may be related to a small area or to an isolated ganglionic pattern. For example: in the somatic sensory area the initial phenomenon may be tingling in one portion of the little finger, and it continues thus through the years although it is followed at times by spread of the aura to arm and face or leg. The Jacksonian motor attack may begin, for example, with vocalization, followed by conjugate deviation of the eyes and by tonic clonic movements of the contralateral face and extremities. Discharge in the occipital lobe may begin with gross colours seen by the patient in only one part of the visual field. Discharge in the auditory cortex may begin with an undifferentiated sound of a particular tone and quality.

In the temporal cortex the initial phenomenon may begin with psychical hallucination such as a certain vivid experience which recurs with each attack. These are positive phenomena which local epileptic discharge may produce in certain areas of the cortex. But there are many other areas that cannot respond thus because of the nature of the function of each. The presence of epileptic discharge in such areas may be betrayed only by the fact that there is interference with the normal employment and use of that grey matter.

Thus when there is discharge in one of the speech areas of the dominant hemisphere, the patient discovers that he is temporarily aphasic when he tries to speak. But if he makes no effort to speak he is not aware that anything has happened to him. This is epileptic interference, the negative effect of discharge.

Functional interference is always present during a seizure. The hand that is tingling because of discharge in the postcentral gyrus has lost capacity for discriminative sensation temporarily. When coloured lights are seen in the right lower quadrant of the visual field the patient is blind to objects that should be seen in that field.

Electrical stimulation has an effect upon the cortex similar to that of seizure discharge. It interferes with normal local function and it produces positive manifestations in those areas of cortex capable of yielding it.

It is my purpose to review[1] the function of different areas of the human cortex in the light of these findings. But first I would ask you to accept tentatively a working hypothesis.

A CENTRENCEPHALIC SYSTEM

The study of clinical neurology and particularly the study of epilepsy drove Hughlings Jackson (1931) to hypothecate the existence of an area of the brain, separate from the motor and the sensory cortex, in which the highest level of functional integration was to be found. Here there must be, he said, a final sensory and motor arrangement that formed the 'neural substratum of consciousness'.

In my own studies it has been more and more obvious that such an area of final functional integration must exist – a ganglionic area in which that stream of nervous impulses must arise that produces voluntary activity, an area in which the sensory pathways culminate in neurone circuits and in which the information relative to past experience is made available, an area in which those nervous mechanisms are to be found which are prerequisite to the existence of intellectual activity and prerequisite to the initiation of the patterned stream of efferent impulses that produce the planned action of the conscious man.

It is obvious that the most important part of this integration does not take place in the cerebral cortex (Penfield, 1938). Transcortical association tracts are not essential to it. For example, excision of the gyri which immediately surround the precentral gyrus does not prevent the use of that gyrus by the patient for the purposes of skilled action that is directed according to visual, auditory or remembered information.

When a motor area of the cortex is stimulated, conscious patients do not believe that they have willed the action. They recognize invariably that movement occurs independent of, or in spite of, their own volition.

Any portion of the cerebral cortex may be removed without producing unconsciousness. On the other hand, injury to the brain stem does result in unconsciousness and epileptic seizures produced by discharge in certain parts of the brain stem are characterized by invariable loss of consciousness.

[1] Illustrative drawings have been provided previously and will not be reproduced here.

Most portions of the brain may contribute in some way to normal conscious processes at certain times but the indispensable 'substratum' of consciousness lies outside the cerebral cortex and probably in the diencephalon.

Herrick defined the brain stem as consisting in 'all of the brain except the cerebellum and the cerebral cortex and their dependencies'. Thus he included the thalami in the brain stem and I shall accept his definition.

As a working hypothesis and definition, I shall refer to those parts of the higher brain stem, which have symmetrical connections with both hemispheres, as incorporated into a centrencephalic system. Obviously this does not include the nuclei of the third cranial nerves nor the geniculate bodies nor other structures that are related to only one hemisphere.

It may be suggested at once that the intralaminar systems of the thalamus and the reticular formation of the brain stem and the non-specific projection systems which have widespread connections with the cortex of both sides satisfy the definition. These doubtless constitute a beginning of anatomical knowledge of the centrencephalic system.

SENSORY REPRESENTATION IN THE CEREBRAL CORTEX

1. *Auditory*

In man, Heschl's gyrus is buried within the fissure of Sylvius. It occupies the superior bank, beginning posterior to the lower end of the Rolandic sensori-motor strip and reaching the bottom of the Sylvian fissure just posterior to the insula.

Electrical stimulation causes a conscious patient to hear an elementary tone or to complain that he cannot hear what is being said. The sound is high or low, continuous or interrupted. The patients described it as 'whistling', 'humming', 'chirping', 'buzzing', 'thumping', 'rushing', etc., or like being somewhat deaf.

The sound or the deafness was often referred to the opposite ear, but this was not invariable.

2. *Somatic Sensory*

1. In the *Rolandic strip*, and especially the postcentral gyrus, threshold stimulation produces a sensation in some portion of the

contralateral half of the body. It is described as 'numbness' or absence of sensation or as 'tingling', 'electricity' or a sense of movement when none occurs. The patient does not inquire as to whether something has touched the peripheral part. He recognizes it as a sensation that has been produced in some unusual manner, not as an ordinary experience.

The sequence of representation is in a fixed and invariable order corresponding with the sequence of Rolandic motor representation.

2. The *second sensory* area of the human brain seems to be located upon the superior bank of the Sylvian fissure anterior to Heschl's gyrus and running down to the insula. Stimulation here sometimes produced sensation that was described by the patient in terms similar to those used in relation to the postcentral gyrus.

In the second sensory area the patient was more frequently impelled to say that he had a desire to move and there was at the same time more frequently inhibition of movement.

In the second sensory area the sensation produced was occasionally bilateral whereas bilaterality of sensation, from stimulation of the Rolandic area, was the rarest of exceptions as far as trunk and extremities were concerned. It was less rare in the face area.

3. *Visual*

Stimulation of the cortex in the calcarine fissure (Area 17 of Brodmann) causes the patient to 'see' brightness, colour, movement, outline situated in some part of the contralateral visual field or directly in front of him. Stimulation of other parts of the occipital lobe (Areas 18 and 19) may produce similar images of colours, lights, black outlines usually on the move. But they are sometimes ipsilateral in position as well as contralateral or central.

Removal of the calcarine cortex produces homonymous hemianopsia. Removal of what may be called the secondary visual cortex[1] does not do so, if it is carried out carefully so as to avoid visual radiations to the primary cortex. Removal of the secondary visual cortex does not interfere with guidance of the contralateral hand in voluntary movement.

[1] Complete removal of all secondary visual cortex with preservation of primary visual cortex has never been carried out. Lashley found this to be an impossibility in the monkey.

From the foregoing observations on 'sensory representation' it seems evident that the calcarine cortex is a way-station for visual impulses which originate in half of each retina and pass on to central integration after leaving the cortex. Transcortical 'association' tracts, from visual cortex to motor cortex, if they exist, are not indispensable to visual guidance of voluntary hand movements.

The postcentral gyrus is a cortical way-station for somatic sensory impulses from the contralateral extremities to some area of central integration. Removal of the postcentral gyrus on the right, for example, deprives a patient of knowledge of the position of the left hand, but he can still guide the hand quite accurately, in voluntary movement, by means of visual information. If he closes his eyes and places the index finger of the normal right hand on the left wrist he can still guide the left hand in voluntary action thanks to sensory impulses that must reach central integration through the postcentral gyrus of the intact hemisphere.

In summary, the second area for somatic sensation (second sensory) and the secondary portions of the visual cortex are related to impulses derived from the ipsilateral side, although to a lesser extent, as well, from the contralateral side. Whatever the function of these dispensable areas may be, the type of sensation produced by stimulation differs little in quality from that produced by stimulation of the primary and indispensable areas.

In no case have hallucinations been produced that resemble things seen or felt in ordinary experience. Such hallucinations, which we have called psychical (after Jackson) rather than sensory, appear only when the electrode is applied to temporal cortex. When stimulating the occipito-temporal region, the change from visual sensory to psychical responses occurs suddenly as the stimulating electrode is moved forward across a surprisingly sharp line that seems to separate the functionally 'visual' from functionally 'psychical' cortex.

It seems evident from these facts that the occipital cortex forms a part of a to-and-fro cortico-subcortical visual mechanism and that transcortical connections from occipital to other areas of cortex are not of primary functional importance.

MOTOR APPARATUS

Stimulation of the precentral gyrus may result in movement which the patient is helpless to prevent or it may produce a simple inability to move the part. In general, the effect of cortical stimulation anywhere, as already pointed out, is to produce activation sometimes, interference with functional employment always.

1. *Corticofugal Connections*

The motor effects will be considered under two headings. (*a*) Cortico-spinal or cortico-bulbar effects, and (*b*) cortical control of subcortically situated motor mechanisms.

(*a*) *Cortical Control of Bulbar and Spinal Motor (anterior horn) Nuclei*

Stimulation produces gross movements of flexion or extension which are, no doubt, mediated through the pyramidal tracts. Bulbar and spinal motor segments seem to have connection with (or representation in) the precentral gyrus in an unvarying sequence. All of these areas that are capable of producing unilateral movement have their cortical connection with the opposite side. Movements of right hand and foot, right eyelids and lips are produced from the left hemisphere. Even the tongue seems to be pushed to the left by impulses that come from the right precentral gyrus and to the right from the left cortex.

(*b*) *Control of Subcortical Motor Mechanisms*

Stimulation of the precentral gyrus also produces more complicated and, what might be called, more dexterous movements: vocalization, chewing and swallowing, alterations in respiration, conjugate looking movements of the two eyes.

2. *Voluntary Movement*

Both of the foregoing types of movement, (*a*) and (*b*) are employed by the human infant at the time of birth. The capacity of the human infant or the chimpanzee infant to vocalize, to suck and to swallow, also to move the extremities, is not altered appreciably by injury to the cortex. Furthermore the adult can control both types of movement on a voluntary basis after complete removal of the precentral gyrus and during its complete absence.

Thus it seems evident that these voluntary movements can be carried out with little or no help from the cortex although these are the very movements that are produced by electrical stimulation of the cortex. When the infants grow older and dexterous use of the extremities should appear, then the absence of precentral gyrus is all too apparent (Kennard, 1940).

The electrode applied to the precentral gyrus produces bulbar and spinal effects similar to those which the electrode might be expected to produce if applied to the motor nuclei of cranial nerves and spinal nerves. So much for the first group of movements.

In regard to the second group, the subcortical mechanisms, the electrode activates or controls breathing, vocalization, conjugate eye movements, mastication, swallowing – all of which acts are obviously subserved by automatic mechanisms in the brain stem.

Thus it is evident that the electrode stimulus cannot imitate the use of the precentral gyrus in voluntary action. It can only demonstrate the peripheral connections of the gyrus.

When the right precentral gyrus in the right hemisphere of a man is intact, skilled voluntary movement of the left hand is possible even though the surrounding cortex has been removed. Therefore skilled voluntary movement must be carried out by means of a stream of nerve impulses which reach the precentral gyrus from the centrencephalic system beneath the cortex. When the patient is conscious these impulses are sent out to both precentral gyri in accordance with his sensory information, according also to remembered experience and the dictates of volition.

The precentral gyrus can do nothing of itself. It can only serve as a keyboard upon which the patterned stream of voluntary impulses plays. This stream of impulses must be somehow analogous to the succession of blows which the fingers of the pianist deliver to the keyboard of the piano.

3. *Information from Electrocorticography*

Dr. Jasper and I have reported the following observation made on the cortex of a conscious and intelligent man (Jasper and Penfield, 1949). Electrodes were placed on the cortex when it was exposed at operation. He then carried out the following move-

ments according to command. He was told to make a fist of the contralateral hand. When he did so the resting rhythm of potentials (25 per second) disappeared in the hand area of the precentral and postcentral gyrus but continued in the face area and in the cortex which lay anterior and posterior to the Rolandic hand area. As he continued the closed-hand posture the rhythm returned in this portion of the cortex.

He was asked to touch the thumb with one finger after the other of the same hand. The result was the same but the resting rhythm did not return to the Rolandic hand area while this complicated manœuvre was being carried out.

These observations and subsequent similar electrographic observations seem to be consistent with the conception of a supracortical stream of nerve impulses from centrencephalic source to motor cortex during voluntary activity.

4. *Extra-Rolandic Motor Apparatus*

It is evident, from experience with electrical stimulation, that the supplementary motor area of the cortex which, in man, is within the sagittal inter-hemispheral fissure just anterior to the Rolandic motor foot area, may be employed to produce postures and manœuvres that involve the limbs, often of both sides, and conjugate looking movements and vocalization as well.

It is evident also that this area of cortex, and the 'second sensory' area as well, may be employed to inhibit or interrupt voluntary movement. One might well assume that these areas of cortex are likewise employed by supracortical control from the centrencephalic system although I can bring forward no proof of such an assumption. Excision produces only minor evidences of motor defect if any.

A SIDELIGHT FROM OBSERVATIONS ON SPEECH MECHANISMS

Stimulation of the cortex never causes a patient to speak nor does it cause him to become aware of disconnected words. It does produce vocalization with attendant control over the respiratory mechanism in the precentral gyrus of either side and the supplementary motor area of each side. Only man has this cortical representation of vocalization and only man speaks.

This, with articulatory control of the lower Rolandic area of both sides, doubtless constitutes the motor apparatus of speech.

In the dominant hemisphere electrical interference may be used to delineate those circumscribed areas of frontal, parietal and temporal cortex that form part of the ideational apparatus for speech. Application of the electrode to such an area may seem to have no effect if the subject is silent. But if the patient is trying to speak he discovers, to his own astonishment, that he has become aphasic. He states afterwards that he knew what he wanted to say but he could not get hold of, could not find, the words.

Thus, it is obvious that the act of speaking, like other forms of skilled voluntary performance, cannot be initiated by cortical stimulation. Initiation probably always comes from elsewhere. The ideational mechanism which is essential to 'finding' the words is evidently situated, at least in part, in the cortex of the dominant hemisphere but no part of this mechanism can be functionally activated by stimulation of the cortex.

On the other hand, strange as it may seem, recollection of specific experiences which may include recollection of speaking can be initiated by cortical stimulation.

CORTICAL MECHANISMS OF RECOLLECTION

Psychical responses from the cerebral cortex, as distinguished from motor or sensory responses, are at times obtained from stimulation of the cortex on the superior and lateral surfaces of the temporal lobe of either side.

The hallucinations thus produced are re-enactments of certain experiences from the recent or distant past (Penfield, 1952b). There may be auditory or visual phenomena or both, and there may be elements of the individual's own interpretation of the experience. Whatever the nature of the neurone mechanism may be, there seems to be an all-or-nothing principle involved in the response, for there is no confusion as there would be by the recall of more than one experience at a time.

Furthermore, the particular psychical response that is elicited seems to be facilitated for a little time just as is the case in motor and sensory areas of the cortex. The same recollection may be repeated as the result of successive stimuli at the same spot or by stimuli at a little distance from each other. Later on, stimulation

at what seems to be the same point may produce an entirely different memory.

Suppose a monopolar electrode is used with a square wave generator producing a current of 60 cycle, 2 millisecond pulses. One or two volts usually proves to be the threshold strength of current required for the elicitation of a somatic sensory response on the postcentral gyrus, with a slight increase to elicit movement from the precentral gyrus. In the case of a patient who has had chronic temporal lobe seizures, the same strength of stimulus may be enough to elicit a psychical response or it may require 3 or 4 volts. We rarely risk the use of greater strengths of stimulus for fear of producing a major epileptic attack, since this is apt to make effective treatment more difficult.

I will refer to cases at random from memory. Let us suppose that a response of music is obtained. When the electrode is applied to the cortex, the patient hears a certain musical selection played or sung. He hears it as he had heard it on some certain occasion. He may say, 'there is a man over there at the piano'; or 'it is lovely the voices in the church', or, 'there is an orchestra playing', etc.

Such patients continue to be aware of the fact that they are in the operating room. A young South African called out in excitement that he heard his cousins laughing and explained that they (he and the cousins) were laughing together at something. His excitement was due to the fact that he realized he was in the operating room in Montreal while they were still in South Africa.

After one patient (D. F.) had been caused to hear the same song over and over by repeated stimulation, she said, 'you have a radio here in the operating room'. She would accept no other explanation even in discussions afterwards.

When the patient is asked to hum the air, he may do so following the music that he seems to hear at, what appears to be, the ordinary pace or tempo. Presumably it is the same tempo at which he heard the music on the occasion which he seems to be re-living.

A little boy heard his mother scolding his younger brother because he had his coat on inside out. A mother heard her son playing in the yard while she was in the kitchen, and she heard the 'neighbourhood noises', cars passing in the street.

Curiously enough, when the patients were questioned as to whether this was something they remembered, they usually replied that the experience was far more real than a memory. But they usually recognized it as authentic. The mother explained that she had heard her son playing in the yard just like that many times. But she did not know which time this was. The little boy recalled that his brother had put on his coat inside out shortly before he came to Montreal. When the mother was questioned, she laughed and said he was always doing it.

Those who were caused to hear a song might not recall when it was they heard it just that way, although they might know the song well enough to sing it. One patient said, 'it is a song my mother used to sing to me'. Another explained that it was the theme song of a radio programme – something about 'Luigi'. Another stated that they sang '"White Christmas" like that' in the church at Christmas time.

In general the recollections produced by stimulation seem to be as clear as they would be a few seconds after the experience. In fact they are apparently as clear as they were during the experience.

What we are in the habit of calling memories tend to become generalizations. We learn to know a song by many hearings, each time perhaps through a different medium. We learn to know a friend by seeing him while he is doing many things. Sometimes we see him from behind, from in front, while talking or walking, smiling or laughing. When we summon the memory of the friend it is usually a generalization which appears.

Each renewed experience of him is like a strip of film from a moving picture. It is not a still picture but a moving progressive sequence of images that occupied minutes of time. These strips of film are still available to the electrode for a long time, perhaps always.

But the detailed information is obviously still available and can be utilized when called upon. For example, after ten years of absence one may be quite unable to recall a former friend clearly. Nevertheless when he is met again, however unexpectedly, one recognizes him and sees at once changes in minute detail. There are new lines in his face, an added stoop of the shoulder, a change in the walk, a greying of the hair. Perhaps his gestures seem

suddenly familiar, the tone of his voice, which one had forgotten, is recognized as identical with the voice of the former friend.

This new experience in which the friend was the centre of attention again was immediately compared with the ganglionic records of that friend which had been ostensibly forgotten but not lost. Thus the new experience seems to rediscover the ganglionic records of past experiences.

There is other evidence also from the study of our material that each new experience is sorted or classified while it is being recorded. Similar experiences seem to be somehow united or associated in the cortex.

When a stimulating electrode is applied to the temporal cortex a stream of successive impulses is delivered at a given rate (for example 60 per second). It seems strange indeed that this should bring back into the patient's consciousness a specific experience from his past. But, however strange this may seem, it is a fact and it calls for physiological explanation.

When electrical stimulation is carried out, it might be assumed that the current is passing through a series of nerve cells, axones, collaterals, synapses – following the same pattern that was followed by nerve impulses when the specific record was first laid down. The stimulatory stream apparently does not follow the pathway taken by all similar recordings. It cannot activate a generalization. It can only follow the course of one recording at a time, reproducing a sequence of events that are bound together by a given interval of time.

Let me refer to the case of a young man (E. C.) who had temporal lobe seizures due to a very slowly growing cholesteatoma that compressed the left temporal lobe. His attacks began with the recollection of an experience that occurred at the age of 13. In this experience he had 'grabbed' a stick from the mouth of a neighbour's dog and had thrown it to a distance. This recollection became the initial phenomenon of each succeeding seizure.

His attacks, which began at 17, were precipitated by witnessing a similar incident. His first attack was precipitated as follows:

He saw a rifle grabbed roughly from the hands of another youth on parade. Then he was suddenly aware of himself grabbing a stick from the mouth of a dog after which he remembered no more. He was seen by others to fall in a major convulsive

seizure. Six months later, while sitting in a night club, he saw a man 'grab his hat from the hat-check girl' whereupon the same train of events was set in action. He was aware of himself grabbing a stick from the mouth of a dog, following which he became confused and had a period of amnesia. He did not know whether he had a major convulsion or not.

At operation in this case electrical stimulation of the temporal cortex was carried out several centimetres from the tumour. This caused the patient to call out: 'There he is. It was like a spell. He was doing that thing; grabbing something from somebody . . . a stick or something . . . up the street . . . That was like an attack, doing that thing.' After an interval the electrode was re-applied to the same point and held in place for a longer period. The patient cried out, 'There he is.' Then he began to turn to the opposite side and had a generalized seizure.

For those not familiar with epilepsy it should be explained that seizures are not infrequently precipitated by the arrival of nerve impulses in the irritable area. Thus a man whose attacks habitually begin with an aura of a tingling in the right thumb may be well aware that rubbing or touching the thumb is liable to precipitate a seizure. It would seem that this is produced by the arrival of evoked potentials at the postcentral thumb area. Touching other parts of his body sends evoked potentials to other portions of the postcentral gyrus but no seizure is produced. A man whose attacks begin with discharge in the visual cortex of one occipital lobe may have a fit induced by looking at a light. Another who has auditory seizures may complain that sounds precipitate attacks.

The young man (E. C.) might watch events of the greatest variety. But only when he saw someone 'grabbing something from someone' was his own psychical seizure precipitated. This would suggest that when he witnessed each new incident which included grabbing, only then did nerve impulses reach the sequence of ganglionic connections in the temporal cortex, which constituted the neuronal record of his own childhood experience of grabbing a stick from the mouth of a dog.

How it is that records can be related or classified according to the abstract concept of grabbing something from someone, whether it be dog, youth on parade or hat-check girl, is difficult

to understand. It presents a fascinating problem to the psychologist. Here is a problem to be studied by the neurophysiologist.

INTERPRETATION OF PRESENT EXPERIENCE

Electrical stimulation, or limited epileptic discharge, may alter a patient's interpretation of current experience so that he makes a false judgment. Thus if such a discharge occurs while the subject is listening to and watching some event, he may have a sudden feeling that it has all happened before or on the contrary that it is very strange, absurd. He, himself, may seem far off, lonely or fearful. All of these feelings are interpretations of present perceptions which have been influenced and altered by stimulation.

Interpretative signals seem to originate in the temporal cortex. It is as though, during the recording of an experience, a judgment were made there by comparison of the present with the past. In a sense this is a disturbance of the process already discussed, of comparing present experience with past recordings. There is comparison of one's present perception, e.g., of a friend, with earlier recordings of that friend. The sound of his voice is reported as familiar perhaps while the grey in his hair is strange.

The fact that such illusions of perception may be produced by stimulation, without other interference in the patient's understanding, is consistent with the conclusion that present experience is recorded in the ganglionic complex of the temporal lobe and past experience is preserved in that recording.

RECORDING OF EXPERIENCE

One other observation may be made that should throw a little light on temporal mechanisms. Discharge in the periamygdaloid area of one temporal lobe produces interference with memory recording so that, for the duration of the discharge at least, the patient will have no future recollection of what transpired. He will have subsequent amnesia for the period. Deep stimulation with an electrode that is insulated except at the tip will produce the same state for the duration of stimulation. This is an example of electrical interference with functional utilization of the area.

Deep stimulation has been carried out many times as follows:

The electrode is thrust perpendicularly into the second temporal convolution at a point 4 cm. posterior to the tip of the temporal lobe. When the tip is at a depth of 3 to 4 cm. the current is switched on and the patient is immediately confused and may speak in an unrelated manner.

At such times the patient is said to be automatic. He may move about and may carry out purposeful action in a more or less confused manner, but he will have no later recollection of the period. The recording process seems to be arrested somehow in both temporal lobes or, more likely, in the central integrating mechanism that projects the memory record to both temporal lobes.

During that period of automatism for which he will be amnesic he is often not altogether cut off from past memory. If an attack of automatism occurs he may return through the city to his home or give other evidence that he remembers an intended course of action.

It seems likely, therefore, that the mechanism of recall of memory is anatomically separated from the mechanism of recording.

DISCUSSION

It was my intention to set before you the responses to electrical stimulation which are characteristic of different areas of the cortex of a conscious human being in the hope that during the discussion in this conference the meaning of these observations might become more apparent. Some such hope has no doubt impelled each of you to come to Ste Marguerite.

One obvious need is to bring our observations on the human brain into relationship with the findings of the experimentalists and anatomists who are at present exploring such structures as the reticular activating systems.

One general conclusion may be drawn from consideration of this material: that transcortical 'association' tracts between functional areas of the cortex are of minor importance. The truth of this statement has been demonstrated by cortical excision, at least as far as the Rolandic motor, the somatic sensory and the visual areas are concerned. Each of these areas seems to continue to

discharge its proper function after excision of adjacent and surrounding areas of cortex.

The precentral gyrus is a *way-station* in the efferent stream of voluntary impulses. This stream originates in the centrencephalic system passing to the cortex (where it may well be altered) and down through the spinal cord system to the voluntary musculature. Stimulation of the precentral gyrus with an electric current causes (*a*) gross muscular contraction or it activates (*b*) subcortical automatic mechanisms that produce somewhat more complicated acts.

Electrical stimulation demonstrates the ganglionic connections of the so-called upper motor neurones, but it cannot produce the complicated acts which the normal adult can carry out voluntarily. The difference in these two sets of motor activity is, in a sense, a measurement of the difference in the pattern of impulses in an electric current as compared with the pattern in the voluntary subcortico-cortical stream of impulses.

Electrical stimulation of a sensory area of cortex can cause the patient to have somatic or visual or auditory sensation, because the impulses pass inward from the electrode to the subcortical circuits of the centrencephalic system. But what it is the patient is caused to feel or see or hear bears only a limited relationship to his perceptions in ordinary life. He is rarely under the impression that this is information about the world around him.

In the sensory areas the electric current delivers impulses that are not organized in patterns like those that must come from retina, cochlea and skin. If they were, perhaps cortical stimulation of sensory areas might cause the patient to see complicated things such as trees or men, and to hear words or music.

But stimulation does cause the subject to see colours, lights, which are recognized as normal. Moreover the images are situated in one part of the visual field or another according to the position of the stimulating electrode in the calcarine cortex. Therefore, as far as the elements of vision are concerned, one may assume that the stream of steadily repeated electrical impulses is the same as, or similar to, the stream of ganglionic impulses that causes the patient to see elementary light or colour normally.

The same is true of hearing. The patient becomes aware of ringing, buzzing, thumping, sighing. These are not different in

quality from such sounds or tones heard at times under ordinary conditions, and the vibration frequency of the sound is not necessarily that of the electrode (40 to 100 per second).

In the field of somatic sensation, when electrical stimulation causes the patient to say he feels an arm moving, although there is no movement, the artificial sensation does not differ from the real.

Therefore, insofar as these pure tones and colours and sensations of simple movement are recognized as normal, the artificial stream of impulses that flows from the electrode placed on the sensory cortex into the centrencephalic system may be considered to have imitated or reproduced a physiological process.

One may be tempted to believe that if it were possible to apply such stimuli selectively to the smallest units, or even to the separate ganglion cells, of the sensory cortex and if it were possible to control the time and place of delivery of stimuli properly, the patient could actually be made to see trees and men, hear words and music, feel a button or a pin. The pattern of the stream of impulses from sensory cortex into the centrencephalic system would then be correct in the timing and placement of impulses.

On the other hand stimulation of the temporal cortex yields a very different result. It seems to re-create specific experiences from the past in a manner that the patient accepts as authentic. Or it may alter perceptual interpretation of new, that is present, experience.

How is it that the temporal cortex differs from the sensory areas? Here the same electrode delivering the same current reproduces an actual experience from the patient's past with startling completeness. It is an episode in which action goes forward and the patient is an actor. He may seem to see and hear and to react as well. It is as though a strip of cinematographic film from the past equipped with sound track had been used, all previously edited as to meaning and emotion by the patient himself!

What is the intimate nature of the recording neuronal mechanism that has been discovered by the electrode? This is a question that I would place before electrophysiologists.

It seems to me that an all-or-nothing principle is involved here, for the experience recalled is a single one, not confused as it would

be if more than one pattern were activated at a time. It is true that the patient has a double awareness. He realizes that he is in a present and in a past experience simultaneously. Furthermore, he continues to record the total situation, for he will remember this strange state of affairs later.

These facts bear out the conclusion, based on other evidence, that the two temporal lobes have similar functions, contain records which are identical and that either one may play the role of both, except for the temporal speech area.

One might well ask the question as to whether the ganglionic complex, which seems to have recorded in it all past experience, is in the temporal cortex or whether stimulation there activates a distant mechanism in which the record has been preserved. The evidence from the study of temporal lobe epilepsy suggests strongly that the recording mechanism is there in the temporal cortex.

On that supposition then I have imagined that the steady pressure of impulses applied by the electrode to the temporal cortex causes one synaptic barrier after another to open for the passage of current, slowly, steadily, in a pattern that was established by the effect of impulses delivered to the temporal cortex from the centrencephalic system at the time of the original experience.

Thus, the re-enactment of the event progresses at the same rate of speed as that of the original experience and thus the re-activation of this ganglionic pattern, projecting its activity back into the zone of central integration within the centrencephalic system, causes the patient to be conscious of the experience for a second time.

It would be going beyond the evidence to conclude that all memory records are necessarily stored in ganglionic patterns in temporal cortex. These observations throw little light on how skills and habits may be preserved within the nervous system or what the organization of speech mechanisms may be. They do not quite explain how generalizations, such as a song or a poem that has been committed to memory as the result of many individual hearings, are preserved ready to be 'called to mind'. When they are called to mind by the man voluntarily the detail of each hearing seems to have been lost.

One of my former patients (D. F.) once wrote to me asking whether at the time of operation I had been stimulating her subconscious mind when I produced in her a recollection of the past. I was amused for a moment. Then I was startled for these records become something like that. Perhaps her suggestion was not far from the truth. The great body of current experience seems to be forgotten by an individual but it is not lost, for the little strips of record that the electrode activates reproduce experiences that are clear and accurate in every detail. There is much evidence from other sources that we make subconscious use of them. Yes, the continuous strip of current experience is converted into a subconscious record and one might well say that it forms the neuronal basis of what has been called the subconscious mind.

This brings us to a consideration of what the essential ganglionic activity may be that accompanies the conscious state, the state of awareness. Do the foregoing observations throw any light on the problem?

It seems evident that the ganglionic record in the temporal cortex is formed at the time of each successive experience. It may be suggested then that the formation of this record is an important part of the neurone mechanism essential to awareness. It may well be that it is while the record is being created, by a sort of projection of neurone impulses to the temporal cortex, that a man is aware of present experience. The record contains those things to which attention is directed and apparently only those.

Thus, to recapitulate, the hypothesis is suggested that sensory information is integrated within the centrencephalic system. A selected portion of this information is then somehow projected outwards to the temporal cortex by that portion of the system which is in functional connection with the temporal cortex of both sides. As it is thus projected, a comparison is made with past similar experiences, thanks to the records of the past that are held there, and judgment with regard to familiarity and significance is made.

There must then be re-projection back to the centrencephalic system by means of the same neurone connections that are activated by the surgeon's electrode. A plan of action is then formulated. This formulation would also seem to be carried out by means of ganglionic activity in the centrencephalic system because of the

fact that the activating stream of motor impulses is sent out from this system. Part of this stream certainly passes outward to the precentral gyrus of each side and the voluntary muscular activity which results is obviously discriminating and appropriate. It is appropriate to the nature of the sensory information, appropriate to the remembrance of past experience and appropriate to the established desires or intentions of the individual.

How it may be that ganglionic activity is transformed into thinking and how it is that thought is converted into the neuronal activity of conscious voluntary action we have no knowledge. Here is the fundamental problem. Here physiology and psychology come face to face. We are far from this final understanding and life is short!

CONCLUSION

This much emerges from study of the cerebral cortex of conscious man.

1. The sensory areas of the cortex transmit the current of afferent impulses, received from the periphery, inward to a central zone functionally common to both hemispheres.

2. Those things which exist in the individual's momentary awareness are somehow projected from this common zone to the cortex on the superior and lateral surfaces of the temporal lobes.

Subsequent electrical stimulation of this temporal cortex occasionally re-creates for the individual the content of this awareness in full detail. Therefore, there must be, it seems, a recording of all present experience in a continuous ganglionic pattern, some or all of which is located in temporal cortex.

3. When the precentral gyri are employed in the execution of voluntary action they respond to a stream of activating nerve impulses that originates in a central area within the brain.

4. The integrating mechanisms prerequisite to voluntary planned action are subserved by to-and-fro cortico-subcortical neurone circuits. The so-called association, or transcortical, connections between cortical areas are not important in that integration.

GROUP DISCUSSION

JASPER: I am sure we are all very grateful to Dr. Penfield for this account of the experiments which led him to the hypothesis of centrencephalic integration. The beauty of this hypothesis is that it can be tested and that the experimental work which has arisen from it has been extremely fruitful.

BREMER: Dr. Penfield's observations are of such fundamental importance that I need hardly apologize for asking him specific questions about the experimental data. Firstly, has Dr. Penfield in the isolation experiments to which he alluded a specific case of complete isolation of the motor cortex? Secondly, has Dr. Penfield ever had occasion to attempt to elicit memories by the stimulation of the underlying white matter, after excision of the temporal area. Thirdly, were events in the distant past ever recalled? Finally, can these memories be evoked in normal non-epileptic patients? I would like to offer also a comment on the observation by Dr. Penfield and Dr. Jasper in which the beta rhythm was activated simply by warning the patient that he would have to move. This could perhaps be explained on the basis of the 'gamma efferents' which are the thin fibres discharging to the muscle spindles which show activity before the motor fibres proper. This anticipatory activation and sensitization of the muscle spindles might still be present in the absence of visible movement.

PENFIELD: I think Dr. Bremer's question about isolation is very important. We cannot, of course, remove all inter-cortical connections. As far as the precentral gyrus is concerned, we have many cases of this sort in which everything in front of or behind or below the precentral gyrus (also within the saggital fissure between foot area and corpus callosum) has been removed in such a way as to interrupt all possible inter-cortical connections in those directions. Very often the face area has also been removed sparing the hand area. The hand or foot area is spared wherever possible. Occasionally we have encircled the precentral gyrus completely except for the cingulate gyrus.

We carried out complete encirclement in the following case: a girl had a very large area of abnormal cortex giving rise to frequent attacks. In her case the precentral gyrus was left by itself with the cortex removed on all sides. It is interesting to note that this girl was still capable of fine hand movements with the precentral gyrus thus circumscribed on all sides.

With regard to the sensory areas we can never get complete removal of surrounding cortex but we have removed the cortex behind the postcentral gyrus and the precentral gyrus in others. The postcentral gyrus continued to function normally.

I know what Dr. Bremer is thinking of when he asks about stimulating the underlying white matter after the temporal lobe has been removed. He wonders whether we are activating a subcortical recording mechanism or some mechanism which lies at a distance from the cortex. Stimulation of the underlying white matter has never evoked a memory and while this is a negative result, it may be pointed out that if you stimulate the underlying white matter of the motor cortex after cortex itself has been removed, you may still get movement. In the case of the postcentral gyrus you may also get sensation from stimulation of its underlying white matter although not as readily as in the case of the precentral gyrus.

Insofar as the age of the memories evoked is concerned, perhaps I did not express myself clearly. I meant to point out that both old and recent memories are evoked with equal ease. There does not seem to be any evidence for the ageing of the memory process and I believe that we retain permanently as memories all those things to which we have attended.

WALTER: I should like first to inquire about the parameters of the electrical stimulation. These may be very important for the type of effect they evoke if one can compare these observations with those during flicker activation. We do not doubt that the evocation of memories by stimulation is a physiological phenomenon because in our experience flicker stimulation also can evoke memories in both normal and epileptic subjects. We have a boy who sees red circles as an epileptic aura, leading to a vision of a boy approaching him and growing larger — a type of macropsia. We can evoke the red circles by flicker but not the macropsia, the subjective sensation being accompanied by seizure patterns moving from the occipital towards the temporal lobes. In non-epileptics, photically evoked memories and visions are often related to a traumatic experience.

My second comment is that the control of movement might be analogous to a change of bias in a servo mechanism. In this case the change of bias could well occur towards the periphery if not in the muscles themselves, as well as centrally. In these circumstances, voluntary movement would be related to cortex in a very subtle way.

PENFIELD: The events recollected are often unimportant and uninteresting psychiatrically.

WALTER: The flicker frequency is very critical. What happens when the frequency of electrical stimulation is varied?

PENFIELD: We have varied the frequency of stimulation from about 20 to 160/sec., particularly in cases in which it was difficult to produce a response. As these variations did not produce noticeable differences, we have settled on square wave stimuli of 2 m.sec. duration, 60 per

sec. Thus the threshold was 1-2 volts for the postcentral gyrus. The precentral gyrus requires a slightly higher voltage and in the temporal area the effective voltage may be the same or may have to be doubled. We don't use stronger stimuli for fear of seizures.

WALTER: The effective flicker rates are below 20/sec.

MAGOUN: Dr. Penfield, in private discussion yesterday, used the simile that his work was like a hand reaching down from the cortex to grasp another hand reaching up from the brain stem. He pointed out that while the two were approximating each other the grip was not yet secure. It seems to me that this simile could be broadened to a hand reaching down from clinical studies to grasp another reaching up from the experimental laboratory. The idea of the centrencephalic system reaching up into the cortex arose in Montreal and now the hand reaching down from the cortex to the centrencephalic system is beginning to emerge from studies in Dr. Penfield's Institute and elsewhere. What is the role of the centrencephalic system relative to the cortex in the detection of perceptual detail? Laboratory studies indicate convergence and occlusion within this subcortical system. It is difficult to visualize discrimination of different modalities within it. Does Dr. Penfield believe that the centrencephalic system is itself a focus or does he conceive of it as a non-specific system playing on various areas of the cortex.

PENFIELD: I don't believe the centrencephalic system ever acts by itself. I think that its action must always be associated with cortical activity, usually in both hemispheres. There is evidence that one temporal lobe is so to speak the carbon copy of the other. They may be used simultaneously. I do not believe that we should think in terms of one level of the central nervous system divorced from other levels. If the centrencephalic system is necessary for consciousness the cortex must still be acting in harmony with it. There may be a double awareness. Nevertheless, I feel that these are essentially normal processes. I would like to cite the example of a patient who called out on the operating table: 'Doctor, doctor, I am hearing my cousins, but they are in South Africa.' Perhaps the presence of the second awareness of this incongruity was made possible by his use of the intact temporal cortex on the opposite side.

HEBB: The answer Dr. Penfield gave to Dr. Magoun, in which he implied that the cerebral cortex and centrencephalic system work hand in hand, removes a misunderstanding of which I was guilty. I thought, to put it in extreme form, that Dr. Penfield meant that conscious processes might continue if all cortex were removed. Since the two work so closely together, may it not be misleading to talk of this system as the 'highest level' or 'centre of consciousness'? But this is termino-

logical only, in view of Dr. Penfield's answer. My second point: I do not see how we can separate memory and consciousness topographically. Is there not another interpretation of the temporal lobe data? Electrical stimulation of a neural mass may mirror its neural function or not, depending on the arrangement of fibres in it. It seems that we must recognize two types of transmission in the CNS. Where fibres are essentially parallel (those originating together in one small region conducting to one other small region, so that they can act effectively together) gross stimulation may approximate what happens physiologically. But stimulation within a tangled network, where normal function requires independent or asynchronous firing, might simply prevent normal transmission, with a 'busy-line effect'. It is very difficult to conceive of memory as a function of a localized region. Thus the distinctive effects of stimulation of the temporal lobe may reflect a special arrangement of fibres within it, rather than showing that memory is resident here and not elsewhere. 'Memory' surely comprises all lasting modification of neural function resulting from earlier activity of the cells concerned, and it seems inevitable that the frontal and parietal lobes are also concerned. I should add, however, that this is only a change of interpretation. It does not change the fact that these data are of very great psychological significance, and it still seems clearly that the temporal lobe has a distinctive function in recall.

PENFIELD: I wish Dr. Hebb would teach me what terminology to use so as to avoid the accusation that I believe in a punctuate or a compartmental representation of consciousness!

ADRIAN: I wonder if I have got Dr. Penfield's idea about the temporal lobe quite straight in my mind. Am I right in thinking that he suggests that all memories from childhood onwards are stored there? The evidence seems to show that only particular kinds of memories, auditory and visual memories, can be evoked by stimulation. He has not presented evidence for the storage of skills and motor memories. Do you think it is the region for all memories? Or only a particular sort of memory?

PENFIELD: There is no evidence for the recording of skills in the temporal lobe. One can only say that a succession of experiences of all types, or at least auditory and visual together with original interpretation of the experience, seem to be stored there. There is no evidence that the temporal cortex is particularly important in the execution of skilled acts. However, when a man plays a sonata, he probably refers to memory records in the temporal lobe.

KUBIE: I would like to raise two points:

First, if I understood Dr. Penfield correctly, I think he implied that these memories were always and only of things which were attended

to. Unless the word 'attention' is used in an unusual way this is not true for all kinds of memory. The evidence from hypermnesis under hypnosis is well established. A man may enter a room and then describe it, having noticed perhaps 20 objects. Subsequently under hypnosis he may add many additional details, showing clearly that he registered, recorded and may reproduce many organized stimuli of which he had been wholly unaware.

Secondly I want to make a plea for a careful examination of the latent emotional importance of evoked memories which may *seem* trivial. Such memories may turn out to be of the greatest importance to the subject. The most highly emotionally charged memories are often masked and represented by seemingly insignificant details, and it would be desirable to re-examine these meticulously.

CORRELATION OF BIOELECTRICAL AND AUTONOMIC PHENOMENA WITH ALTERATIONS OF CONSCIOUSNESS AND AROUSAL IN MAN

By

RICHARD JUNG

Correlations of conscious experience and physiology can be studied satisfactorily only in human subjects. Consciousness and attention may be tested approximately by the perception of sensory stimuli and by verbal communication. However, both attention and consciousness are also altered by the arousal effect of the stimuli. Therefore our investigation is restricted methodically to a few aspects of the problem. Comparisons of objectively recorded responses of the central and autonomic nervous systems together with verbally communicated subjective experiences can give only limited information about some basic neurophysiological mechanisms for the regulation of conscious perception and attention.

Definition: Consciousness is considered as a selective and restraining function for limiting actual psychic experience amongst the many potentially psychic phenomena which remain unconscious. Attention is a co-ordinating aid for conscious perception and may be compared to a spotlight which illuminates details in the dark unconscious field of the internal and external world (Weber and Jung, 1940). From clinical evidence it is assumed that consciousness and attention are functions of the brain.

To illustrate this definition I may be allowed to give a schematic diagram of my conceptions of consciousness and attention (Fig. 1). The main conclusion seems to be that consciousness should be considered together with attention: both functions are co-ordinated and selective so that consciousness will contain only very few things in a focus of attention with a fringe representing the half conscious background of the 'sphere'. This figure shows how the searchlight of attention assists consciousness by selecting inner experiences and outer

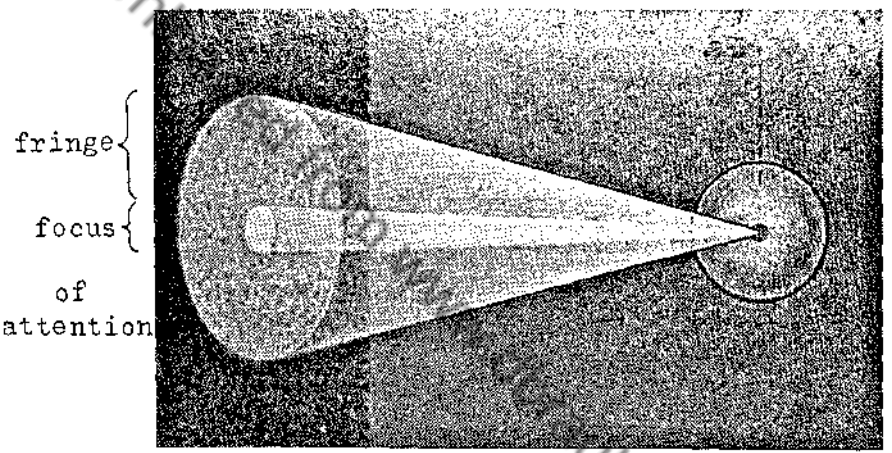


FIG. 1

Schematic diagram of the selective function of consciousness with the searchlight of attention, illuminating details of the inner and outer world. The searchlight should be considered as movable to select different objects and as having a regulating diaphragm to illuminate a narrowly concentrated or a diffuse wide field of attention.

perceptions from the sense-organs, so illuminating a sector of the internal and external world. The beam of light is focused on the central spot giving brightness and clarity. A surrounding fringe or 'sphere' allows a peripheral field with a more hazy picture. The searchlight is movable and can change for selection of objects. It can be concentrated or broadened to illuminate a narrow or a wide field. This diagram has its limitation and does not show the more dynamic side of the 'stream of consciousness'. Another metaphor may be more useful for this purpose: 15 years ago, when working on the epileptic aura (Weber and Jung, 1940) we used a further illustration for consciousness and attention and their relation to other psychological functions: following a suggestion of K. Jaspers (1923) we compared conscious activity with a play on a stage. On this stage various actors appear for a limited time as the actual selected contents of consciousness, illuminated by the spotlight of attention. After a short performance the actors of conscious thinking and feeling disappear behind in the unconscious background of the stage. The spotlight of attention may be broad and shine with a diffuse light on the whole stage or it may be concentrated on one actor with a small but very bright spot as when we focus our attention on one object.

I do not intend to discuss the well-known phenomena of the blocking of the alpha-waves with visual attention (Berger, 1930; Adrian and Matthews, 1934) and of the EEG-changes in different states of sleep (Loomis *et al.*, 1938) familiar to everybody. I wish to speak about some observations on the EEG, respiratory and autonomic reactions in arousal from normal or pathological alterations of consciousness and their possible relation to perception and attention. In addition to these observations the effects of electrical stimulation of the specific and unspecific projection system in the human thalamus are reported to bridge the gap between the study of human subjects and animal experiments.

Methods: Simultaneous recordings of the electroencephalogram, electrocardiogram, galvanic skin reflex, finger-plethysmogram and respiration were obtained in 10 normal individuals and 10 patients with *petit mal* epilepsy. The method and some results are described in an earlier paper (Jung, 1939). The arousal reactions to sensory and verbal stimuli were studied in varying states of drowsiness and sleep and during *petit mal* attacks. Additional observations on the EEG only were made during syncopal faints with loss of consciousness.

During stereotactical operations (method of Riechert and Wolff,

1951) electrical stimulations of the human thalamus and basal ganglia were made in various conditions (intractable pain, hypercinesia or schizophrenia). The electrical stimuli were thyratron discharges of 0.5 to 1 m.sec. duration applied by bipolar concentric electrodes, 1 or 3 mm. apart in the brain. Voltage of stimuli was varied between 1 and 18 volt, electrode A.C. resistance 500–800 ω. Some of the patients were under local anaesthesia, but most of them were in a state of light hibernation with megaphen. This causes little change in the EEG and there ensues a semi-sleeping state from which the patients can be aroused so that they may answer questions. The effects on the EEG of these stimuli were recorded with an 8-channel electroencephalograph (Figs. 6, 7)

ELECTROENCEPHALOGRAPHIC AND AUTONOMIC RESPONSES TO SENSORY STIMULI IN DIFFERENT STATES OF CONSCIOUSNESS WITH VARYING PERCEPTION

1. *Normal Alterations of Consciousness (Wakefulness and Sleep)*

In normal adults the EEG was recorded together with autonomic reactions and respiration in the wakeful state, in drowsiness and sleep. Various stimuli (shouts, pistol shots, pin pricks and cold on the skin) were applied and verbal commands (to take a deep breath or to open the eyes) were given. In the wakeful state all stimuli of the first sort cause autonomic reactions in the galvanic skin reflex and the plethysmogram following a more or less distinct short block of the alpha-waves. When the stimuli are expected the autonomic responses are less pronounced and the alpha-block may fail to appear. In drowsiness and sleep some slowing of pulse rate and respiration occurs, but the autonomic reactions remain the same or become larger (Fig. 2). In the EEG, however, very different arousal reactions appear: in the drowsy state alpha-activation instead of blocking occurs and the on-effect (P. Davis, 1939) is often more marked (Fig. 2*b*). In medium or deep sleep the K-complex, described by Loomis and co-workers, is observed with several slow waves (Fig. 2*c*) or later alpha-activation. The alpha-activation and the K-complex have longer latencies (100–300 m.sec.) than the alpha-blocking.

In the wakeful state, during the first experiments the stimuli caused more emotional reactions and a generalized sympathetic discharge with galvanic skin reflex, vasoconstriction and tachy-

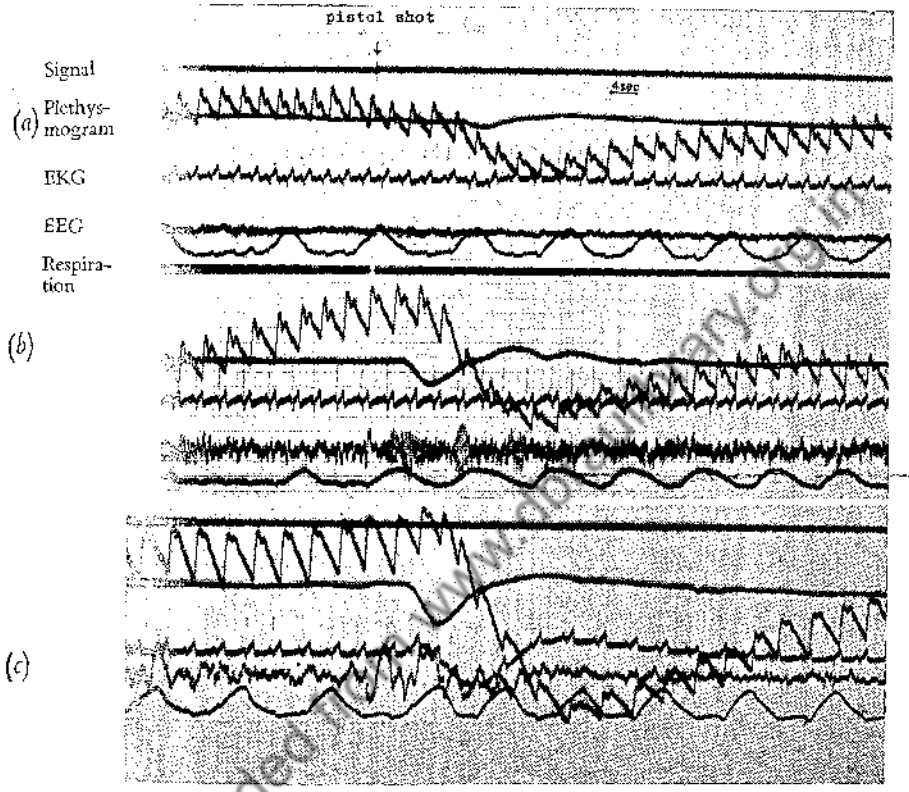


FIG. 2

Different arousal reactions after acoustic stimuli (pistol shots) in various states of consciousness. Normal subject with simultaneous recordings of EEG, EKG, galvanic skin reflex, finger plethysmogram and respiration.

(*a*) State of attention in the waking individual. Little alpha-activity in EEG. Relatively high pulse rate around 80 per sec. Stimulus evokes small vasoconstriction in the plethysmogram, practically no change in galvanic skin reflex and EEG. Moderate acceleration of respiration.

(*b*) Drowsiness at the onset of sleep with a few slow waves in EEG. Pulse rate around 60 per sec. Stimulus causes on-effect and later activation of alpha-rhythm in the EEG. Marked autonomic reactions of galvanic skin reflex and plethysmogram, acceleration of pulse rate and respiration. Stimulus caused arousal and was perceived.

(*c*) Deep sleep with large slow waves in EEG. Slow pulse rate with respiratory arrhythmia between 50 and 60 per sec. Marked vasodilatation with early dicrotic wave in plethysmogram. Stimulus causes K-complex followed by atypical large slow waves in EEG. Strong autonomic reactions in plethysmogram and galvanic skin reflex, short acceleration of pulse and respiration. Subthreshold arousal, subject did not awake and could not remember the stimulus later.

cardia. Later with some habituation the galvanic skin reflex and the alpha-blocking became less pronounced after cold stimuli and after a deep breath so that only vasomotor reactions remained (Jürgens, 1940). After many repeated experiments one subject became so used to the stimuli that in the wakeful state the autonomic reactions of EEG-changes were much diminished or altogether absent even after strong acoustic stimuli such as pistol shots. In drowsiness and sleep the autonomic responses to stimuli, ineffective in the wakeful state, became again very intense and constant although the subject did not always awake. Even very low noises such as a whisper or a clicking of the hammer of the pistol were able to elicit arousal reactions in the EEG and the autonomic system. Later questioning in the waking state revealed that many stimuli that caused these reactions in deep sleep could not be remembered. Verbal commands during sleep were not obeyed although definite changes of the EEG or autonomic reactions occurred. In some subjects complex verbal communications given in sleep could be remembered approximately. In these instances however when the sleeping person was addressed the EEG always changed from the sleep pattern more to the waking state with diminution of slow waves and appearance of alpha- or beta-waves.

From these observations one may conclude that the arousal reactions of the EEG are dependent upon the different state of activity of the brain which in some way is associated with different levels of consciousness. The autonomic responses associated with arousal do not change in different states of consciousness, except that conditioning and expectation of the stimulus tends to suppress and diminish the reactions in the waking state.

Voluntary attention with mental exercise (calculating) had a similar effect on the EEG or the automatic responses as had sensory stimuli. However the duration of vasoconstriction was longer with mental exercise than after sensory stimuli. Also mental exercise was found more effective in preventing drowsiness and sleep than sensory stimuli.

A clear-cut correlation between EEG and conscious perception could not be found in the different states of consciousness of normal subjects. It can only be said that perception was mostly suppressed when the slow waves of deep sleep were present. In

drowsiness and sleep all stimuli tended to evoke an arousal reaction, the form of which was dependent upon the actual pattern of the EEG, varying with different levels of consciousness. When the arousal reaction changed the sleep pattern of the EEG to a higher level of light sleep or a waking record, perception was again facilitated. The reappearance of autonomic responses during sleep to otherwise ineffective stimuli indicates that sleep may eliminate a conditioned suppression of these responses which has developed in the waking state.

Inasmuch as the different states of drowsiness and sleep had so many intermediates, graded transitions and physiological variations from moment to moment, it seemed more promising to investigate conscious perception in pathological disturbances of consciousness which occur in attacks of definite time limits and of more uniform character such as in *petit mal*.

2. *Petit Mal*

Petit mal attacks cause an alteration of consciousness and perception for a definite time with a clear bioelectrical equivalent in the spike and wave discharges of the EEG. Its frequent occurrence and easy reproduction by hyperventilation makes *petit mal* especially suited for these investigations (Jung, 1939; Cobb, Sargent and Schwab, 1939; Schwab, 1941; Cornil, Gastaut and Corriol, 1951).

Petit mal discharges can be blocked by intense sensory stimuli, the most effective of which are loud noises and pain (Jung, 1939). Although not all these stimuli have a blocking effect some diminution of the spikes and waves in the parieto-occipital area is mostly seen and eventually a sudden end of the attack may be induced (Jung, 1939).

When a cessation of respiration occurs during the attack (as it happens often after hyperventilation), the stimuli may elicit an inspiration. The beginning of this first inspiration can be recorded and correlated in time with the EEG. Sometimes the respiration is activated without an effect on brain potentials or with incomplete block, but mostly the first inspiration begins earlier, 100-200 m.sec. before the spikes and waves are blocked (Fig. 3).

Effective blockings of *petit mal* discharges are always followed by discharges in the sympathetic nervous system as recorded with

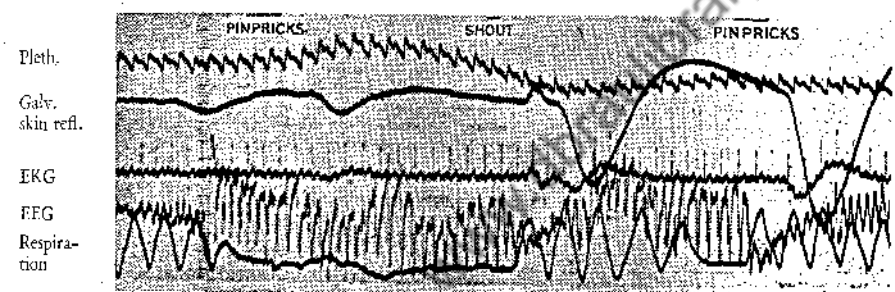


FIG. 3

Petit mal attack with EEG, respiration and autonomic reactions. Arousal caused by sensory stimuli activates first respiration, then blocks EEG and lastly evokes autonomic reactions. The first pin pricks are not effective. Shouting causes transient blocking of the spikes and waves. Respiration stops in the beginning of the attack but is activated by the 2. and 3. stimulus, before the spikes and waves are stopped in the EEG. Pin pricks cause a new blocking after respiration has begun. Strong galvanic skin reflexes follow such arousal block, but fail to appear after the first ineffective and not perceived stimulus; conscious perception occurred only for the second and third stimulus. (After Jung, 1939.)

the galvanic skin reflex and plethysmogram (Fig. 3). Stimuli which fail to block the spikes and waves often do not elicit peripheral autonomic discharges or cause diminished or atypical responses. When autonomic or respiratory effects occur without blocking, a following stimulus usually blocks the spike and wave discharges more easily.

The blocking of spike and wave discharges has a latency of 0.5-1 sec. This latency is always longer than the individual reaction time in the interval between *petit mal* attacks, or longer than the startle reaction as detected by muscle potentials. In most cases it is also longer than the latency of respiratory activation. The latency time for blocking the spikes and waves is always shorter than the latency of the peripheral autonomic responses (Jung, 1939).

The alteration of consciousness during the *petit mal* attacks varied in different cases. In some patients there was complete loss of consciousness and perception and total amnesia was apparent. In a second group, as in *petit mal* status, there was only loss of attention with conserved perception, but amnesia occurred later. In a third group perception was still possible but all motor reactions were blocked. Effective sensory stimuli which blocked the *petit mal* discharges were always perceived and normal attention and consciousness was regained after this arousal from the attack. Ineffective stimuli remained unnoticed or at least unremembered in most cases. But in some patients even complex verbal commands were perceived and remembered and appropriate answers were given later, after the attack had ceased, with a much longer reaction time, as described by Schwab (1941). However, during the attack no verbal reactions were obtained, except in *petit mal* status where slow speech was possible after a short blocking of spikes and waves.

Complete blocking of spike and wave potentials is always bilateral and may occur nearly simultaneously in all cortical areas. With incomplete blocking fairly constant local differences are observed: blocking generally is more effective in parieto-occipital than in frontal regions but remains bilaterally symmetric in both hemispheres.

In a case of *petit mal* status with continuous regular spike and wave discharges over several hours, associated with clouded con-

sciousness, disorientation, slowing of motor responses and of speech and with partial amnesia, the blocking effect in different brain regions was investigated further. In this 12-year-old boy a transitory block of the regular spikes and waves for a period up to 3 seconds, predominantly in the parieto-occipital regions, could be obtained by stimuli of all sense organs: olfactory, visual, acoustic (noises or verbal command), taste, touch, deep pressure and pain (Fig. 4). Repeated stimuli of longer duration, such as continued pin pricks, flickering light or verbal addresses, were only effective in the first seconds, when the patient apparently tried to pay attention to them. Voluntary movements, speaking, opening as well as closing of the eyes also caused a similar short block of the spike and wave discharges, but usually with less effect on the frontal spikes. Movements of the patient such as intentionally pressing another person's hand blocked the discharges only at the commencement but not later when the movements were continued for a longer time. Laughing and yawning had the same blocking effects. There was no essential difference whether the movements were induced by verbal command or were made spontaneously. Some apparently involuntary movements, however, were associated with an increase of spikes. After nearly all kinds of sensory stimuli the spike component was suppressed in both hemispheres simultaneously. The slow waves sometimes were only diminished in amplitude. After verbal stimuli the slow waves sometimes continued in the occipito-parietal regions (Fig. 4*c*). With all other stimuli the block was more effective in the occipito-parietal cortex. When incomplete effects occurred, both frontal regions might continue to show spikes and waves although the block was well developed in the other brain regions (Fig. 4*b*).

Information about the psychic state during the *petit mal* status remained incomplete. There was disorientation in space and time in the first hour of the attack and the patient could tell us that he perceived the stimuli, but later amnesia occurred for most of the events.

Voluntary attention and concentration or emotional upset has a similar effect in preventing or eventually blocking *petit mal* attacks (Lennox and Gibbs, 1936; Jung, 1939). Many epileptic patients had the repeated experience that they were able to prevent their fits by willed attention and concentration and by sen-

sory stimuli which they added voluntarily (Weber and Jung, 1940). But no patient was able to show evidence of 'active' attention after the *petit mal* attack had begun. An exception was apparently the *petit mal* status where unfortunately information about what was going on inside the patient remained incomplete.

3. *Syncopal Faint*

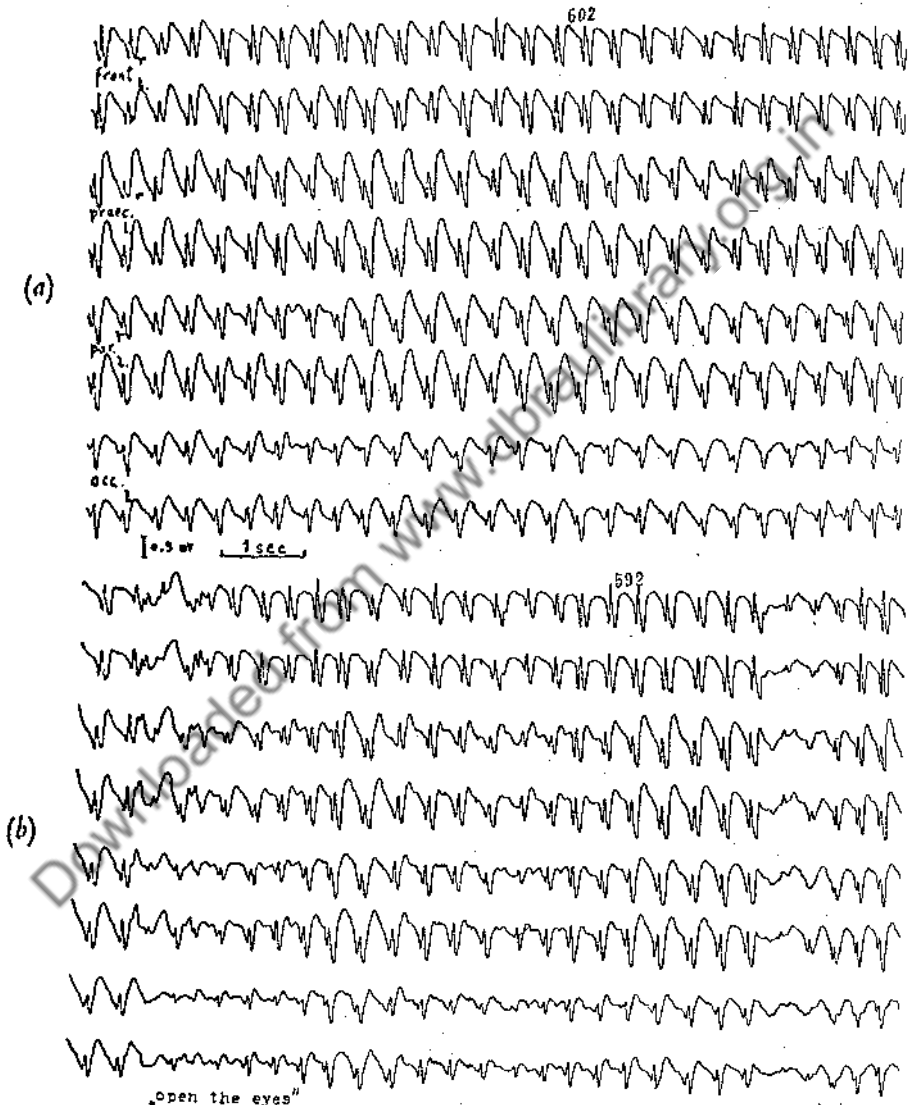
In students and doctors with a tendency to fainting, but otherwise healthy, faints were produced by pain stimuli or orthostatic stress. The EEG was recorded from different brain regions mostly without autonomic reactions and respiration. When loss of consciousness occurred after some premonitory pallor and sweating the EEG showed large slow waves 1-2/sec. with irregular shape. During the faint sensory stimuli and verbal commands were given. Although all subjects were apparently unconscious, they reacted to verbal commands, opening the eyes and closing them as requested. After the request and with the reaction the slow waves in the EEG diminished or were blocked for a few seconds, and after that an acceleration of the frequency of the waves was observed mainly in frontal regions (Fig. 5). No complete arousal with alpha-waves and no waking EEG record could be obtained by stimuli during the faint. When the fainting attack (of 20–30 sec. duration) was over, nothing of the command or the reaction or of other stimuli was remembered.

It seems, therefore, that during the faint verbal stimuli of complex nature can be elaborated in the brain into correct reactions. When these occur the EEG shows a period of incomplete arousal, although conscious perception or recollection is not demonstrable.

Voluntary attention and mental exercise was able to postpone the onset of faints.

ELECTRICAL STIMULATION OF THE SPECIFIC AND UNSPECIFIC PROJECTING SYSTEMS IN THE HUMAN THALAMUS

In the course of stereotactical operations on the human brain (Riechert and Wolf, 1951, 1953) we have made a series of electrical stimulations in the thalamus and in other basal ganglia. In collaboration with Riechert, Hassler, Baumgartner, Bauer and



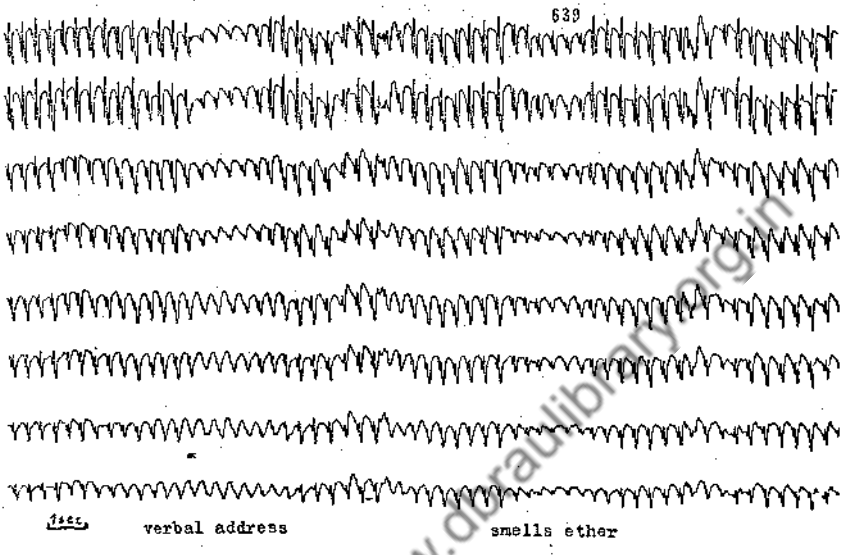


FIG. 4

Short blocking effects of sensory and verbal stimuli and of movements in *petit mal* status.
(*a*) Without stimulus, continuous regular spikes and waves.
(*b*) Opening and closing the eyes on request causes a short block of the spikes and waves which are resumed later with regular discharges.
(*c*) Verbal address is followed by suppression of spikes. Smell of ether blocks the spikes and waves in occipito-parietal regions and diminishes them in frontal regions.

Rossi subcortical electrograms and surface EEGs during thalamic stimulation were recorded in 30 cases to obtain information about the location of the deep electrode. Some of the records seem to confirm for the human brain the results of animal experiments. Therefore they will be reported briefly here. As we have heard in this symposium nearly all our knowledge of the electrical correlates of the specific and unspecific projecting systems is drawn from animal experiments and more information about similar stimulations in the human thalamus is urgently needed. Figs. 6 and 7 show two examples of the very different effects of stimulating the specific somato-sensory system in the ventro-caudal nucleus and of stimulations of the unspecific system in the intralaminar thalamus.

The recording of brain potentials from subcortical regions was disappointing. The brain potentials from different thalamic

nuclei did not give any results which could be used for localization of the electrode tip, which is so important for therapeutical coagulation. In contrast to these subcortical electrograms, stimulation of different thalamic regions gave more characteristic results at different locations of the stimulating electrode, when controlled with the EEG in the usual leads from the skull.

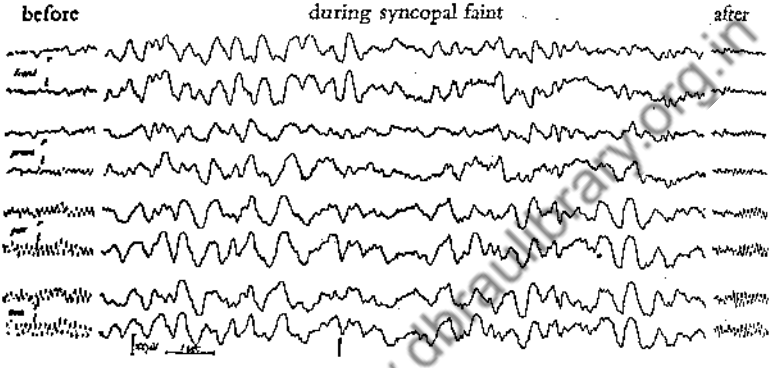
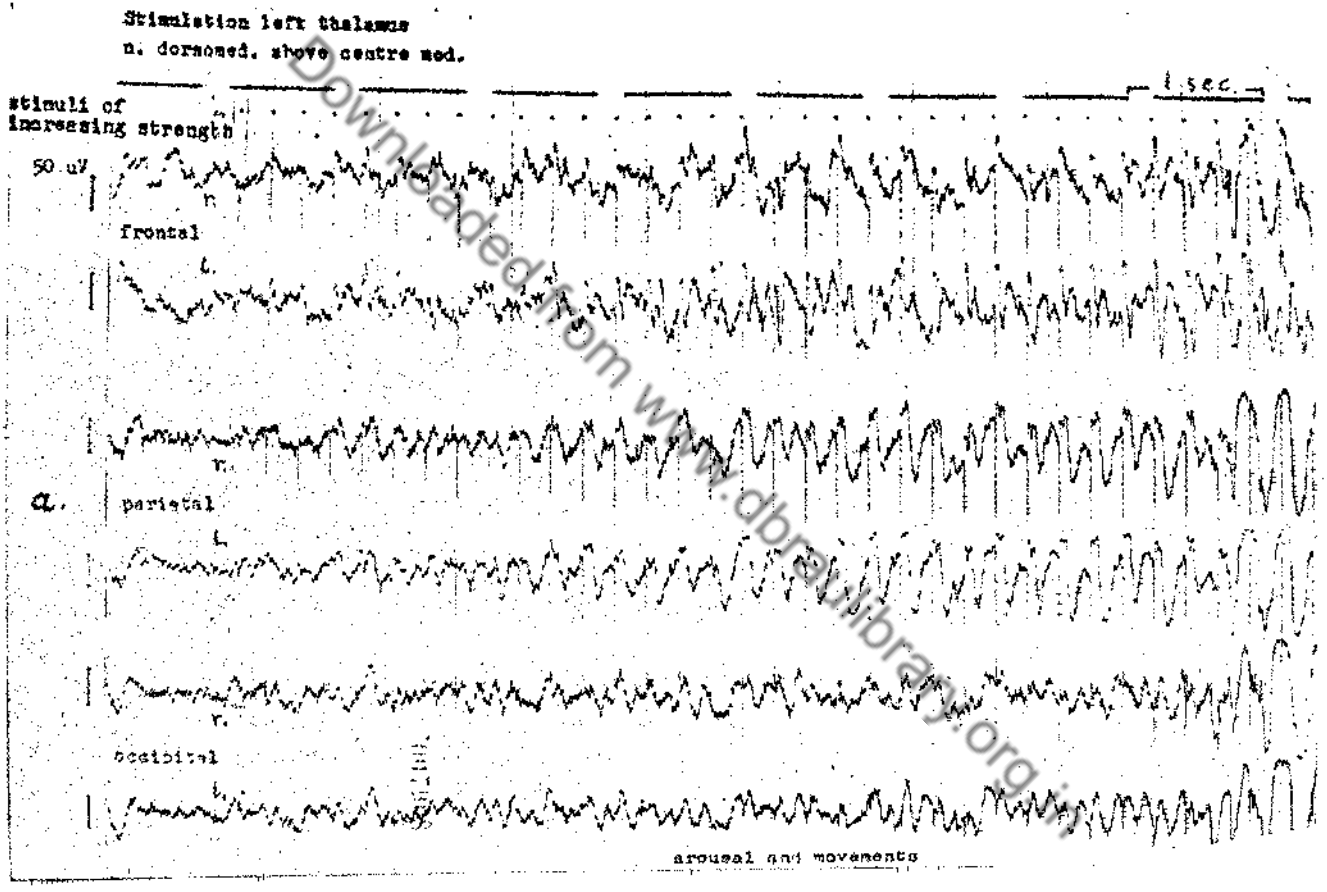


FIG. 5

Arousal effect of verbal command during a faint with amnesia. Command to open the eyes (↑) and correct reaction could not be remembered after the attack. Flattening and acceleration of EEG waves (after Jung, Neurophysiologische Untersuchungsmethoden in Handb. d. inn. Medizin V/1 Berlin, Springer, 1953).

Unspecific diffuse responses: In most cases thalamic stimulation evoked diffuse responses of many cortical regions in both hemispheres, apparently as an activation of the unspecific projecting system of the thalamus (Fig. 6). Low frequency stimulation (between 1 and 4 per sec.) of the medial and lateral thalamus produced in the EEG bilateral, slow waves with long latencies of 40 to 100 m.sec., sometimes preceded by spike-like discharges 20 to 30 m.sec. after the stimulus. All these responses were more pronounced in frontal, temporal and parietal leads, but could be seen in all cortical regions which can be traced in the EEG. The cortical hemisphere over the stimulated side showed mostly somewhat higher amplitudes of the waves than the unstimulated side (Fig. 6*a*, *b*). In some cases bilateral symmetrical waves or spike-and-wave-complexes could be obtained (Fig. 6*c*) as found in animal experiments (Jasper and Drooglever-Fortuyn, 1946). Sometimes as in Fig. 6*b*, the stimulation



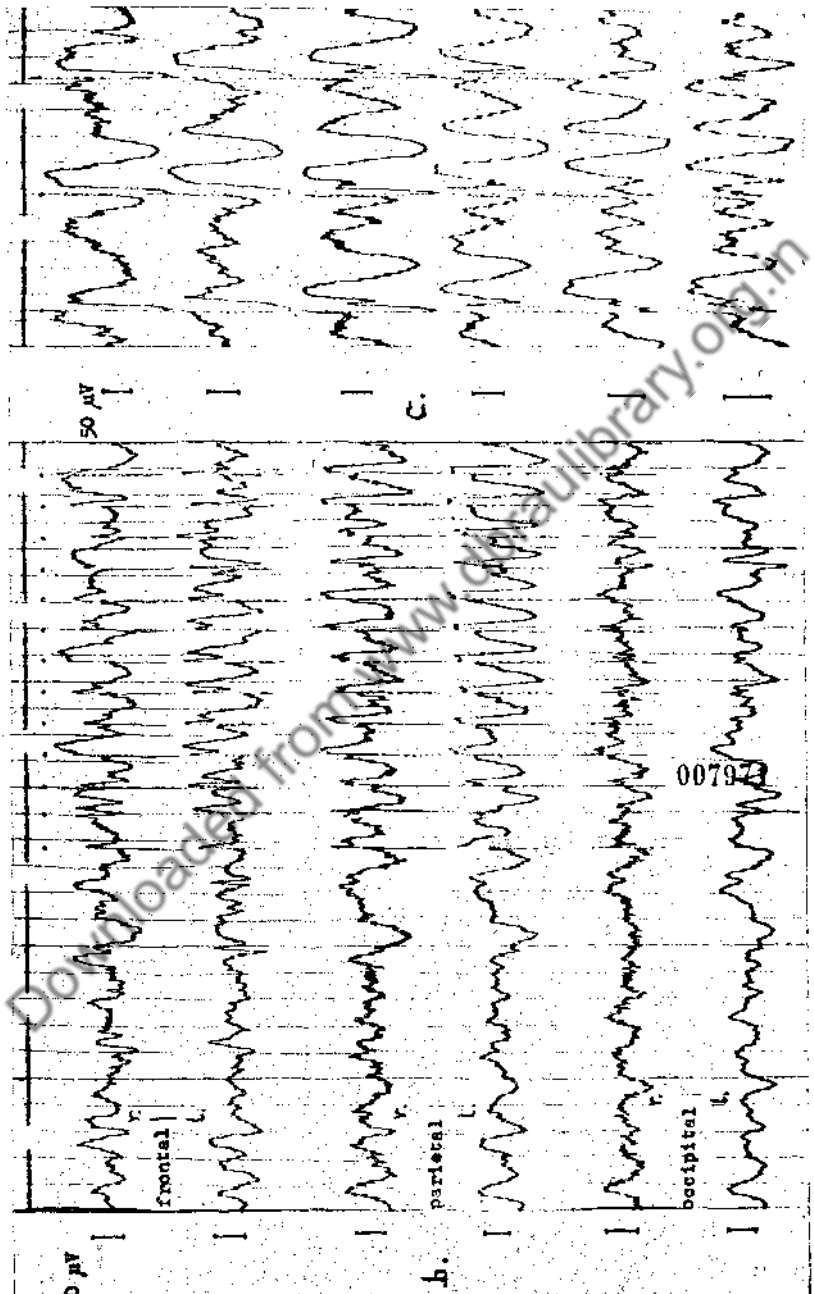


FIG. 6 (see pp. 328, 329)

Stimulation of unspecific projection system in human thalamus and its effects on EEG. Stimulation of left dorso-medial nucleus above centre median. Erethic imbecile with occasional fits after infantile brain damage (13 years Lei. 7. VII. 53). Hibernation (100 mg. Megaphen) 'Unipolar' recording against references on homolateral ears.

(*a*) Stimuli of increasing strength (4 fold: 2 V. from beginning to 8 V. at end, 4.5. per sec.) cause long latency slow waves in the parietal region and spikes with inconstant slow waves in the frontal regions. Continuous increase of amplitude with stimulus strength until large slow waves appear at 8 V. More marked effect on the homolateral (left) side. Arousal with opening of eyes.

(*b*) Medium frequency stimulation 4.5 per sec. with constant strength (4 V.) causes recruiting potentials: long latency slow waves in parietal, and spikes and waves in right frontal region. Moderate arousal effect.

(*c*) Low frequency stimuli of 1 per sec. and higher intensity (10 V.): Large spikes and waves bi-symmetrical over both hemispheres. Latency of the spike about 30 milliseconds, wave begins 80–100 milliseconds after stimulus. No arousal effect.

effects were more similar to the recruiting responses of Dempsey and Morison (1942).

The region from which these diffuse responses could be obtained was not confined to the intralaminar nuclei although stimulation of these seemed to have a lower threshold for the diffuse cortical responses. With higher voltage these responses could be induced after stimulation of many points of the medial part of the thalamus and from some parts of the lateral and ventral nuclei only 2 or 3 mm. above the ventro-caudal nucleus. Similar cortical responses were seen also after stimulation of the globus pallidus. Hypothalamic or mesencephalic structures were not stimulated.

Medium frequency stimulation between 4 and 20 per second had similar effects on the EEG, but the long latency slow waves were cut off by the next stimulus. Clinically this stimulation had definite arousal effects on the patients under hibernation. They opened the eyes and looked around with an expression of surprise. In contrast to the stimulation of the specific somato-sensory system the patients could not report any sensations felt during the stimulation, except when motor effects appeared with stronger stimuli over 8 volt. After arousal by lower voltage stimulation the patients were unable to describe what they felt except their awakening from a drowsy state. The arousal effects were clinically similar to those of addressing the patient verbally, or after the command to open their eyes, but showed very different EEG-changes. The effects were certainly quite distinct from *petit mal* seizures with staring.

High frequency stimulation over 20 per second was not used in most cases to avoid the danger of an epileptic fit. In 3 cases stimulation of 20 to 100 per second had the same arousal effects on the EEG as the medium frequency stimulation but complete flattening and blocking of the EEG waves was not observed with the low voltages used.

Specific localized responses: It was much more difficult to find responses in the EEG after stimulation of the specific somato-sensory projecting system in the ventral nucleus. Only three cases of intractable pain were examined in which a lesion of the ventro-caudal nucleus was made after stimulation. Clear localized results were seen only in one case of severe spinal pain which is shown

in Fig. 7. After each electrical stimulus of the sensory thalamic nucleus a localized evoked potential appeared in the homolateral parietal region corresponding approximately to the projection of the post-central gyrus. This evoked potential consisted of a sharp surface negative wave of about 30 m.sec. duration with a very short latency of less than 5 m.sec. after stimulation at the electrode tip in the sensory nucleus ventro-caudalis. No slow waves were seen. The patient experienced a sharp pain on his left side especially in his knee, similar to his spontaneous pain, when the thalamic nucleus was stimulated and a cortical effect

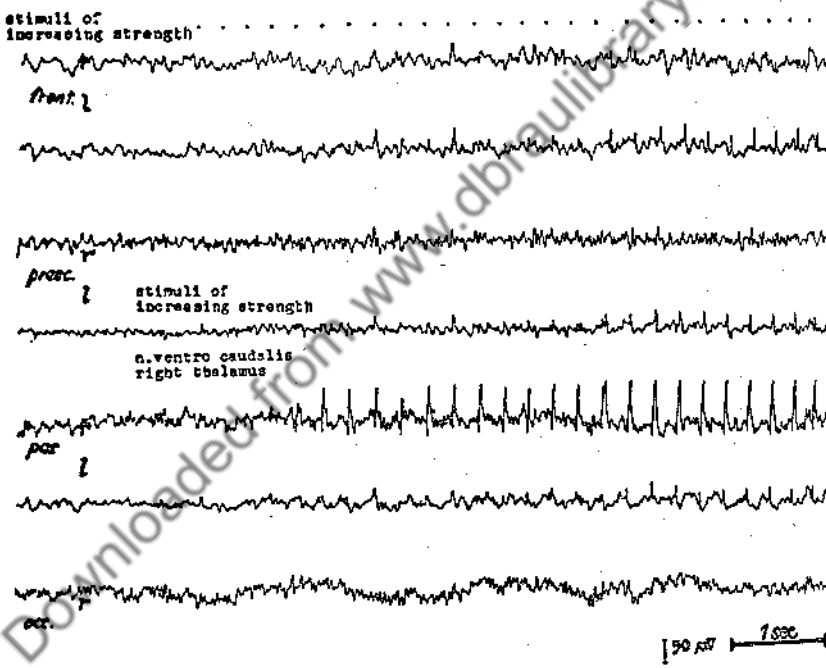


FIG. 7

Stimulation of specific projection system in human thalamus, and its effect on EEG. Electrical stimulation of right ventrocaudal nucleus in a case of intractable spinal pain (45 years Pflu 13.5.53). Hibernation (50 mg. Megaphen) 'Unipolar' recording against references on homolateral ears.

Stimuli of increasing strength (2 to 10 V.) and 4 per sec. cause short evoked potentials in homolateral right parietal region over post-central gyrus. Definite threshold and very short latency of a few milliseconds. Fairly constant amplitude although stimulus increased more than 5-fold from beginning to end of record. Subjective pain sensation in contralateral left body side after each stimulus.

was obtained in the EEG. Later coagulation of the same region resulted in hemianalgesia and hypesthesia for touch and passive movements on the left side of the body. After coagulation a renewed stimulation failed to cause any evoked potential or pain effect.

These stimulations of the specific and unspecific projection systems in the human have to be confirmed and elaborated by further observations before they can be used as indicators for localization of the electrode. We have not yet enough material of EEG records after stimulation of the specific somato-sensory nuclei to be sure of the consistency of the effects, and we need more high frequency stimulations of the unspecific system to know whether a blocking of cortical waves occurs as observed in animal experiments. The preliminary results which we have shown indicate that the human thalamus may contain similar systems of cortical projection as were found in laboratory animals.

DISCUSSION

From these observations in human subjects a few conclusions may be drawn concerning the physiological mechanism for attention and arousal. The main result seems to be that a system, regulating arousal effects after sensory stimuli, can be activated in normal as well as in pathological alterations of consciousness. Another important result may be found in the observation that electrical stimulation of the thalamus will cause arousal effects and EEG-changes without sensory experience.

Otherwise the results of a correlation between objectively recorded physiological facts and subjective phenomena of conscious psychological experience are not very impressive. They are particularly hampered by methodical limitations: we cannot record physiological reactions and at the same time get exact information about what happens in the psyche. The 'internal' aspect of the story has to be obtained later. It is hard to assess how far memory defects, so common in alterations of consciousness, distort the content of the verbal communication. A description of conscious states cannot be given in exact terms, if consciousness

is a selective process of limiting psychic contents as defined above.

There seem to be three main types of short seizure-like alterations of consciousness and attention: the amnestic type 1 is found in faints and in some cases of *petit mal* status: preserved reactions to stimuli with somewhat slower reaction time but with loss of conscious recollection. The motor blocking type 2 is found in some *petit mal* attacks: blocking of motor reactions to sensory or verbal stimuli with a conserved perception and memory for these stimuli. The combined type 3, observed in many *petit mal* seizures, shows both blocking of the motor response mechanism and of conscious recollection occurring with complete amnesia.

When we compare the changes of the EEG with the alterations of consciousness the results seem to be somewhat disappointing. No absolute correlation is possible between the form of the EEG and the state of consciousness or perception (Janzen and Kornmueller, 1939; Duensing, 1949). But this could hardly be expected if we consider the complexity of conscious states and perceptions and the interference of memory processes in the testing procedure. It seems more promising to correlate the physiological changes with attention. Then our observations presented in Part A suggest three tentative general conclusions which, however, do not contain much new information:

1. The appearance of slow waves in the EEG is connected with a diminution of attention and awareness which eventually may lead to complete inattention and unconsciousness. Exceptions are the short bursts of slow waves appearing after sensory stimuli in sleep or after electrical stimulation on the thalamus.

2. Acceleration of brain potentials and disappearance of slow waves both of normal and pathological origin, after all sorts of sensory stimuli, is associated with an arousal effect and increase of attention and readiness.

3. 'Active' voluntary attention may have the same effects on the EEG, the autonomic system and respiration as have 'passive' sensory stimuli. This may indicate that both primary voluntary attention and secondary attention following sensory stimuli may induce these general effects over the same neural systems.

Two factors seem to be important for the arousal effect of the stimuli: intensity and significance. The role of significant and verbal stimuli is essential for the interpretation of the cere-

bral mechanisms involved in arousal. Verbal stimuli although not very intense, as whispering the name, may be more effective than loud noises as Li and co-workers (1953) have also observed. This indicates that the neural mechanism of arousal cannot consist only of collateral excitations from sensory tracts to the brain stem reticular system. Verbal stimuli will certainly need very complicated integrative patterns and the use of cortical analysers to clear the significance of the stimulus. Therefore complex interactions between cortical and subcortical mechanisms have to be postulated to account for the arousal effect of weak verbal stimuli. This interaction may apparently be conserved during sleep and during the very abnormal cortical EEG-patterns of a faint (Fig. 5) and of some *petit mal* attacks.

If it is allowed to present some further speculations about the neural basis of attention and consciousness the following may be said with all reserves necessary for such hypothetical suppositions.

A regulating system exists in the human brain which co-ordinates physiological and psychological functions in two reciprocal directions: sleep and wakefulness being the two antagonistic states in normal activity. Depression and arousal, decrease and increase of attention may be described as additional tendencies of antagonistic psychic functions. In Hess's terminology that would mean: *trophotropic* influence with restitution, passive behaviour and prominence of the *milieu interne*, associated with slow cortical waves, and *ergotropic* influence with readiness, active behaviour and turn to the environmental world, associated with arousal patterns in the EEG after sensory stimuli (Jung, 1941).

Depression of activity, decrease of attention and sleep is related to a slowing of the brain waves with very different patterns. The regulating system may be active not only in physiological changes between sleep and attention but also in pathological disturbances of consciousness: in normal sleep there is gradual onset and a smooth regulation and transgression of different levels of consciousness with different patterns in the EEG, which can change either spontaneously or under the influence of external stimuli. In a faint the onset of the EEG-change is more rapid, the slow waves are more uniform and continuous than in deep sleep. In *petit mal* the beginning is sudden and paroxysmal, the EEG-pattern more regular with 3/sec. spikes and waves. In all these

different states of normal and pathological alterations of consciousness an arousal reaction can be evoked by sensory stimuli producing attention (Figs. 3–5). The arousal may have some correlations with the activation of respiration and with reactions of the autonomic nervous system (Fig. 3). Voluntary attention may also prevent or postpone the onset of the unconscious state in normal sleep as well as in a faint and in *petit mal*.

Some support for the comparison of such different conditions as *petit mal* and sleep may be drawn from two sets of observations. (1) Experimental results in animals demonstrate that cortical responses resembling *petit mal* (Jasper and Droogleever-Fortuyn, 1946) as well as natural sleep behaviour (Hess, 1949) can be elicited after stimulation of the intralaminar thalamus. (2) Neurophysiological observations in man show that children between 2 and 10 years may have a transitory EEG-pattern during drowsiness, very similar to *petit mal* (Gibbs, 1950). *Petit mal* therefore is regarded as an abnormal reaction of this regulating system to convulsive phenomena in the child brain. This abnormal reaction may not be a local convulsion in the system itself but a sort of faulty regulation responding to convulsive discharges which may be localized elsewhere in quite different regions of the brain. The slow waves of *petit mal* are believed to be an exaggerated defence mechanism against the interference of convulsive excitations.

Results of thalamic leads in *petit mal* patients can support this theory. We have found that the spike and wave discharges did not start in the medial thalamus. Cortical convulsive discharges of other forms may precede and the spike and wave discharges may develop last in the medial and intralaminar thalamic regions. These observations are in contrast to the just published results of Williams (1953), who found the spikes and waves starting in the thalamus. We cannot yet explain these and other contradictions to Williams's findings also in the clinical observations. We could not find evidence for selective interruption of afferent mechanisms, postulated by Williams in *petit mal*. Anyway the co-ordinated *petit mal* discharges seem to be a further support for the existence of a regulating system in the human brain for the co-ordination of different states of consciousness and attention.

I do not wish to say something about the 'seat of consciousness'. This conception was criticized often enough, very recently in a

clearly written review by Schiller (1952). But one may be safe in believing from the evidence we have, that consciousness is a function of the brain. Clinical observations of the older generation of German neuropsychiatrists (v. Economo, 1917; Reichardt, 1919; Kleist, 1934) and many papers of the last years which cannot be revised here have shown, that brain stem mechanisms are an essential part for regulation of consciousness, attention and sleep. These observations and our results after stimulation of the human thalamus allow some analogies with animal experiments on brain stem centres (Hess, 1949; Jasper, 1949; Magoun, 1950) which have shown the existence of a regulating system for sleep and arousal.

Evidence for the localization of this regulating system in human beings could be obtained only by thalamic stimulation during stereotactic operations. The results of these stimulations with diffuse effects (Fig. 6) may be compared with those of Morison and Dempsey (1942), Jasper (1949), Magoun (1950) and Starzl and Magoun (1951) on the diffuse thalamic projection system in cats. Of course location of the stimulus site is less precise in the human and confined to roentgenologic and stereotactic controls and the clinical and subjective stimulation effects. No anatomical verification is available until now. No stimulations of human hypothalamic, mesencephalic or rhombencephalic reticular structures were done. Therefore direct evidence for the function of these systems is still lacking in the human.

The role of the lower brain stem reticular substance in different states of consciousness and attention therefore remains still a matter for speculation. One little fact only seems suggestive for the participation of the bulbar reticular system in arousal: the early activation of respiration in the arousal reactions of some *petit mal* patients, occurring 100–200 m.sec. before blocking of cortical potentials is obtained (Fig. 3). If we accept that respiratory rhythms are regulated by the pontine and bulbar reticular substance, it seems that after sensory stimuli the co-ordinated function of this brain stem centre precedes the activation of the cortex. In this case the cortical areas might be compared to effector organs as the respiratory muscles, activated both by similar brain stem structures. The working mechanism of the regulating system may be thought similar to Hess's vegetative regulation of the cortex (Hess, 1949) and to the centrencephalic system which Pen-

field (1952) supposes for voluntary activation of memory patterns

Science has similar limitations as has consciousness. We never shall know the whole story but only parts of it, owing to the limits of our scientific methods. The way to conscious experience is essentially a psychological one. The adequate method for investigation of consciousness proper remains introspection and inter-human communication with speech as the main transmitter. Neurophysiology can only show some correlations to the basic cerebral functions as preconditions for consciousness.

SUMMARY

1. Possible correlations of the EEG and autonomic functions with different states of consciousness are investigated by simultaneous recording of EEG, EKG, galvanic skin reflex, finger plethysmogram and respiration in normal individuals and in patients with *petit mal*. The arousal reactions to sensory and verbal stimuli are studied. New observations on electrical stimulations of the specific and unspecific projection systems in the human thalamus are reported.

2. Consciousness is defined as a cerebral function for selecting actual psychic experience from unconscious material. Attention is compared to a searchlight illuminating details for conscious perception. A schematic diagram illustrating the co-ordinated function of consciousness and attention is given.

3. The autonomic and EEG-changes following sensory stimuli are compared in the waking state and in normal sleep. The autonomic responses show only minor changes in different states of consciousness, whereas the EEG has very different forms of arousal responses varying with the level of consciousness.

4. Sensory stimuli, applied during *petit mal* attacks may block the spike and wave discharges, evoking an arousal effect and peripheral autonomic discharges in the galvanic skin reflex and plethysmogram. The latency for blocking the spikes and waves is longer than the individual reaction time outside the attack. The effects of arousal stimuli have the following time sequence: 1, activation of respiration; 2, blocking of EEG; 3, autonomic reactions. Effective stimuli, blocking the EEG, were always perceived. Ineffective stimuli without EEG-change often remained unnoticed or unremembered.

5. In a case of *petit mal* status a short blocking of the otherwise continuous spikes and waves was obtained by stimuli of all sense organs and by voluntary movements and speaking. The spikes and waves were blocked predominantly in the parieto-occipital regions as also observed in ordinary *petit mal* attacks.

6. During syncopal faints with large slow waves in the EEG the seemingly unconscious subjects reacted to verbal commands. After verbal address, and with the reaction, the slow waves diminished, accelerated, or were blocked. There was complete amnesia for command and reactions.

7. Three types of alterations of consciousness in seizures are described: 1. *Amnestic type*: reaction to stimuli is preserved but amnesia occurs; 2. *Motor blocking type*: motor reactions to stimuli are abolished but perception and memory for the stimuli is conserved; 3. *Combined type*: blocking of both motor response and recollection occurs with total amnesia.

8. The effects on the EEG of electrical stimulation in the human thalamus are described. Diffuse bilateral responses in both cortical hemispheres, predominantly frontal and parietal, with slow waves and recruiting responses occur after unilateral stimulation in medial and lateral thalamic nuclei. These are interpreted as activation of the unspecific projecting system of the thalamus. Medium frequency stimulation of this system is associated with arousal of the patient without sensory experience. Localized homolateral responses in the post-central cortex after stimulation of the ventro-caudal thalamic nucleus is interpreted as stimulation of the specific somato-sensory projecting system. This effect is associated with pain in the contralateral body side.

9. These observations indicate that a regulating system exists in the human brain which co-ordinates physiological and psychological functions into reciprocal directions of sleep and wakefulness. The relations to Hess's vegetative regulation of the cortex by trophotropic and ergotropic functions and to Penfield's centrencephalic system are discussed.

GROUP DISCUSSION

JASPER: We are very grateful to Dr. Jung for this presentation. Perhaps we could hear from Dr. Courtois who has been doing some interesting work in this field.

COURTOIS: We have studied the state of consciousness in 29 patients with generalized, bilateral, synchronous, 3 per sec. wave-and-spike discharges, with various tests with respect to motor, somato-sensory and higher functions (speech, memory and comprehension). The reflexes were also tested.

There was a marked difference in degree of impairment of the various functions tested during the attack. Some patients, although unresponsive, were able to understand and recall words or commands given during the attack and repeat the words or carry out the commands when the attack was over. However, in other cases there was complete or partial amnesia for the attack. No retrogade amnesia has been noted. Some somato-sensory functions could be completely lost while comprehension and memory were but little interfered with.

Speech appears to be very easily impaired while other functions, including rhythmic movements, may be undisturbed.

The various somato-sensory modalities may be unequally affected. Possibly light touch is the modality most easily affected, then sensation of passive movements. Pain sensation appears to be the most resistant.

In many cases it is possible to show a change in reflexes during the wave-and-spike discharge. The plantar response may change from flexor to extensor, accompanied by withdrawal of the leg. The pupillary light reflex may be decreased or absent. Ankle clonus and the Hoffman sign have been observed.

It has not been possible to establish an absolute correlation between the voltage of the wave-and-spike discharge and the degree of disturbance of consciousness. However, in the group of patients least affected clinically the voltage was more often lower than in the group with complete loss of consciousness.

GASTAUT: In 1951, I investigated with Professor Cornil the problem of consciousness in cases of *petit mal* epilepsy on which spike-wave discharges were produced by intermittent photic stimulation. We published at that time the following conclusions which are very similar to those of Dr. Courtois: (1) The electrical discharges represented by a single spike-wave do not appreciably affect awareness, for the subject continues to perform a perfectly normal rhythmic automatic activity and remembers a complex sound which is made to coincide with any phase of the spike-wave by means of a variable-delay trip circuit; (2) discharges made up of a small number of spike-waves grouped in one short paroxysm still do not modify the perception of complex sounds, although they slightly affect rhythmic automatic activity and voluntary activity: increase in reaction-time and delay in rhythmically repeated movement. They also considerably disturb verbal activity: interruption of speech or confusion of words spoken.

In these results I sought evidence of the existence of two degrees — automatic and voluntary — of human behaviour; a concept greatly cherished by Pierre Janet.

PENFIELD: I would like to call attention to the very interesting observation which Dr. Jung made that during a *petit mal* attack a patient may perform an act which he is told to do without any recollection of it. It is very difficult to distinguish between this and temporal lobe automatism. The discharge of *petit mal* may be regarded as centrencephalic. In this case the memory-recording mechanism is out of action while the effector mechanism is intact. In temporal lobe automatism the same would be the case although the discharge originates usually in one temporal lobe. The state is produced in each case by subcortical interference by epileptic discharge.

JASPER: We have a very interesting paradox here in that in the one case we have a blocking of the recording mechanism with continued adaptive behaviour as though conscious and in the other case (*petit mal*) there is an arrest of response, as though unconscious — without loss of memory recording.

JUNG: I would just like to remark that only in a few cases of *petit mal* may one see the same effect of blocking the recording mechanism that I reported for the faint and the *petit mal* status that behaved more like a temporal lobe automatism, as Dr. Penfield remarked. The subject does what he is told but has no recollection of it. More usually one finds the other type of blocking of the response mechanism; as Dr. Gastaut has said, some *petit mal* patients fail first to respond to a command and then respond later and may have nearly full recollection of it. You can see the other type of isolated blocking of the recording mechanism in *petit mal* also but it is rare and is found mainly in fainting.

KUBIE: I would like to suggest that the rhythm of the respiratory centre may rest primarily on a biochemical basis, and that the respiratory centre may activate the centrencephalic system rather than the other way round. Secondly, in studies of states of consciousness which involve the recording and the recall of sensory data, the sensory modality should be kept in mind, that is whether they are predominantly exteroceptive, proprioceptive, or enteroceptive, or a mixture. It is possible that these different modalities may not all be organized, evoked and reproduced in the same way.

WALTER: I should like to add a word of caution about the wave-and-spike phenomena; we are inclined to think that the wave and the spike of *petit mal* are one and the same thing, but in fact wave-and-spike is always a very complex phenomenon. Furthermore we have observed patients with long runs of wave-and-spike in whom the only effect of

stimulation was to change the geometry of the various components without affecting the gross amplitude.

PENFIELD: What kind of stimulation did you use?

WALTER: Asking questions, asking for the performance of actions and various kinds of psychological tests.

OLSZEWSKI: The point I would like to mention is the importance of recording – when working on the central internuncial system – of many types of responses simultaneously, as it was done by Dr. Jung. The central internuncial system is the site of many different mechanisms – vegetative, respiratory, facilitating and inhibitory and so on – and the morphological substratum of these mechanisms does overlap. The understanding of the organization of these mechanisms will not be possible without recognition of this fact.

The central internuncial system can influence the electrical activity of the cortex not only by way of neuronal transmission, but also through other mechanisms. I am wondering whether Dr. Jasper would like to ask Dr. Ingvar to tell us about his recent experiments which illustrate this important point.

JASPER: Would you like to report this very important observation on the isolated cortex, Dr. Ingvar?

INGVAR: Observations have been made in experiments in cats in which an area of the cortex had been isolated neuronally by subpial dissection. The brain stem was intact and the experiments were carried out under local anaesthesia and curare. With the technique used, no neuronal connections could be demonstrated to exist between the isolated area and the surrounding cortex using several methods – evoked potentials, after discharges and application of strychnine or metrazol locally. Histological controls have furthermore failed in demonstrating any connections.

With this technique it was observed that the isolated area was spontaneously active. The activity was of several types of fast and slow frequencies, and it may be worth while mentioning that very often 3 per sec. rhythms were observed from the slab. In a couple of experiments a 3 per sec. spike-and-wave pattern was recorded from the isolated area also.

Another group of observations concerns the effect of stimulation of the reticular system of the brain stem upon the activity in the isolated area of the cortex. When the slab was silent it was on occasion possible to induce activity in it by reticular stimulation. The latency of this effect in the slab from the onset of the stimulation was long: between twenty and thirty seconds. On other occasions when the slab was spontaneously active a more rapid effect of reticular stimulation was observed. Thus, a change in the electrographic pattern from spikes to

slow waves could be observed. On other occasions the activity in the slab stopped for a few seconds to come back again.

Looking for an explanation for these phenomena, we observed the pial circulation through a microscope. It was possible to see quite dramatic changes all over the cortex, including the isolated area. A second or two after the onset of reticular stimulation the cortex was observed to flush and the circulation to speed up in the small veins. These circulatory effects could outlast the stimulus and gradually subside over a period of several minutes. It may be worth while mentioning that the circulatory changes were observed even after large doses of hexamethonium and in one experiment, after adrenalectomy. Sections of the spinal cord did not seem to interfere with the vascular phenomena but in two experiments they were abolished by mesencephalic brain stem section. In spite of the absence of vascular changes visible under the microscope in some experiments certain effects on the electrical activity of the cortical slab were seen, on occasion, with a latency of about 20 secs. At this preliminary stage we are guessing that apart from vascular mechanisms, humoral factors may play some role in the effects of reticular stimulation upon the neuronally isolated area of the cortex.

I should like to add finally that there were indications of some topographical localization of this effect in that stimulation at some points in the brain stem could give only the usual arousal pattern in the surrounding cortex but no vascular effects, while other points would give both. This observation would, however, require confirmation.

ADRIAN: Are these bursts seen in the isolated cortical slabs related to respiration?

INGVAR: The cats were examined under artificial respiration and care was taken to eliminate mechanical stimulation of the cortex by the electrodes from the slight movement of the brain due to respiration. The bursts were not found to be related to the respiratory rhythm.

BREMER: I was struck once more by the fact that the rhythmical bursts observed in isolated cortical slabs do not differ essentially from the spindles which characterize the residual activity shown by an area simply undercut. They seem to be related to nothing more than the suppression of afferent impulses. These bursts, which occur sometimes with striking regularity, appear to have a relation with other autorhythmic phenomena. In an isolated nerve fibre in the crab, Fessard and Katz recorded the same burst activity, and Osterhout, in a single cell of Nitella sensitized by guanidine, could demonstrate the most striking spindles. It seems to me that there is a fundamental analogy among all these rhythmicities.

MORISON: This may be getting close to one facet of the spreading

'depression' of Leao. The appearance of the cortex in Dr. Ingvar's experiment is similar to that in the spreading depression. Conditions in his experiments are obviously so good that the depression and convulsive discharge does not spread to the normal cortex but might well affect the isolated slab. As is well known, the spreading depression may be accompanied by seizure activity.

THEORETICAL PROPERTIES OF DIFFUSE PROJECTION SYSTEMS IN RELATION TO BEHAVIOUR AND CONSCIOUSNESS

By

W. GREY WALTER

The notion of consciousness is not a very promising starting point for a physiological discourse. The classical methods of neurophysiology deal rather with what may be called 'sciousness'; the activity of single units or systems in relation to carefully selected and controlled stimuli or signals. It is the congregation of such activities within the nervous system that may be considered the physiological basis of consciousness, and this congregation cannot legitimately be dissected into its components. The difficulty is not that, in some vague and mystical way 'the whole is greater than the sum of its parts' but, much more simply, that it is the *relation* between the various multiple activities that is of importance. The technical outcome of this situation is that the experimenter must resign himself to handling equipment of great apparent complexity, and to dealing, in effect, with a number of simultaneous differential equations. Fortunately, it is possible now to make instruments which can present such information to the experimenter in a reasonably intelligible form, thus relieving him of many operational duties and affording him opportunity to study at the same time the behaviour and conscious activities of his experimental subjects. The observations and conjectures to be elaborated here are based mainly on information obtained during experiments with rather specialized equipment on the electrical activity of the brain in relatively normal human subjects.

METHODS

The technical details of the methods have been described elsewhere (Walter in Hill and Parr, 1950; Walter and Shipton, 1951; Walter, 1953a, b), but certain features may be summarized here in order to explain the nature of the illustrations.

The first system to be used was a combination of frequency analysis and statistical computation. This technique has the very considerable advantage that responses to regular or rhythmic stimuli can be identified against a random or irregular background even when their amplitude is comparable with that of the 'noise'. It was discovered that during rhythmic stimulation particularly of the eyes by flashes of light, measurable but very complex responses were present in most people in regions remote from the sensory projection area. Such responses were particularly susceptible to mental influences, and were greatly reduced, for example, during drowsy or inattentive states of mind. These observations were first reported about seven years ago and have since been confirmed by many workers, but the method has definite limitations. Analysis of frequencies can be performed only over fairly long periods of time — of the order of 10 seconds, so that fluctuations from second to second are suppressed altogether or averaged out. Furthermore, although the validity of frequency analysis does not depend upon any assumptions about the sinusoidal or other form of the original voltage changes, it does admit certain ambiguities in that a non-sinusoidal waveform will be indicated as containing a certain proportion of harmonic activity as though it were made up of several components, whereas actually its appearance as a function of time may be *inherently* non-sinusoidal. It is often possible to check results of frequency analysis by the appearance of primary waveform, and by spatial analysis, but in the case of the small, evanescent and widely dispersed responses to stimulation in human subjects this is only rarely feasible and it is often quite uncertain whether the particular features of the diffusely projected activity as revealed by analysis during stimulation are due to super-position and interaction of many components or to an inherent skewness or irregularity of a single evoked discharge.

In order to resolve this dilemma and permit the study of transitory phenomena in greater detail, an entirely different type of display system has been developed. This device was originally referred to as a Toposcope because it was intended for projection in map-like fashion of the topographic details of brain activity. Like so many elaborate machines this has evolved into something considerably more flexible and although the topographic resolution remains unimpaired, it has been found of particular value for examination of the time-relations and phase-relations of events in different parts of the brain. The input to the display system is derived from 22 channels of amplification and the changes of voltage from these amplifiers are converted into variations of brilliance in 22 cathode ray oscilloscopes, rather as in a television or radar system. The CROs are arranged in a pattern corresponding to the positions on the head of the electrodes from which

their respective amplifiers derive their signals. This arrangement provides immediate indication of location of activity and since the 22 channels are connected to only 16 electrodes in network fashion an indication is also given of the orientation of the apparent source of activity, wherever it may occur. The resemblance to a television display system is made even closer by the provision of an internal scanning system; this resembles quite closely that employed for many types of Plan Position Indicator in that an oscillator working through a velodyne-synchro circuit is made to produce the appearance of a line of light on each CRO. This line or radius-vector is equivalent to the hand of a clock since it rotates around the face of the tubes at a rate depending on the velodyne speed; the rate of rotation is indicated in the usual way on the dial of a voltage tachometer close by the cluster of CROs. The assembly of tubes and tachometer may be regarded as a set of clock faces on which the hands are visible only when they are illuminated by a signal, and the time scale for the rotating hands is indicated by the tachometer. For example when the tachometer indicates 10 revolutions per second, 100 m.sec. is represented by rotation of 360° of the radius vector and 1 m.sec. is therefore equivalent to 3.6 degrees. It is convenient to refer to such readings in terms of the familiar clock face — so that in the example given, if one tube indicates a signal at 12 o'clock and another at 3 o'clock, the time interval between them would be 25 m.sec.

The speed of the rotating vector can be controlled either by the operator or by the signals in one selected channel which are made to generate voltages to synchronize the vector in frequency and phase. Stimuli such as flashes of light can be generated by rotation of the vector and these can be delivered singly or in a variety of patterns. Manual control of the vector speed is used when the effects of stimulation are being studied; automatic control is more useful when 'spontaneous' activity is to be examined. In the first case the stimuli themselves, which are displayed on a small monitor tube at the top of the indicating unit, are used as fiducial marks from which the time relations of evoked components can be measured. During automatic control, the principal component of the activity in the channel selected to drive the vector is always held at 12 o'clock in the CRO corresponding to this channel, and this component may therefore be used as a fiducial mark to estimate the time relations between this and all the other channels. Photographs of brain activity displayed in this way are obtained by time-exposures of 35 mm. film. The duration of the exposures is pre-selected and is usually about one second. The shutter and film run-on are operated electronically; when the vector is under automatic control the exposures are also made automatically whenever

a certain degree of synchronization and regularity appears in the brain activity displayed in the governing channel. The operator is thus free to observe or converse with the subject during the experiment.

This system is, in effect, a sort of multiple stroboscope, since the whirling vectors are illuminated only by the signals. When the vector speed is a factor or a multiple of the signal frequency, an illusion of immobility is seen in the CROs displaying the synchronized activity. Recording by photography confers the further advantage that images of regular signals are superimposed during the exposure period and can therefore be distinguished more easily from random components or 'noise'. The resolution is such as to permit measurement of the phase and position of signals equivalent to about four microvolts even in the presence of random components equivalent to 15-20 microvolts.

OBSERVATIONS

The phase and frequency indicating toposcope was first used to check observations already made with the help of frequency analysis. The complexity and wide dispersion of activity evoked by stimulation were soon corroborated, so that although the possibility of ambiguity in frequency spectra still remains as a general hazard, the specific conclusion with regard to harmonic evoked components and their wide distribution may be regarded as amply confirmed.

As already reported elsewhere (Walter, 1952) human subjects show a much more variable and intricate response to stimulation than would be expected on evidence obtained from experiments on anaesthetized or mutilated animals. There are well marked personal characteristics and dramatic variations in accord with the state of mind of the subject. These will be dealt with in more detail later.

With the frequency and phase-locking device it has been possible to study the relation between 'spontaneous' and evoked activities in terms of their respective geometries and time relations. As is well known, the effects of flicker in human subjects were for a long time referred to as 'driving the alpha rhythm'. This phrase is undoubtedly inadequate as a general description of the effects of visual stimulation but in many people conventional records show an apparent augmentation of the response to flicker

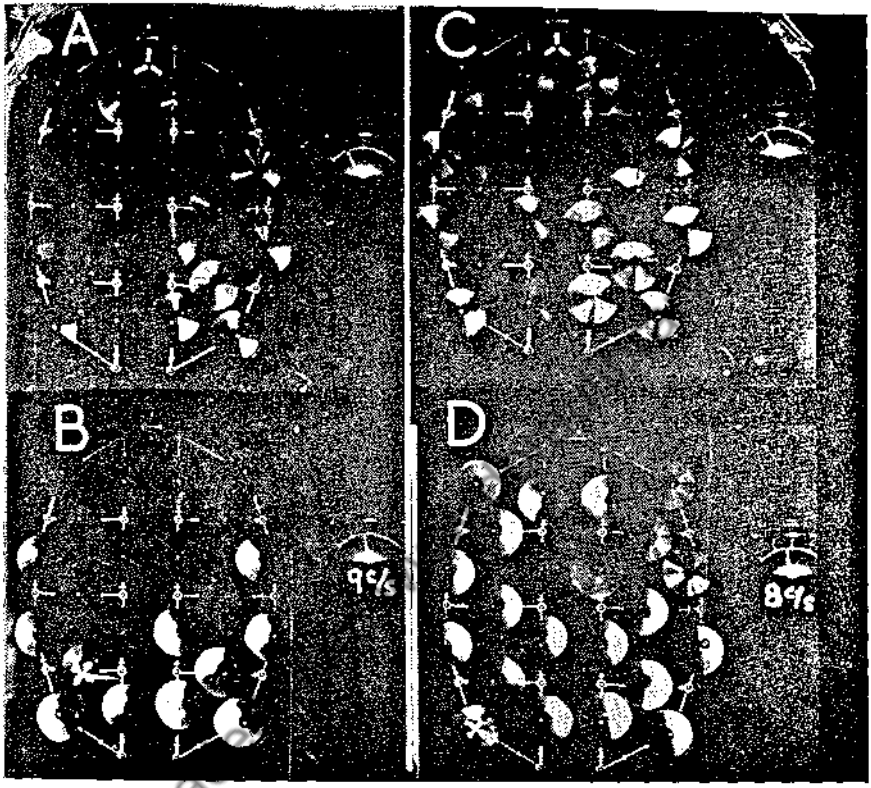


FIG. 1

(A) Responses to flicker at 5 × 3 *f/s* in a normal subject compared with his alpha distribution (B). Responses are evoked mainly in the right occipital region, but the stimulus pattern is reflected only in the right fronto-temporal region, corresponding with the extreme anterior projection of the alpha activity. On this occasion the response pattern was considerably embellished. (C) Responses evoked by similar stimuli in another subject with a much more extensive alpha distribution as shown in D. In this subject the spontaneous 8 cycles/sec. component showed a phase reversal in the fronto-central regions and the time relations suggest the possibility of a sweep under the occipital channels. In C a distorted reproduction of the stimulus patterns appears in several occipital channels, a clearer one in the frontal channel on the right side.
In this and succeeding reproductions, except where stated, the exposures lasted one second. In records of 'spontaneous' activity the motive channel is marked with a cross.

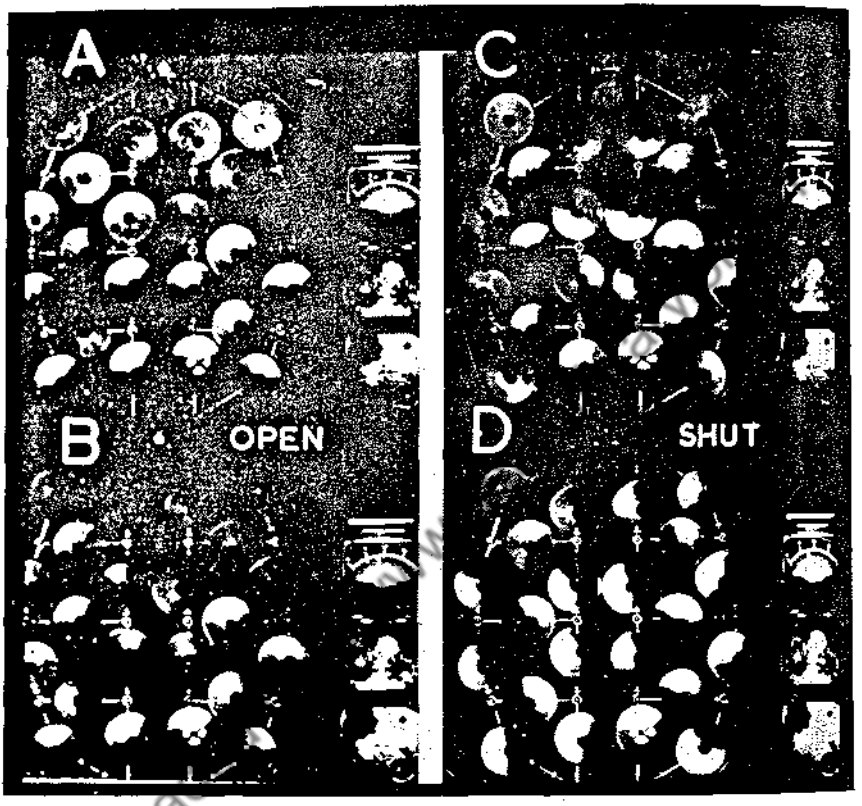


FIG. 2

Two pairs of exposures from a normal subject with persistent alpha rhythms. The motive channel in all is right occipital.
(A) Eyes open at rest. There is almost perfect synchrony of 8 cycles/sec. alpha rhythms over a wide area.
(B) Eyes open, during conversation. The alpha phases are more varied, and suggest a sweep from temporal to occipital channels.
(C) Eyes shut, still conversing. The alpha phases are quite different from those in (B) and there is indication of parietal phase reversal as well as a sweep.
(D) Eyes shut, at rest. The alpha rhythms now penetrate to all regions and there are indications of several phase reversal 'foci' as well as a sweep from front to back.
Such records illustrate the way in which the detailed time- and space-relations of alpha rhythms are associated with the degree and nature of conscious attention. Conventional records taken at the same time showed no significant variation in amplitude or frequency in the posterior channels.

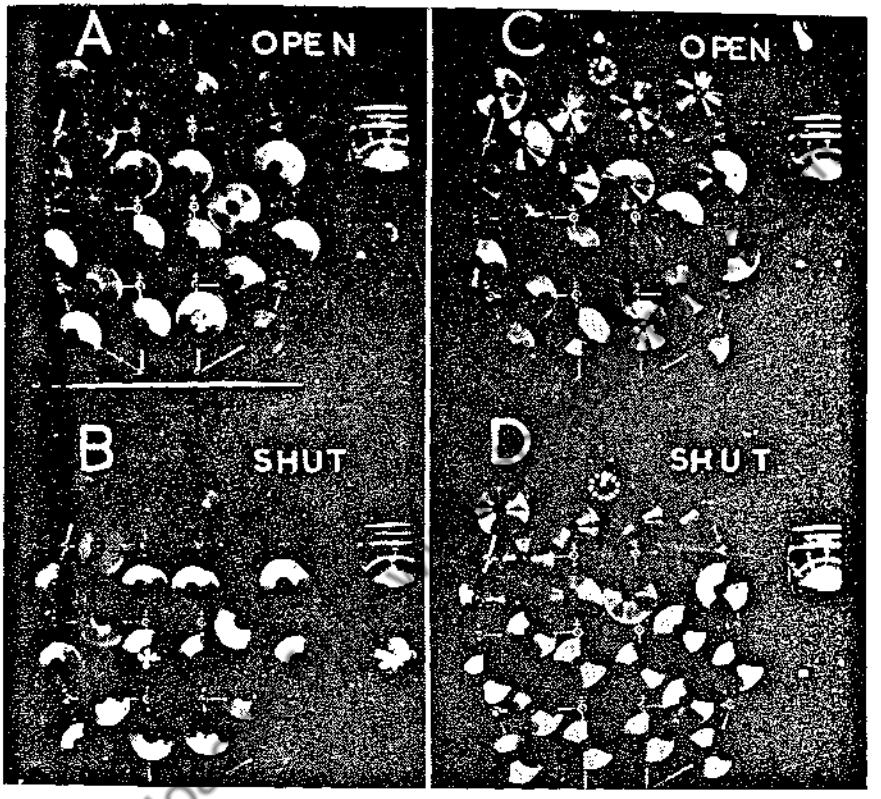


FIG. 3

Alpha rhythm distribution and evoked responses in a psychotic but intelligent youth, troubled by obsessive fantasies.

(A) With the eyes open alpha phase is constant over a wide area, the frequency is 9–10 cycles/sec.

(B) With the eyes shut the phase relations suggest a clockwise sweep under occipital channels on both sides, the radius being smaller on the left than on the right.

(C) Stimulation at 5 f/s. with eyes open. Evoked responses are widely distributed, some harmonics appearing in several channels.

(D) Stimulation at 5 f/s. with eyes shut. The evoked responses are at twice stimulus rate, and penetrate to many regions, particularly those affected by spontaneous alpha activity as shown in B, but the response is synchronized in nearly all channels.

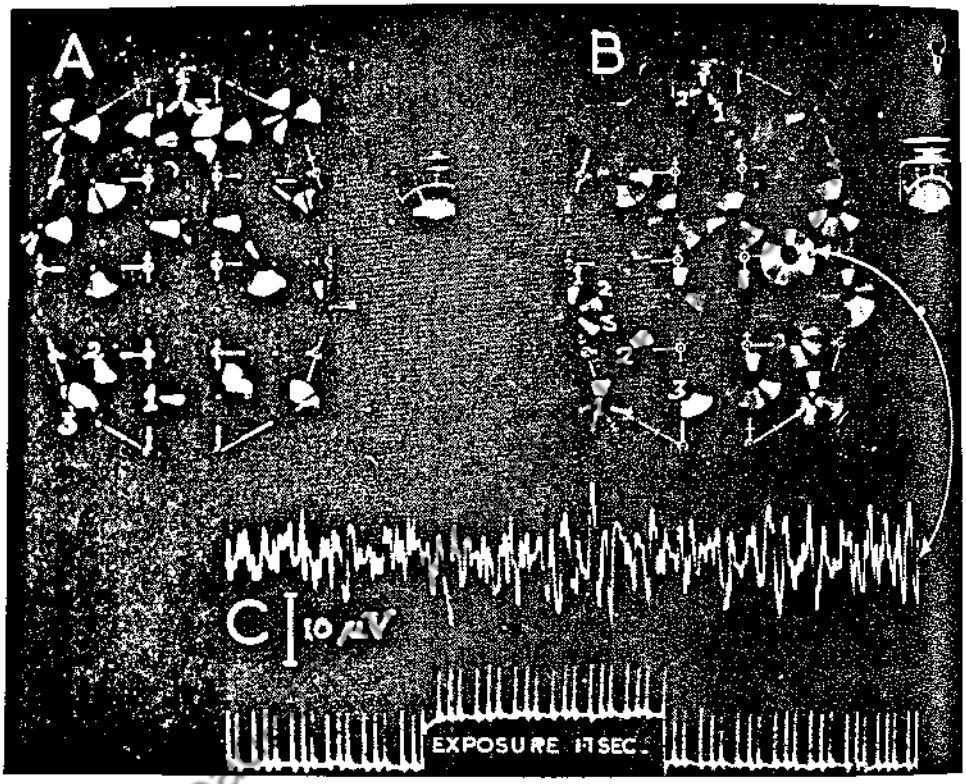


FIG. 4

(A) Responses evoked in a normal subject by flicker at 5×3 f/s. In the left occipital region the appearance of 'abscission' can be seen in the three contiguous channels where the separate responses to each of the three flashes of the group can be identified; a compound of these three regions could reproduce the original pattern, and this appears in the frontal channels with various latencies and time relations.
(B) A similar record from another subject. The flash-pattern is more compressed, the repetition rate (3.5 per sec.) lower and the exposure longer (1.7 sec.), but abscission is visible in the left occipital region and resynthesis in several other channels. The threefold response appears in six different guises, and with latencies from 200 to 300 microseconds (C) A primary record and monitor for flash and exposure corresponding to the exposure of (B). This shows that six groups of three flashes each were delivered during the exposure. The difficulty of recognizing any particular pattern is clear; the conventional trace is from the right transverse temporal channel.

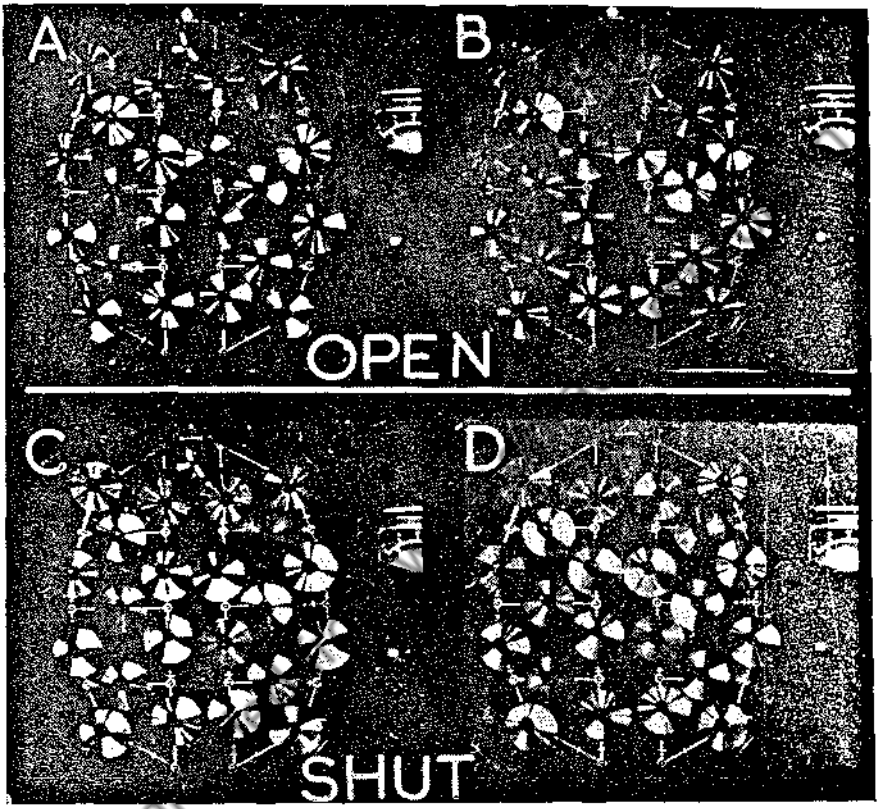


FIG. 5

Variety, dispersion and persistence of response to flicker in a normal subject.
(A) Eyes open, flicker at 2.5× 3 f/s. The stimulus pattern is reproduced intact in the right oblique occipital channel but in the anterior regions appears in many versions.
(B) Eyes open, one second after termination of stimulus. Traces of the stimulus pattern remain, particularly in the right temporal channels, mixed with rudiments of the returning spontaneous rhythms represented as Maltese crosses (2.5× 4 = 10 cycles/sec.).
(C) Eyes shut. Again the stimulus pattern is reproduced in many forms and in nearly all regions.
(D) Eyes shut, one second after termination of stimulus. The stimulus pattern is preserved for a longer time and with less distortion than when the eyes were open.

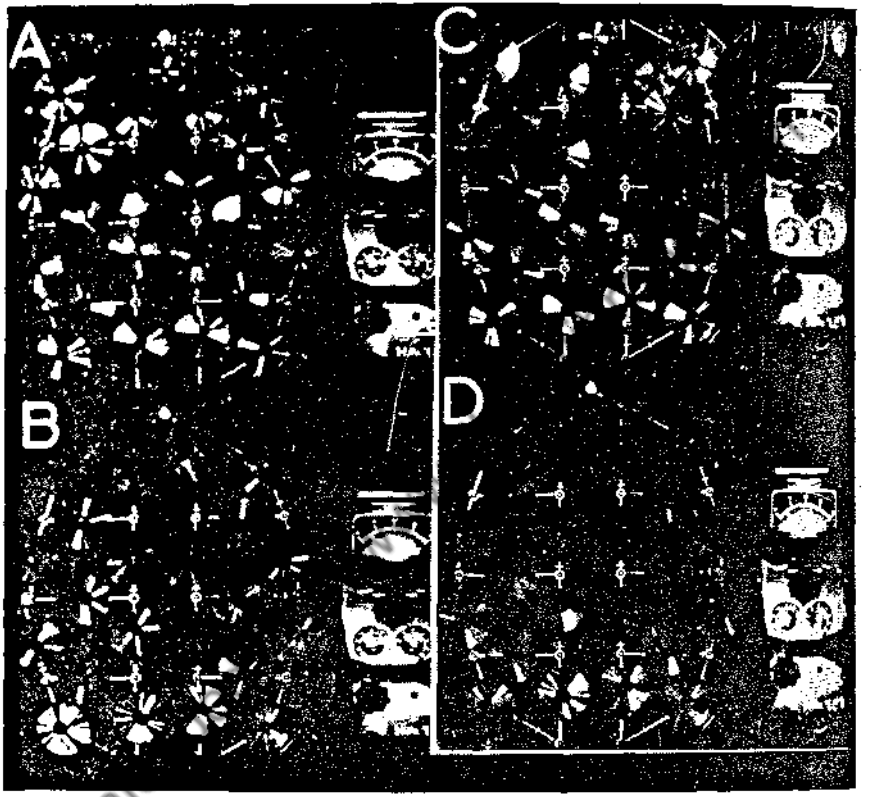


FIG. 6

The effect of habituation on the dispersion and preservation of responses to flicker in a normal subject.

(A) Eyes open, flicker at 3 × 3 f/s. at the beginning of stimulation; the responses are varied and widely dispersed.

(B) Immediately after termination of stimulus; the patterns persist in many areas.

(C) Same conditions, but after 50 exposure periods. The dispersion and variety of patterns are less marked, particularly in the temporal regions.

(D) Immediately after termination of stimulus at end of experiment; only in the occipital regions is there any sign of persistence or preservation of the stimulus pattern.

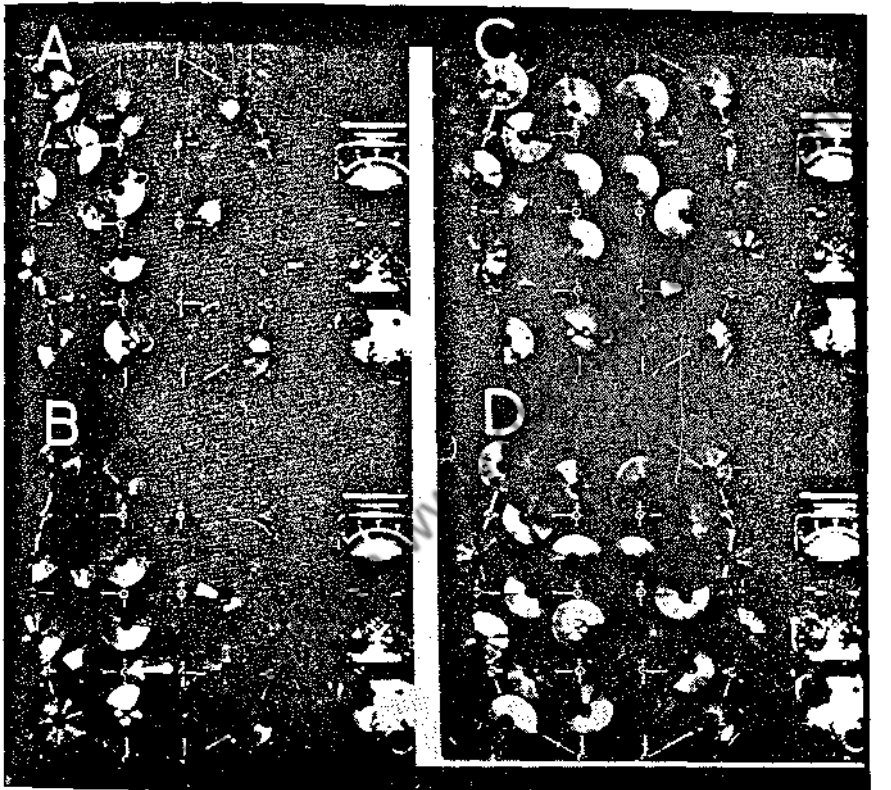


FIG. 7

Spontaneous activity in an intelligent youth, three years after right hemispherectomy. The right hemisphere shows little sign of independent spontaneous rhythms but the transverse temporal channel exhibits a component which cannot be attributed to electric spread from the left cortex because of its time- and phase-relations. In (A), (B) and (C) the motive channel (indicated by a cross) was in the left occiput, in (D) the left centro-occipital channel was used. The frequency of the activity on the left side varies from 6 to 8 cycles/sec., and the phase relations sometimes indicate a focus as shown by the arrow. Eyes shut throughout.

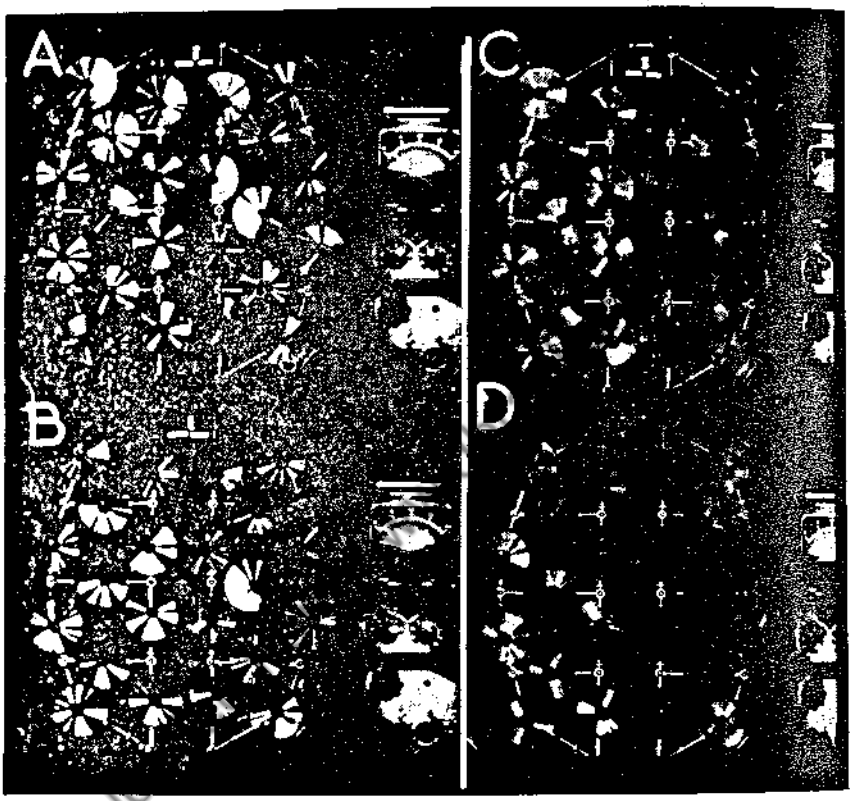


FIG. 8

The spread and persistence of responses to flicker in the case of hemispherectomy.
(A) Flicker at 2×3 f/s. The response appears in many areas, even on the mutilated side, particularly in the transverse temporal channel.
(B) The same a few seconds later; this shows the short term variations of the normal response pattern, but on the right side the transverse temporal channel again displays peculiar individual characters which cannot be due to physical conduction and are markedly stereotyped.
(C) Flicker at 4×3 f/s. The difference between the two sides is more marked at the higher stimulus rate, and the right temporal response has disappeared.
(D) One second after termination of the stimulus; persistence of the pattern is more prolonged and varied on the intact side.

at rates in the neighbourhood of an alpha frequency. In most people, however, the impression of 'driving' is probably illusory; frequency analysis shows clearly the presence of the alpha and evoked rhythms as separate components at, say, 9 and 11 cycles respectively, but there is good reason to suppose that some interaction takes place between the fluctuations seen as alpha rhythms and the effects of rhythmic stimuli. Perhaps the most striking evidence for this is the subjective impressions of subjects with fairly prominent alpha rhythms. Such people consistently describe vivid and detailed pulsating patterns as the stimulation rate passes through the alpha band, and can learn to estimate the flicker frequency very accurately by means of these 'visual beats' just as the frequencies of electrial oscillations are measured by setting a calibrated oscillator to beat with an unknown signal.

Records have been taken with the toposcope from a number of subjects with a variety of alpha rhythms, and exposures taken during rest with the eyes open and closed have been compared with those obtained during exposure to a variety of visual stimulus patterns. As would be expected, there is the widest imaginable variation between individuals, quite apart from clinical cases. But in general there seems to be some relation between the geometries and phase relations of spontaneous and evoked rhythms. This is seen particularly clearly in people whose alpha rhythms have a symmetrical distribution in the two hemispheres, and also in those subjects in whom an alpha component can be detected in the anterior as well as the posterior regions (Fig. 1).

There are many exceptions to prove this rule in the sense of testing it; where evoked responses appear in regions which show no alpha activity at rest they are often grossly exaggerated and even pathological, but unfortunately it cannot be asserted that the familiar pathological effects of flicker are always associated with absence of resting alpha activity in the affected region. As will be seen later, the resting rhythms seem to have a more complex connection with the forwarding of incoming signals to remote regions, so that in certain conditions, particularly when the activating stimuli are automatically synchronized with a spontaneous rhythm, extravagant effects may be produced just in the alpha-rich regions.

Special attention has been paid to the time relations of alpha

wave or peaks in different regions in these assorted normal subjects. It has been suggested by Stanford Goldman for instance (1948) that the alpha activity sometimes takes the form of a spiral sweep over the posterior regions of the head and existence of such a mechanism would be most encouraging to the proponents of a 'scanning' hypothesis of alpha activity. Subjective impressions of 'Catherine wheels' and whirlpools are quite commonly reported during flicker; movement of the subjective pattern is in fact invariable, so a spatial fluctuation on a time base of cerebral responsiveness cannot be excluded. Up to the time of writing (April 1953) the evidence is still inconclusive. In many subjects the most striking feature of topograms taken during rest is the *simultaneity* of the alpha peaks over very wide regions. In the toposcope, the summit of a potential gradient over the scalp, indicated in ordinary records by a 'phase reversal' is apparent as a 180° difference of position of the bright sector in the CROs on the two sides of the summit. Thus in one subject (Fig. 1 D) the alpha component at 8 c/s. extended into the frontal regions but the bright sector was centred at 3 o'clock in most posterior regions, the second anterior longitudinal channels showed no signal, and the first anterior longitudinal channels showed a bright sector at 9 o'clock, indicating a potential summit between the second and third electrodes from the front, that is, well anterior to the central sulcus. In this subject nearly all regions showed activity at either 9 o'clock or 3 o'clock, but in the left parieto-occipital channels there was some evidence of a sweep, the activity in the motive channel in the left occipital oblique CRO being, as specified for the lock-system at about 12 o'clock, that in the adjacent occipital transverse one at about 2 o'clock and in the longitudinal at 3 o'clock. This suggests the possibility of a clockwise sweep in this region. In another subject with a less widespread alpha rhythm at 9 c/s. (Fig. 1 B), there was no indication of a phase reversal focus but again the occipital regions showed slight discrepancies in time relations of the alpha peaks in adjacent channels; here again this could be considered evidence of a clockwise sweep effect.

In nearly all subjects from time to time there are clear signs of a time lag in the spread of alpha activity, but almost as frequently the activity appears practically simultaneously in widely separated

areas. The distribution of these two states is not quite chaotic; on the whole, the more profound the tranquillity of the subject, the greater the degree of synchronization (Fig. 2). There are exceptions to this rule also. In one subject the alpha rhythms were sometimes rather larger and more widespread with the eyes open than shut (Fig. 3) and with the eyes open the activity was amost perfectly synchronized in all posterior regions while with the eyes shut characteristic phase differences were invariable. Now most people feel more relaxed with their eyes shut, but this subject, a brilliant but psychotic schoolboy, was seriously troubled, particularly when his eyes were shut, by obsessive fixed ideas about chemistry, and he had been in trouble with the police because of persistent minor delinquencies.

It would seem that the physical basis for the alpha activities is a great deal more complex than has been realized and that study of the electric fields concerned as if they were simple linear voltage gradients in a single plane cannot be expected to give very helpful results. The observations already described suggest that the geometrical and chronological structure of the alpha mechanisms depend very much upon the attitude and mentality of the subject, and in this respect at least are very different from the scanning generators in most mechanical systems with which they have been compared. In a television channel, the scanning generators in the camera have a constant field- and line-repetition rate; the details and brilliance of the scene projected on the photo-electric mosaic do not usually control or modify the frequency, amplitude or phase of the scanning circuits. The same is true of the television receiver, except of course that the local scanning circuits are synchronized with those in the camera by special pulses from the transmitter; here again the picture details are not supposed to affect the scanning mechanisms. This analogy has been drawn because in certain circumstances, a television receiver can *display as a fault* an effect which may provide a clue to alpha activity in the brain. In England this fault is known as 'pulling on whites' and the symptom is a tendency for the length of a scanning line to depend on the brilliance of the picture detail at the end of the line, a highlight here tending to trigger the flyback of the line scanner prematurely. The effect is an unpleasant shimmer of the picture, since features anywhere in the field which are on the same

horizontal line as a bright object to their right tend to appear too far to the left, and vice versa.[1]

It would seem that, to some extent at least, the alpha mechanism tends to 'pull on whites': we may carry the analogy a stage further and recall that had commercial television systems been developed a few years later in the history of Information Theory, the scanning circuits would almost certainly have been designed to allow for modulation of scanning-rate by picture-detail and this is probably very much more like the processes in the brain.

We may now consider information obtained from the study of events in the brain which accompany the provision of regular pattern stimulation. As already mentioned these observations have been made on relatively normal subjects during exposure to very simple standardized visual stimuli. There is no technical reason why more elaborate stimuli should not be used and the investigation of responses to stimuli varying in form – as well as in time – as described by Marshall and Harden (1952), are of particular interest. Here again the variations between subjects and from time to time are very great, but examples have been selected to demonstrate the most persuasive evidence that signals reaching the visual regions are dealt with in a particularly intricate and elegant manner. The exposures in Fig. 4 were taken from two different subjects but under similar conditions. The exposures had durations of one and 1.7 secs. respectively and stimulation was in groups of three flashes, in the first case at 5 and in the second at 3.5 per sec. In Fig. 4 A the response to the first flash of the group is in the left longitudinal occipital channels at 3 o'clock, that to the second in the left transverse occipital at 5 o'clock and that to the third in the left oblique occipital is a bifurcated one at 12 o'clock. Since these three channels are connected to the same three electrodes it would appear that the differences in them must be due to variations in the geometry or orientation of the responsive structures beneath the electrodes. On the right side only a single bifurcated response is seen at about 12 o'clock; this cor-

[1] The corresponding fault in the United States would be 'pulling on blacks' but is infrequent since the American picture uses 'blacker than black' as synchronizing signal; electrical interference rather than extremes in the legitimate picture are more likely to produce this fault in American receivers. On this analogy the brain would seem to resemble the British more closely than the American television system, at least as far as their weaknesses are concerned, but whether this is a cause for pride or humility on either side is not, at the moment, clear.

responds to the pattern in the left oblique channel from the third flash. In the anterior regions a wide variety of dispersed and dissected patterns can be seen. At stimulation rates above 3 per second with three flashes there is often an exaggerated response to the third or fourth of a group of stimuli. In Fig. 4 B the stimulation rate is lower but dissection of the pattern is evident again in the left occipital channels. In this record re-collection of the components of the response is visible in the temporal regions; on the left in a compressed, and on the right in an extended version. As will be shown later, the regions where re-collection or re-assembly of response components are most evident are also those where the response pattern tends to persist for the longest time after the end of a stimulation period. The conventional EEG record reveals little of these effects, as is shown in Fig. 4 C; the irregular background 'noise' is too high to permit discrimination of the signal, but the pattern is reasonably clear in the associated toposcope channel.

The effect apparent in the left occipital region in these two exposures seems to be evidence of what has been called 'dissection' of the elementary response by rhythmic fluctuations of some kind in the visual and visual association regions. The term 'dissection' has caused some misunderstanding since in these conditions the separation of the components of the stimulus pattern is from a scale of time into a scale of space. It is suggested therefore that the term 'abscission' should be used to describe this particular effect. The implication of this term is that elements of a sensory time pattern are cut off and projected in a spatial pattern, transmitted in this form, like beads on a string, to other regions, and there reassembled in their original form as well as in variations of this. For the purpose of discussion, the process of abscission, as seen from the association areas, may be considered as abstraction, a drawing off of the strung beads. The hypothesis suggested to account for records of this type invokes alpha activity as the mechanism performing the process of abscission; interaction between the stimulus pattern and various components of the alpha rhythms in their abscissive role seems the simplest explanation for the enormous variety and versatility of the patterns evoked in non-projection regions.

In the experiments during which these records were obtained

the stimulus 'pattern' was a succession of groups of three flashes of light and the evidence suggests that such a time-pattern or rhythm results in the successive response of different brain regions. The inference is that the excitability or responsiveness of the visual areas varies with time in a rhythmic fashion and in such a way that the peak of responsiveness reaches different parts at different times. This of course is a lengthy way of defining a space-time scanning mechanism. The corollary of abscission for a stationary visual space-pattern lasting for one cycle of the change in responsiveness is the transformation of the spatial pattern-projection into a succession of signals on a time-base. This again is the specification of a scanning generator. From the physiologic standpoint there are obvious connections between these observations and the experiments of Bartley (1936), Bishop (1933) and Gastaut *et al.* (1951), all of whom discovered cycles of excitability in the visual cortex with periods of the order of 100 m.sec., but did not investigate the spatial distribution of the cycle over the cortex.

The possibility that these observations are due to some quite insignificant artefact has been considered; perhaps the most convincing evidence in favour of the reality and importance of the phenomena is that they depend to a very great extent upon the alertness of the subject and the novelty of the situation. A further point in favour of the reality of the dispersed, abstracted responses to stimulation is that they tend to persist for a short time after the end of stimulation. This is shown in Fig. 5, the top pair of exposures being taken with the eyes open and the bottom pair with the eyes shut. In this subject also stimulation was by groups of three flashes and the group frequency was 2.5 per second with the eyes open and 3.0 per second with the eyes shut. In each pair the one on the left was taken towards the end of an exposure to flicker and the one on the right a second or so after the flicker had been turned off. In both experiments a particularly vivid display of evoked patterns was produced by stimulation of this type; the subject also reported vivid subjective experiences with visual, tactile and vestibular components, associated with considerable affect. It is worth inspecting this figure with some care to discover how and where the stimulus pattern is reproduced and to what extent it has been corrupted, particularly in the more anterior channels. The exposures on the right, which were taken after the

end of stimulation, demonstrate – particularly clearly with the eyes closed – the persistence of the triplet pattern of the stimulus in the temporal region, rather more on the right side than the left.

Preservation of evoked patterns is a regular feature of normal records obtained by this technique. In most people who experience the situation for the first time, the stimulus pattern remains visible in the brain above the noise level for a few seconds after the stimulus is terminated. It must, of course, last very much longer in the intimate structure of the cerebral hemispheres, but it would be correct to say that the time constant of exponential decay is of the order of a second or two in most fresh subjects. In some patients with mental disorders the preservation time is 10 or 20 times as long, becoming indeed perseveration rather than preservation. It is naturally of great interest and importance that the effect is most pronounced in the temporal region, even when the stimuli are visual, and that, to some degree, a complex time pattern can be preserved. If a single stimulus is used the effect appears as a simple 'after-discharge' but with grouped stimuli the effect is seen to be in the nature of a reverberating echo rather than a damped oscillation. If one taps a drum three times, the diaphragm will continue to vibrate after the last tap, but will obviously not preserve or reproduce the triplet rhythm; if the experiment is performed in an echo chamber, however, the echo will equally obviously retain the pattern of the original sounds. These experiments suggest that there exists somewhere in the temporal region a mechanism capable of maintaining over a period of several seconds at least the pattern of visual signals. Studies of the geometry of these cerebral echoes suggest that they involve both cortical and deeper structures.

The long latency of the responses evoked during pattern stimulation is one of their most peculiar features. As is well known, the latency of the cortical response to single flashes of light is rarely greater than 60 m.sec. and the very first effects may be seen still sooner. Yet the latency of pattern responses is usually of the the order of 200 m.sec. and the response is not seen fully developed for several seconds after the start of the stimulation. These facts suggest that such responses involve more than simple sensory projection, and it is tempting to relate this long interval

to the similar values which are found in measurements of perception and reaction time.

The relation of these effects to the state of consciousness is illustrated clearly by comparing results obtained from a fresh subject with those when the subject has lost interest in the situation. The effect of boredom is demonstrated in Fig. 6 taken from another subject. In this record the top pair of exposures were taken during stimulation and the bottom pair after the stimulus had been terminated. The left hand pair were taken while the subject was fresh and the stimulus situation a considerable novelty, those on the right were the last two exposures of the experiment and were taken after about 50 sets of observations. Even during the flicker exposure the remote and abstracted responses are considerably less at the end of the experiment than at the beginning. The most striking evidence of boredom, fatigue or adaptation is seen in the bottom right hand exposure taken immediately after the fiftieth flicker period. By this time there is practically no sign of preservation of the remote responses and even the occipital regions show only a faint echo of the stimulus pattern. For comparison with other methods of recording, the potential difference corresponding to the after discharge in the occipital channels of this exposure had an average value of 4 microvolts.

The extent to which habituation, adaptation, fatigue, boredom and distraction influence these features of evoked responses is perhaps the most personal and individual characteristic of human brain activity. The evocation of dramatic responses in the temporal and frontal regions in normal people by flicker stimulation is a commonplace in EEG laboratories; in 3 or 4 per cent of a normal population, wave-and-spike patterns indistinguishable from those found in *petit mal* attacks may be evoked in this way, and recent studies of healthy university students have shown that activity of an 'epileptic' type may be evoked by flicker in as many as 50 per cent, but in these people dramatic evoked patterns appear only during the first dozen or so of exposures to flicker and only when no warning or explanation is given of the nature of the experiment. Some degree of novelty and suspense are essential and as soon as the experience has shown that the stimulus is innocuous and irrelevant, the magnitude and distribution of the

wave-and-spike discharges sinks rapidly to below noise level so that after 10 or 20 trials such responses can never again be elicited. It is the *persistence* of these exaggerated effects after many repetitions that distinguishes the epileptic from the normal person, rather than any feature of the response itself, or of the subjective accompaniments which, as reported by normal subjects, often resemble very closely a brief *petit mal* attack. When in a normal subject, the remote responses have faded after repeated exposure to a certain pattern, the brilliance and variety of the disseminated effects can often be restored by an apparently trivial alteration in the stimulus pattern.

It would naturally be of great interest to discover which structures in the human brain subserve these intricate functions. Records taken through the skull of intact subjects can provide information from which the position and orientation of the equivalent electric sources can be determined with considerable accuracy but correlation with detailed anatomy is scarcely permissible in view of the notorious variation in the relations between brain and superficial landmarks. Some light can be thrown on this subject by study of patients in whom known lesions exist, particularly when these are the result of deliberate surgical intervention rather than of disease or injury. Figs. 7 and 8 are exposures taken during experiments made on a young man of 22 who had started having left sided seizures at the age of ten and had a right sided hemispherectomy performed by the late Sir Hugh Cairns three years ago. The operation was described by Sir Hugh as removal of the whole of the right cerebral hemisphere, leaving behind the thalamus and the caudate nucleus. There have been no seizures since the operation, the left limbs are slightly spastic and there is a left homonymous hemianopia. Intelligence is high and powers of abstraction are well developed; the patient is interested in social science but is uncertain whether to take a two years course for a diploma or a three years one for a degree.

The exposures in Fig. 7 were taken during rest with the eyes shut. The frequency-and-phase-lock was connected to the channel marked by a cross in each case. The left hemisphere shows considerably more synchronized activity than the right, the synchronizing component being at 6-7 cycles/sec. with a phase reversal at the left anterior occipital electrode. The striking

feature is the constant appearance of synchronized activity on the right side in the transverse temporal channel. This is not due to electric spread from the intact hemisphere because the form and time relations have individual characters. The four exposures are reproduced to demonstrate the regularity of synchronization combined with individuality of phase and duration. Records taken during and just after flicker stimulation are shown in Fig. 8. The left hand pair were taken during stimulation by a group of three flashes at two per second and again the right side is far from idle. The right transverse temporal channel is actually the most active at the group frequency of stimulation. The peculiar form of its response is worthy of particular attention; the two left hand exposures are reproduced to show that this was not a rare or accidental effect. There is a wave lasting about 150 m.sec., followed by two sharp waves with a separate spike in the upper exposure. Here again it is worth examining all the channels in these exposures to appreciate the variety and subtle interlacing of pattern. The peculiar responsiveness of the right side diminished rapidly with repeated exposures at higher rates as shown in the top right hand exposure. The right hand exposures demonstrate also the dramatic difference between the two sides in the preservation of the evoked response – the top exposure was during stimulation, the lower one just after; stimulation is at the rate of three triple flash groups per second. The activity on the left side persists over quite a wide area, but that on the right subsides almost at once; only one longitudinal temporal channel displays a misty imprint of the vanished sign.

Observations such as this suggest that the presence of cortex is not essential for the development of widely disseminated responses to stimuli, but that preservation, storage or, not to put too fine a point on it, memory, does demand the collaboration of cortex and sub-cortical projections. Careful inspection and geometric analysis of photographs such as those reproduced shows that in intact subjects the appearance of disseminated, abstracted and preserved effects of evoked activity is due to the combination or congruence of two, perhaps more, orthogonal components. This interpretation has proved difficult to explain but a homely analogy may be useful. The domestic sewing machine does not imitate the human seamstress whose needle passes through the

fabric alternately from top and bottom; it contains two threads, one held by a needle oscillating vertically through the material and another in a shuttle oscillating horizontally below the fabric. By ingenious co-ordination of these two motions the threads are knit into a single seam. If one thread is missing or when co-ordination is faulty, the seam may look intact, but it can easily be unravelled by drawing on one end of the thread. It is this sort of mechanism which is suggested by the observations summarized above; an interweaving of reciprocal electric filaments to generate an intricate and durable texture of significant association.

Observation has so far taken us little further than this in human studies, but our conjectures may be informed by analogies more precisely fashioned to the special needs of this problem. Some years ago it was realized that as soon as trustworthy information about the mechanism of brain function began to accumulate rapidly, there would be enormous difficulties in appraisal of the mutual significance of isolated observations. The number of observed facts is the exponent of the number of possible hypotheses to relate them. When there are few facts and many impossible connections the subject may be understood without great difficulty, but when there are many facts from divers sources and nothing can be assumed impossible, special tactics must be used to permit an ordinary mind to see the wood rather than the trees. Perhaps the simplest and certainly the most agreeable device in such a situation is to construct models, on paper or of metal, to reproduce the main features of the system under observation. In such models care must be taken to observe the principle of parsimony; to imitate as many as possible of the relevant functions with as few parts as possible. Successful models then show not only a mimicry of the specified features, but reproduction of other activities not in the original specification. This is because in our appreciation of a complex problem we tend to enumerate functions as though they were separate entities, not realizing how many are really combinations of relatively few elements. True, as science evolves even the number of identifiable elements may increase considerably, but this number is still vastly smaller than the number of compounds. A few hundred years ago the number of chemical elements was fixed at four; we now recognize a hundred, yet the number of chemical compounds is indefinitely

large and almost all can be synthetized from knowledge of elemental properties. Models of physiological functions have the same purpose as atomic or molecular models in other sciences – to help in the identification and specification of elements and their compounds, to promote analysis of mysterious mixtures and encourage synthesis of novel material. It should be recalled that, in relation to human activity, experiments on animals are also essentially experiments with models.

The particular model which is relevant to the problems and observations outlined above is one that was constructed to reproduce the behaviour of an animal constrained to modify its behaviour when faced with the association of two series of events. It is, in effect, a conditioned reflex analogue. A complete description of this machine has been given elsewhere (Walter, 1953a) and need not be recapitulated here. The important requirement is that for adaptive behaviour to have survival value it would seem necessary for a signal entering the nervous system to be operated on in two ways, and for these two derivations of the original signal to be disseminated throughout the brain 'for information only, to whom it may concern'. The two operations have been described as differentiation or clipping and extension or stretching respectively. The effect of the first is to generate from a prolonged stimulus a short pulse at its beginning, that of the second to protract the response after its end. The clipped form is postulated as necessary in case the signal should turn out to be important as an unconditioned or specific stimulus, to *be meant* by something, the stretched form is required in case the signal be important as a conditioned or neutral stimulus, to *mean* or imply something. A signal may easily be implied by something and imply something else; *a priori* assumptions by the nervous system as to which association is more probable are unjustifiable and dangerous.

The two sets of signals derived from the sensory input are literally *propaganda*; they must be propagated but need not be attended to unless they are frequently and regularly repeated in the same pattern. The rank of 'memoranda' is not attained until a clipped signal from one source and a stretched one from another appear together often and close enough to acquire significance over and above that which would be expected by chance. A neuronic system to provide these facilities has been sketched out;

it is the block diagram of the conditioned reflex analogue and represents schematically the peculiar properties of what – on this hypothesis – may be expected to underlie the brain functions we recognize as conscious attention to events and adaptation to circumstance. There are postulated two relays from every sensory input; both should project diffusely to as many regions as possible of the unspecialized – perhaps even to specialized – cortex. One of these relays should pass through a differentiating or in physiological terms, rapidly adapting, circuit to provide the clipped form of the incoming signals. This should appear in electrical records as a brief 'on effect', a spike or short burst of waves at the onset of the stimulus. The other relay should pass through a circuit with a pronounced tendency to after-discharge, giving the effect of stretching and seen in electrical records as a response considerably outlasting the duration of the stimulus. Activity in both these relays should be suppressed in drowsiness, anaesthesia, boredom – in any conditions in which 'awareness' or the ability to assess the significance of events is impaired. As well as this, a rich and bewildering variety of anomalies and abnormalities would be expected. Inhibition of the after-discharge mechanism for example, makes the system pessimistic, sceptical, suspicious and depressed. Prolongation of the clipping action has effects similar to that of the after discharge, but leads also to completely irrational reversals of probable meaning – thunder means lightning – superstitions, fantasies, and delusions.

Encouraged by the discovery of orderly and objective complexities within the brain we have derived from a simple model predictions of the detailed effects of sleep, anaesthesia, habituation and distraction, warning of the occurrence of depressive, manic and deluded mentality and statistical specifications for the origin and spread of epileptic seizures. As a material basis for these functions and their disorders we have postulated two diffusely projecting systems arising close to the input for sensory signals and terminating in all, or nearly all, cortical regions. The signs of activity in these systems as they impinge on cortex we believe to be the interwoven electric fields represented by records such as those here reproduced. To what extent these observations and forecasts match those from other sources will be a matter for demonstration and debate.

GROUP DISCUSSION

FESSARD: The fact that Dr. Walter can so frequently observe steady states in the spontaneous rhythms has impressed me. How abrupt are the transitions from one state to another?

WALTER: The answer to this question is complex because it depends very much on individuals. Some individuals maintain for several minutes constant phase- or time-relationships. In the extreme cases these people are quite mad. In the medium case such a person is characterized by a crystal-sharp abstract imagination. In most people though, phase-changes are very common and varied and differences corresponding to various mental states are easily measurable. In sleep, particularly, phase shifts are common and rather abrupt.

ADRIAN: I would like some clarification of your theory about the activities which go on in different areas. In regard to the visual projection system you suggested that one third of the signals were picked up in one place, another third in another, and so forth. Surely the projection area should receive the whole picture?

WALTER: One must remember that recording through the intact skull of the human, one is probably far from the primary projection area. The 'abscission' effect is seen in the secondary and tertiary areas 18 and 19 rather than 17. The re-composition and abstraction effects appear in the frontal and temporal regions.

PENFIELD: If a patient were listening to continuous clicks or to continuous music would the pattern be changed as it is following visual stimulation?

WALTER: I think, yes. However, it is difficult to work with acoustic stimulation because it is not so easy to tell microphonic effects from the cochlea from cortical evoked potentials in the temporal lobe nearby. In addition, in the case of the auditory apparatus in man there is very rapid adaptation which is not true in the case of flicker.

PENFIELD: Are you depending on the disorganization of the alpha rhythm?

WALTER: No, mainly on evoked effects. As a matter of fact you can see elaborate patterns in places where no alpha can be detected.

PENFIELD: If the input has something to do with what a man can remember or be conscious of, I would expect to have a constant stream of impulses to both temporal regions, a stream that recreates what he is attending to. The flicker stimuli are surely not the sort of thing that a man would recall and I should think he would try to turn his attention to something else.

WALTER: The subject actually sees not just a flicker but all sorts of fantastic and elaborate moving patterns. This subjective impression

may be the result of interaction between the alpha rhythms and the afferent impulses in the way indicated in the figure of 'abscission'. These subjective patterns are often very vivid and memorable, but as interest lapses, so the electric patterns wane.

PENFIELD: So that sometimes he is thinking about these things and sometimes not.

WALTER: That's true, and in fact some epileptics do or do not have seizures during flicker according to the way they are thinking of their impressions.

BREMER: Would you think that a brief flash of light given during the after-effects would wipe out the memory trace?

WALTER: I do not know. I have never tried that; it will be most interesting, the traces are less persistent with the eyes open than when they are shut, so it looks as though new signals were competing with the old traces.

KUBIE: Did you ever compare the effects upon patients with organic mind blindness or visual aphasias and agnosias or with hysterical blindnesses?

WALTER: So far, we have deliberately confined ourselves to the study of normal people without going into more complex problems. However, in some cases of hysterical blindness the remote effects are often very mild. In one case, however, there were no evoked responses and the alpha rhythms remained unchanged.

HEBB: Dr. Walter has raised the problem of learning but I do not recognize the aspects with which we usually deal in what he has said. Perhaps I might ask two questions. What is the basis of the long lasting changes of memory? And what does Dr. Walter mean by 'important for the organism'? In other words, how does a stimulus differ, from a physiological point of view, when it is 'important' and 'not important'?

WALTER: I think the answer to this question would take us too far from the subject of the symposium; I have developed these notions in detail elsewhere. However, I am suggesting that what goes on in the brain must result from the intermingling of signals from two different sources and the cortex assists in the confluence of the streams from two sources.

HEBB: But what are the physiological changes? Do you think in terms of synaptic changes to explain the long lasting effects of learning?

WALTER: We do not know the substrate for these changes. Whether some chemical changes take place or new dendrites grow up or perhaps electro-chemical reverberations are initiated; some new state is set up as a result of these two confluent streams.

HEBB: If two streams come from two different sources where do you

think the meeting takes place? If it is in the reticular system, where it is likely that all the stimuli meet, why should two particular stimuli meet – why should not any stimulus be 'important' on this basis?

WALTER: I suggest rather the signals come through the reticular structures and meet in cortex. What happens there depends on the history of the organism. In the young animal there can be no *a priori* assumptions. All impulses come together and they are mixed up, not just at random but in a systematic fashion. The final effect on the brain will depend on the extent to which the clipped signals from one source and the stretched ones from another coincide, as compared with chance expectation.

MORISON: I have the impression that this model gives us information about perception more than learning.

WALTER: You need at least two neurone systems to get conscious perception. Otherwise you have only 'sciousness' of which the simple learning element may be considered as one unit. I do not consider consciousness as an entity, but as a process, a relation between observations, and therefore an element of association

FESSARD: Don't you think that in the mixture of messages, motivation – as the psychologists call it – is a decisive factor in giving the final action its shape?

WALTER: I have suggested that from the statistical standpoint, one can choose a favourite or an outsider and motive of course plays a role in this choice, as does personality. Maybe psychiatrists can help us in the definition of motive in these terms. It would be very interesting to investigate the growth of the statistical standards which govern choice of action.

FESSARD: How long does it take for these changes you mention to disappear?

WALTER: A few seconds in most people, up to minutes in certain pathological states.

FESSARD: I agree that differentiation is a very common feature in the responses of elementary structures such as nerve fibres, but prolongation is much less frequent, unless one deals with complicated structures.

WALTER: After-discharge is a common physiological phenomenon, even in spinal cord and we postulate two diffusely projecting systems, one of which does differentiate and one which is characterized by some sort of after-discharge.

FESSARD: Would you say that after-discharge is an autorhythmic process or a reverberatory one?

WALTER: I think possibly both, in brain.

PENFIELD: Do you feel you have seen in these photographs only the effects of the entrance into the brain of the afferent impulses or are you

seeing something that gives you an idea of the intellectual state of the subject?

WALTER: There are differences between different people. Both the states of mind, psychologically speaking, and the electrographic picture vary enormously. In some people, the relations between behaviour states and electrographic pictures can be reproduced over a fair period, but there is always the adaptation or boredom effect unless a special significance is attached to the signals by making them imply something of elementary importance. One can never 'repeat' an experiment on a brain.

BREMER: The after effect retains the rhythmic structure; this is very amazing and I wonder if an after-discharge can explain that. However, it seems to me that even these phenomena in the cortex find an analogy in lower levels of the C.N.S. In the case of the spinal strychnine tetanus, when the tetanus has been initiated by rhythmic stimulation for a few seconds following the end of the stimulus, the tetanus is seen to have the same rhythm as the rhythm of the inducing stimulus.

JASPER: In the cortex, however, this is a rather rare phenomenon and it happens only when the frequency of the stimulus is very near to that of the spontaneous rhythm, and I wonder whether this applies to Dr. Walter's case.

WALTER: Of course in these conditions, it is not exactly a frequency. It is rather a rhythmic pattern, and there is no obvious relation between the signal intervals and the spontaneous rhythms when persistence occurs.

RIOCH: The duration of these patterns seems to be of the same order of magnitude as the time during which a concept may be maintained unchanged in 'consciousness' as indicated by introspection and also as indicated objectively in patients by the rate of change of content of thought reflected in their speech.

WALTER: Interrogating the subjects, we get the impression that the persistence time is indeed of this order of magnitude.

GASTAUT: In your records you show that in every case the photic responses are equal in the frontal temporal and in the occipital regions. This fact is never observed in the usual ink-tracing records. The same is true for the after-effects which are never present in our records. Could you explain that? If I understand your method correctly, the same brilliance means the same amptitude.

WALTER: This method is not designed to indicate amptitude accurately. There is a short linear range and in these reproductions 10 microvolts produced full brilliance. Then there is the relatively high resolution against noise which is usually between 5-10 microvolts; few of these effects would be identifiable in conventional records.

FUNCTIONAL PROPERTIES OF THE THALAMIC RETICULAR SYSTEM

By

HERBERT H. JASPER

Evidence and arguments have come from many sources for a central reticular core of closely interconnected neurones which has been loosely termed the reticular system. Rather than a specific function for a given sensation or movement, this system would seem to have a more general functional significance for the activity of the brain as a whole, with particular reference to conscious mental processes.

Penfield (1952) has been drawn to the necessity of postulating such a system of neurones from his observations upon the effects of local epileptic discharge and epileptic seizures in general, as well as from studies of the effect of electrical stimulation of the brain in conscious human subjects. Penfield has proposed the term 'Centrencephalic System' for a hypothetical system of neurones in the brain stem which have equal functional relationship with the two hemispheres and closely interrelated connections with widespread areas of each hemisphere. He has elaborated upon this conception in his own communication to this Conference. Basically Penfield's logic rests upon the same premises as those of Descartes, who found the necessity for a central structure in the brain which could serve as the anatomical basis for the coherent unity of mental processes.

From quite a different point of departure, Magoun and his colleagues have found it necessary to postulate an 'ascending reticular system' which is capable of 'activating' the cerebral cortex as a whole. This conception developed from previous work on the 'descending reticular system' which was shown by Magoun and Rhines (1948) to have such important effects upon spinal reflexes and muscle tone. The ascending reticular system, which extends from the medulla to the rostral pole of the thalamus, was shown from electrophysiological and behavioural

studies to be of importance for the function of the brain as a whole with particular reference to what was termed 'arousal' or states of alertness, as opposed to states of inactivity simulating sleep or unconsciousness.

From still another point of departure Morison and Dempsey (Morison and Dempsey, 1942a; Dempsey and Morison, 1942a) had previously described a system of neurones in the thalamus called the intralaminar or recruiting system. Electrical stimulation of this system of neurones did not evoke specific localized cortical responses. Instead, it had the remarkable property of being able to control the electrical rhythms of widespread areas of the cerebral cortex in the cat. These studies were confirmed and extended by the present author with J. Droogleever-Fortuyn (1947), in addition to the demonstration that the bilateral wave and spike characteristic of the electroencephalogram of *petit mal* epilepsy could be reproduced by stimulation within the intralaminar portions of the thalamus. This gave experimental support to the hypothesis that there exists a centrencephalic mechanism in the higher brain stem from which the discharges of *petit mal* epilepsy originate, and that this system must be somehow closely related to mechanisms of consciousness, for it is consciousness which is principally affected in the *petit mal* epileptic attack. The evidence was strengthened by the demonstration that not only the electrical pattern but also *petit mal*-like seizures could be reproduced in unanaesthetized experimental animals by electrical stimulation in the mesial thalamus (Hunter and Jasper, 1949).

For the present Conference I propose to review certain studies carried out in our laboratories on the thalamic portion of the brain stem reticular system. In presenting our own observations and hypotheses, I wish to acknowledge from the start my indebtedness to many colleagues with whom I have worked, particularly Jan Droogleever-Fortuyn, John Hunter, Robert Knighton, George Austin and Julius Stoll and, for more recent studies, I am greatly indebted to the collaboration of Cosimo Ajmone-Marsan and John Hanbery.

For anatomical relationships with our physiological studies we have all had the most valuable assistance of George Olszewski, who has presented his own point of view regarding the reticular system in this Conference.

SPECIFIC AND UNSPECIFIC THALAMOCORTICAL PROJECTION SYSTEMS

Lorente de Nó (1943) first described two types of cortical afferent fibres which he called 'specific' and 'unspecific'. The identification of these two types of fibres was based upon cyto-architectonic studies of the rat.

The specific afferent fibres to the cortex consisted of the main projection fibres from sensory relay nuclei of the thalamus to sensory cortex and possibly also the principal afferent projections from other thalamic nuclei to other areas of cortex, such as those from the nucleus medialis dorsalis to frontal cortex, from lateralis posterior-pulvinar complex to parietal cortex.

The unspecific fibres were from two sources: (*a*) those coming from undetermined regions of the thalamus independent of the specific thalamic nuclei and (*b*) transcortical or transcallosal association fibres.

Specific afferent fibres terminate principally in layer 4 of the cortex, with a distinctive terminal structure or arborization called the 'brush' by Lorente de Nó. This is illustrated in Fig. 1. The unspecific terminations from either the thalamus or from other cortical areas seemed to have collateral branches ending in all layers of the cortex, probably synapsing with cortical cells (short pyramids and spindles and deep star cells) which do not receive direct synaptic connections with the specific afferent system. The unspecific fibres tended to terminate in all layers of the cortex, branching sparsely in the molecular layers, without the distinctive brush formation so characteristic of the specific afferent terminals.

Recently Chang (1952a) has provided both cytoarchitectonic and experimental evidence for two distinctive forms of terminal afferent structure in the cortex. Following the original description of Cajal (1934) cortical synapses are described as of two kinds: (1) axo-somatic and (2) axo-dendritic. The axo-somatic terminals seem to end principally on the cell bodies of cortical neurones, while the axo-dendritic terminate on cortical dendrites. Chang has proposed the terms peri-corpuscular and para-dendritic to describe these two principal forms of synapse in the cortex.

The specific afferent terminals are chiefly of the peri-corpuscular type, with their characteristic terminal arborization in the fourth

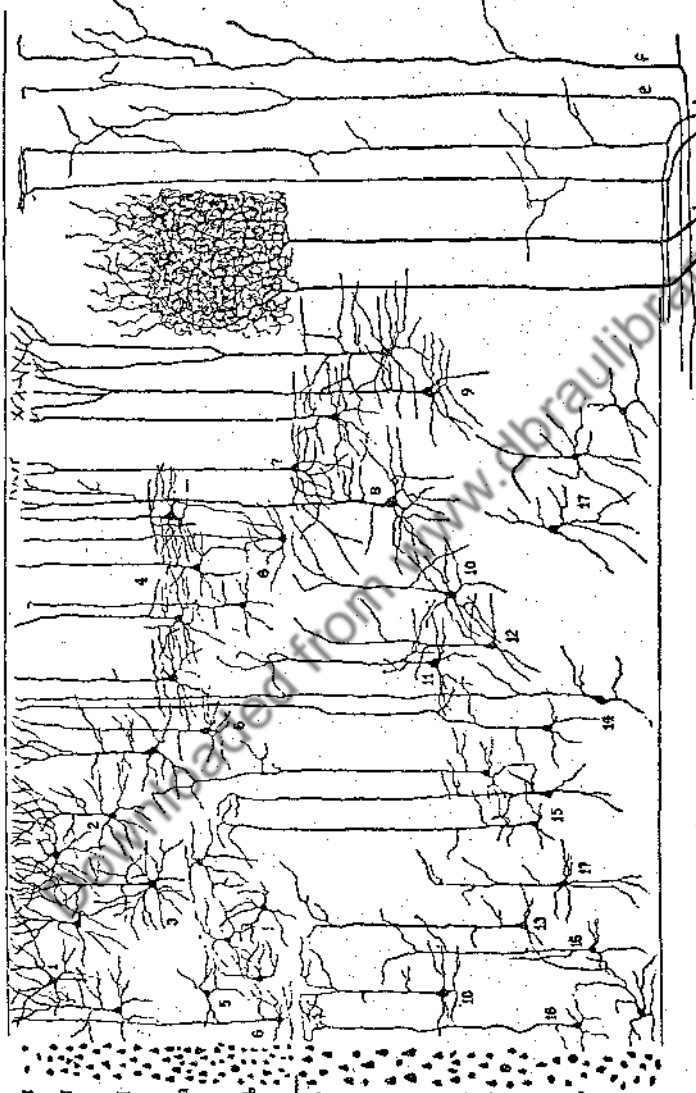


FIG. 1

Diagrammatic representation of cortical afferents as described by Lorente de Nó (1949). At the left are shown the cortical layers of cells taken from the parietal lobe of the adult mouse. In the centre are shown the bodies and dendrites of the principal types of cortical cells (descending axons not shown). At the right are shown the specific cortical afferents (*a* and *b*) ending in typical dense arborization in layer IV. Unspecific or 'pluriareal' afferents of thalamic origin are shown in *c* and *d*, giving off branches at all levels of the cortex, but perhaps chiefly in layer VI.

layer of the cortex. The para-dendritic terminals have a diversified origin according to Chang, being collaterals from different pyramidal cells, the terminals of trans-callosal fibres from the opposite hemisphere, or association fibres from other cortical areas, as well as unspecific thalamic projection fibres. Electrophysiological confirmation of the more superficial termination for the unspecific fibres has been given in the work of Bremer (1952), Chang (1952a), Amassian (1953), and in our studies with Li (Jasper and Li, 1953).

Chang suggests that the para-dendritic terminations which characterize the unspecific afferent fibres must have a very different function in the cortex than the peri-corpuscular or specific afferent terminations. The para-dendritic could act in modifying the state of excitability of the cortex by facilitatory or inhibitory effects regulating the transmission in specific synaptic circuits. A similar conclusion was arrived at independently by Bremer as a result of his studies of interaction between trans-callosal and specific afferents in the modification of the evoked potential complex. The fact that interaction was observed to occur chiefly upon the surface negative component of the evoked potential complex led him to propose a more superficial termination of the inter-hemispheric commissural fibres where they could affect the apical dendrites of pyramidal cells. One cannot be sure, of course, that the unspecific thalamo-cortical afferents have the same form of termination as do the transcortical fibres, though both seem to interact chiefly on the surface negative components of specific evoked potential complexes.

Morison and Dempsey (1942a), when searching for an anatomical explanation of their classical observation that electrical stimu-

(Caption for Fig 2)

Specific evoked potentials from the sensory cortex of the cat (monopolar, negative up) in response to brief single electric shocks administered to the sensory relay nucleus of the thalamus (Ventralis Posterior). The upper line in each pair of cathode-ray oscilloscope tracings was recorded from a surface electrode (silver ball about 1 mm. in surface contact on pia). The second line in each pair was taken with a microelectrode (glass pipette about 1 mu. diameter) at different depths from the surface adjacent to the gross electrode down to a depth of 2.2 mm. Note that the deep electrode records a large negative wave simultaneous with the surface positive wave when the deep electrode reaches a depth of about 0.8 mm. and there is a complete reversal in phase from this level on down. Layer IV in this cortex is about 0.8 mm. beneath the surface. Numbers on each pair of records represent millimetres depth of microelectrode from surface. Time line at bottom indicates 5 microseconds intervals. Vertical calibration lines equal 400 microvolts.

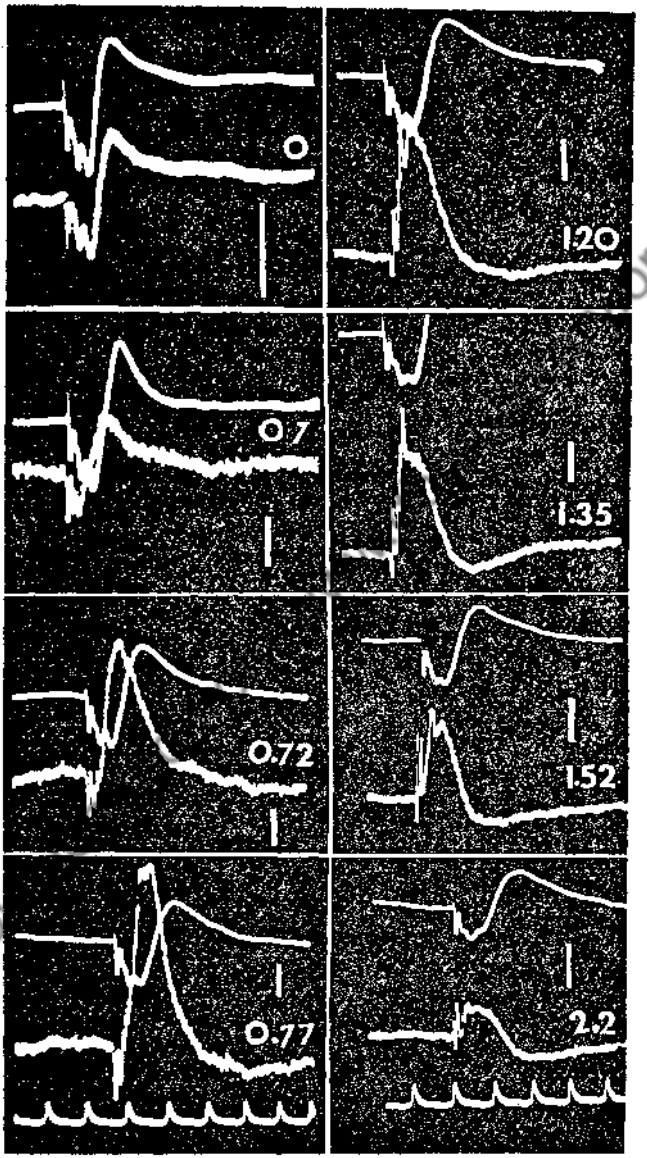


FIG. 2

lation in the intralaminar portions of the thalamus had a remarkable effect upon the rhythmic electrical activity of widespread areas of cortex, suggested that such effects might be mediated by unspecific thalamocortical projection fibres as described by Lorente de Nó. This was supported by the demonstration by Morison and Dempsey that the electrical responses of the cortex to stimulation of specific thalamocortical projection systems was of a different form and apparently showed a considerable degree of independence from the cortical responses to stimulation within the intralaminar portions of the thalamus. They described the relation between the specific and unspecific systems as being characterized by 'semi-independence'.

THE LAMINAR MICROELECTRODE STUDIES OF SPECIFIC AND UNSPECIFIC THALAMOCORTICAL PROJECTIONS

The form and distribution of electrical responses at different depths of the sensory motor cortex in the cat while stimulating specific or unspecific thalamic nuclei has been studied recently in our laboratories with microelectrodes in collaboration with Dr. Li and Dr. Cullen. The details of these studies are to be published elsewhere, but the pertinent data may be summarized here.

As the microelectrode was inserted progressively into the depths of the cortex the specific evoked potential underwent very striking changes when the electrode reached the region of the fourth layer of the cortex. In the sensory cortex, for example, the surface positive wave became a much larger negative potential when the tip of the microelectrode reached the fourth layer, where it is known that the terminal arborizations of the specific afferent system lie (see Fig. 2).

The form and distribution of recruiting responses of the cortex throughout its layers was found to be different than that of the specific responses. In the first place the unspecific responses to somato-sensory cortex in the cat, (e.g. resulting from repetitive stimulation of the nucleus centrum medianum) were much more labile than were the surface positive waves of the specific evoked potentials in the same area of cortex. In those experiments showing good surface negative recruiting response, the microelectrode showed also a predominantly negative response throughout the upper 0.5 mm. of cortex.

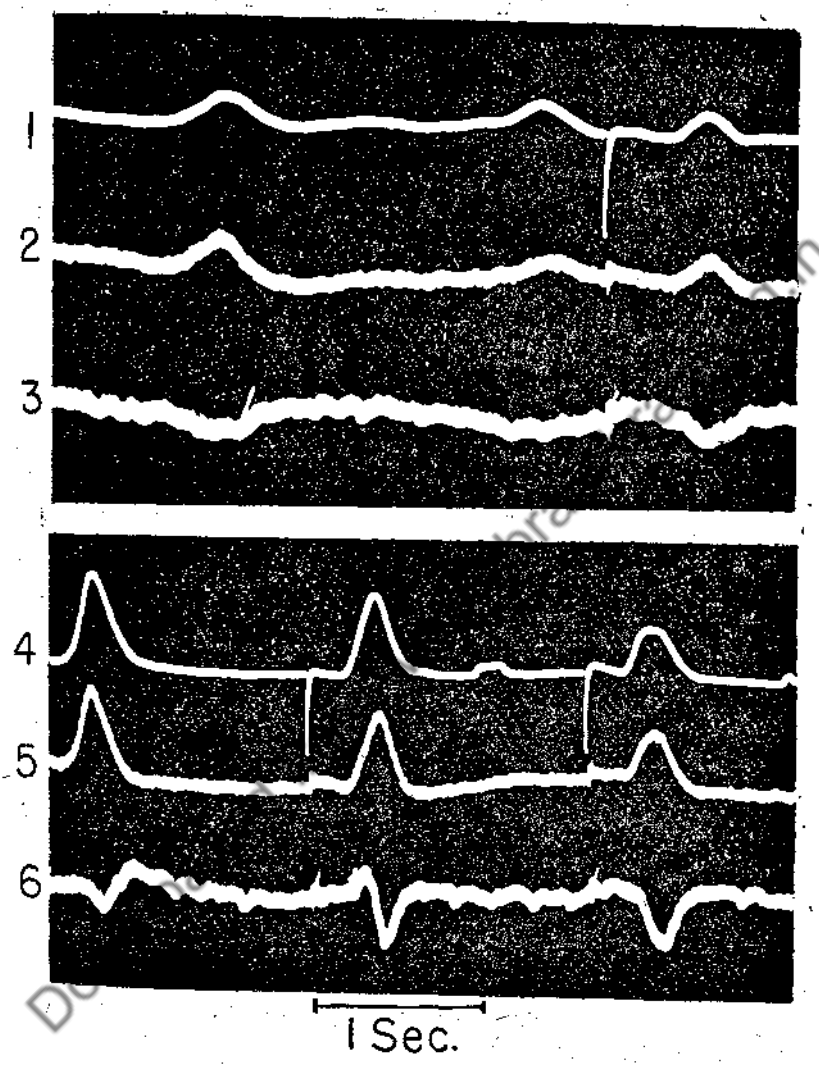


FIG. 3

Recruiting responses recorded from the surface and at different depths with microelectrodes in the somato-sensory cortex of the cat. Records 1 and 3 were from a surface electrode. Records 2 and 4 were from a microelectrode at a depth of 0.40 mm. from the surface, records 3 and 6 from a second microelectrode at a depth of 1.30 mm. In the upper three tracings note the spontaneous surface negative wave which becomes positive at the depth of 1.3 mm. The recruiting responses shown in the lower three simultaneous tracings also show an inversion in electrical sign at the depth of 1.3 mm. Stimulus frequency 6/sec. Latency of surface negative response was 22 microseconds. Stimulation point in rostral Centrum Medianum.

Recording in deeper layers in some experiments the recruiting waves remained negative and in phase with those at the cortical surface. In other experiments there was a much more gradual change in electrical sign between about 0.5 and 1.5 mm. in depth, a complete reversal in sign (deep positive with surface negative) occurring below about 1.5 mm. from the surface (see Fig. 3). The marked increase in voltage in the region of the fourth layer which is such a striking feature of the specific evoked potentials was not observed, except to a limited degree in some experiments, in the laminar analysis of recruiting responses. In certain experiments a marked increase in amplitude did occur in about the region of the fourth cortical layer, but we could not be sure in these instances whether both specific and unspecific fibres were being excited simultaneously by the thalamic stimulating electrode.

It is interesting to note that the so-called recruiting response, namely, successive increase in amplitude of cortical response with repetitive stimulation at frequencies close to the frequency of the spontaneous rhythms of the cortex, can be demonstrated also in terms of unit discharge of cortical cells. Initial slow wave responses may not be accompanied by the discharge of cortical neurones and are considered to be of the nature of synaptic potentials. By repeated stimulation, as the synaptic potential increases in height, individual cortical units begin firing on the negative crest of the synaptic potential. This control of cortical discharge by rhythmic electrical stimulation simulates that which occurs spontaneously with the bursts of slow waves at about 8 to 10 per second which are characteristic of the sensory cortex of the cat under barbiturate anaesthesia or in the relaxed animal without general anaesthetic. Unit firing from stimulation of the specific system is of quite a different character. Since recruiting is not necessary, units discharge at shorter latency and prolonged after-discharge may occur, as shown in Fig. 4.

We cannot at this time elaborate on the details of this analysis but suffice it to say that these observations have given electrophysiological confirmation to the anatomical studies which show not only a different distribution of unspecific fibres within the ayers of the cortex, but that stimulation of the unspecific system may exert a quite different effect upon cortical activity than do

afferent volleys arriving over the specific projection systems. Definite interaction between the two systems, however, can also be shown, but these are obvious, particularly in the surface negative wave of the specific evoked potential complex, as has been previously described in collaboration with Ajmone-Marsan (Jasper and Ajmone-Marsan, 1952).

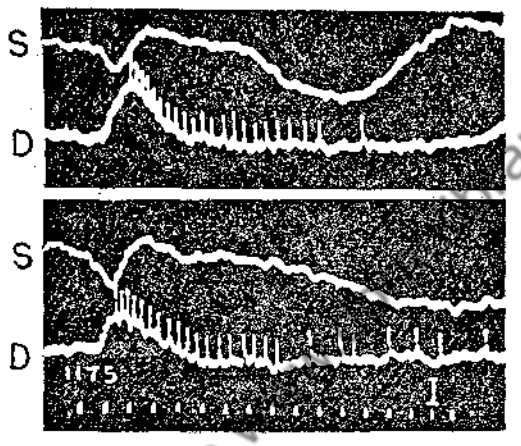


FIG. 4

Evoked potentials recorded simultaneously from surface and deep microelectrode (1.17 mm.) in the somato-sensory cortex of the cat in response to a single electric shock delivered to the anti-brachial nerve. Note deep negative wave with repetitive single unit discharge at the peak and on the descending phase, and beyond. S refers to surface and D refers to deep electrode in each pair of records. Note that the evoked potential is surface positive and deep negative.

From previous studies, as well as the present ones, it can be concluded that the unspecific system has a separate and distinctive synaptic distribution through the cortex, and it has a particularly close relationship to the spontaneous or resting rhythms, such as the alpha rhythm. It affects the response of the cortex to specific afferent volleys, such as those over sensory pathways, by affecting the elaboration of the afferent volley within the cortex, particularly as manifest in the surface negative potential and in the sensory after-discharge. It seems possible, therefore, that the elaboration of response of sensory cortex to an incoming volley of impulses over the sensory pathways can be controlled and regulated, timed and possibly facilitated or inhibited by existing activity within the

unspecific projection system to sensory cortex. Similar relations seem to exist between specific and unspecific projection systems in other cortical areas.

Since much of the evidence for the location and functional properties of the brain stem reticular system is based upon changes in the electrical activity recorded from the surface of the cerebral cortex we should perhaps summarize our conclusions regarding the significance of cortical electrical activity as revealed by microelectrode studies carried out with Dr. Li (Li *et al.*, 1952; Li and Jasper, 1953).

With microelectrodes in the depths of the cortex one finds continuous spontaneous discharge of individual nerve cells in the form of brief spikes of less than one millisecond in duration. They are of constant amplitude, all or none. There are also recorded, from the same electrodes, isolated or rhythmical repeated slower potential waves, the briefest of which are 10 to 20 milliseconds in duration. These waves are of variable amplitude, not all or none. With anaesthesia or anoxia the unit spikes are suppressed more or less completely before there is a perceptible change in the slow waves. The slow waves cannot be considered, therefore, as composed of envelopes of cortical cell discharge, since they may occur independently. Under certain conditions, however, unit discharges occur on the negative peak of the slow waves, or, especially in the deeper layers, unit discharges may be inhibited during the positive phase of the slow waves.

Stimulation of the ascending reticular system may cause an increase in the number and frequency of unit cell firing in the cortex, as in normal awakening or arousal. Stimulating parts of the meso-diencephalic portion of the reticular system may, on the contrary, cause an arrest of unit discharge. Both of these effects may occur with 'flattening' or 'desynchronization' of the usual tracing of electrical activity taken from the cortical surface. This suggests that the ascending reticular system may not be entirely an 'arousal' or activating system, but may have inhibitory components as well, similar to its organization with respect to the descending system in the medulla.

With regard to the interpretation of the usual slow waves seen in the surface electrocorticogram (which fails to record any unit cortical cell discharge), even the so-called epileptic or strychnine

'spikes' (which are actually waves of 20 to 40 milliseconds in duration even when recorded with microelectrodes) may be grouped together under the term *synaptic potential*, broadly defined. By synaptic potential we mean changes in membrane polarization of constituent neural elements without discharge of neuronal cells to produce a propagated all or nothing type of action potential of brief duration. They serve to affect the excitability, and to time the discharge of cortical cells.

The oscillatory character of the familiar 'rhythms' of the cortex probably represents a form of autorhythmicity, as described so frequently by Bremer (1949). Synchronization between units may be due largely to electrical field effects within a given area, and to afferent vollies impinging upon the local synaptic network from a distance.

ANATOMICAL DISTRIBUTION AND PATHWAYS OF THE UNSPECIFIC THALAMOCORTICAL PROJECTION SYSTEM

In Fig. 5 is shown the most recent version of our analysis of the anatomy of the thalamic reticular system in the cat. This map represents a summary of a long series of observations carried out with many colleagues since the original studies with Droogleever-Fortuyn (Jasper and Droogleever-Fortuyn, 1947; Jasper, 1949).

The clear areas (unstippled) represent thalamic zones whose local stimulation gives rise only to local cortical responses of the short-latency specific type restricted to a topographically related cortical area. Repetitive stimulation within the specific nuclei does occasionally produce what Morison and Dempsey have called the 'augmenting type of response' which may spread somewhat from the primary projection area into surrounding areas of cortex and must be distinguished from the long-latency more widespread responses characteristic of the non-specific system.

In the stippled areas are shown the regions which in repeated experiments have given rise to the typical recruiting cortical responses. The cross-hatched area in the section of frontal plane 12 indicates that zone in which most of the pathways of the non-specific system are found to lie and from which relatively short-latency widespread cortical responses can be obtained by suitable stimulation as reported in work done with Dr. Hanbery (Hanbery

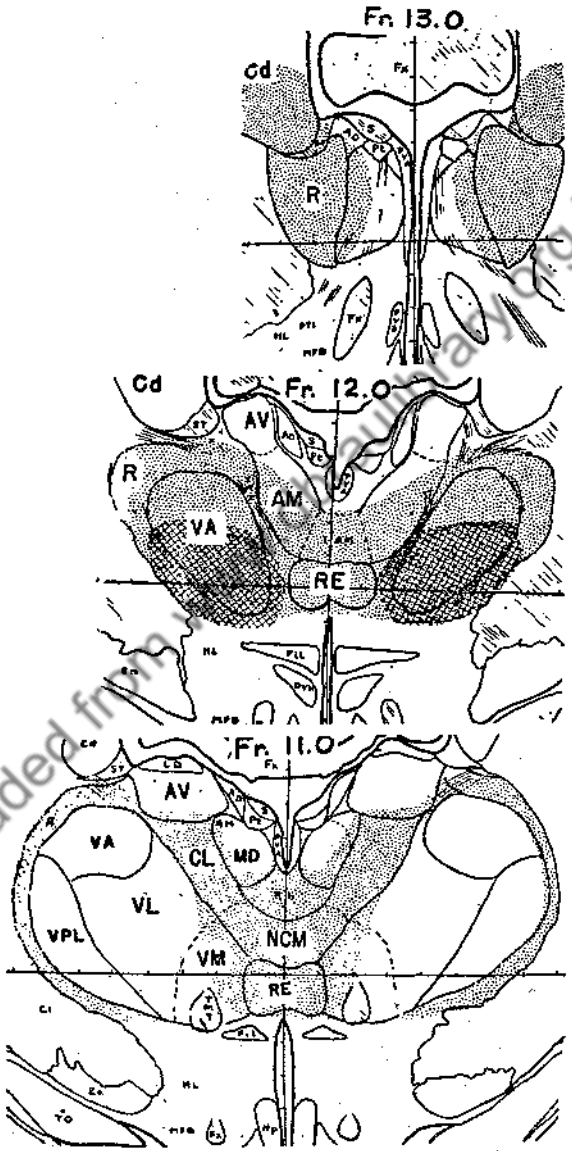


FIG. 5 A

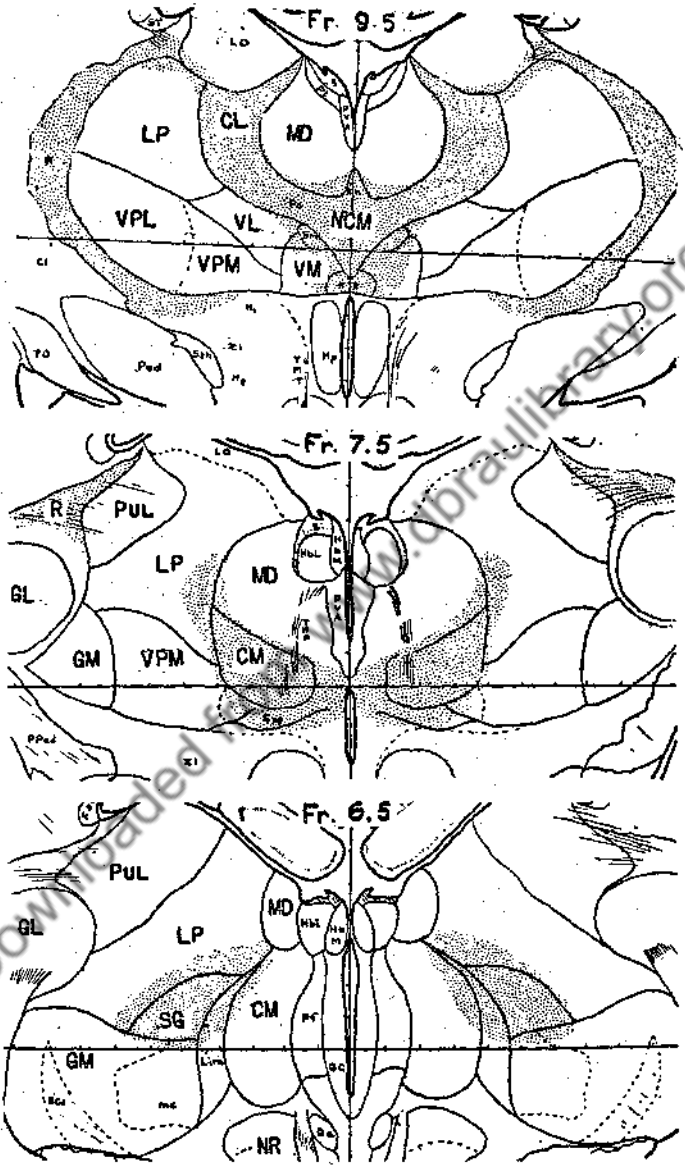


FIG. 5 B

(Caption for Fig. 5)

A. Composite diagrammatic representation of the unspecific thalamo-cortical projection system as determined by thalamic points whose local stimulation gives rise to typical recruiting responses of the cortex in the cat. The stippled areas indicate the unspecific system, the clear areas the specific projection systems. These are coronal sections in various frontal planes of the stereotaxic instrument (Fr. 13.0 to Fr. 6.5). The cross hatched area in Fr. 12.0 indicates the region where we find the greatest concentration of rostrally directed pathways of the unspecific system (from Centrum Medianum). Abbreviations are as follows: Cd — Caudate, R — Reticularis, Va — Ventralis Anterior, AM — Antero-Medialis, AV — Antero-Ventralis, RE — Reuniens, VPL — Ventralis Postero-Lateralis, VPM — Ventralis Postero-Medialis, VL — Ventralis Lateralis, CL — Centralis Lateralis, NCM — Nucleus Centralis Medialis, VM — Ventralis Medialis, Pulv — Pulvinar, LP — Lateralis Posterior, MD — Medialis Dorsalis, CM — Centrum Medianum, SG — Supra Geniculatus, GL — Geniculatus Lateralis, GM — Geniculatus Medialis, NR — Nucleus Ruber.

B. Schematic diagram of thalamo-cortical and cortico-thalamic relationships. Specific nuclei are shown as open circles, the reticular system by the stippled area extending into mesencephalic areas. Each cortical area is supplied by both specific and reticular projections. Two way connections are shown between specific nuclei and each type of cortical area. By 'elaborative' is meant such areas as the peri and parastriate cortex of the visual system. Correlative areas are the 'association' areas in temporal, parietal and frontal regions. Particularly strong connections are indicated from the latter areas back into the reticular system. 'Collateral' fibres from ascending sensory pathways directly into the reticular system are also shown.

and Jasper, 1953). This system continues to give good cortical recruiting responses when stimulated repetitively, even following destruction of specific thalamic nuclei — sensory relay as well as 'association nuclei'.

One might gain the impression from the terminology employed for this system of projections, namely, 'diffuse' or 'unspecific' that we are dealing with a relatively indefinite area within the thalamus. For those who have not had the privilege of carrying out such experiments, it may be advisable to note here that the recruiting system of the thalamus is a definite and clearly identifiable system from electrophysiological studies. Confusion arises only with the more localized augmenting responses obtained when stimulating the so-called 'association nuclei' of the thalamus.

When exploring the thalamus with a stereotaxic instrument millimetre by millimetre or by fractions of millimetres, using standard minimal stimuli and a bipolar stimulating electrode which does not permit spread of current, it becomes obvious that many portions of the thalamus give rise to only restricted local cortical responses or to no obvious cortical responses from the sites of the recording electrodes. Widespread recruiting cortical responses are obtained from only very well limited portions of the thalamus. In many experiments moving of the stimulating

electrode only a fraction of a millimetre would suddenly enter a zone yielding recruiting responses when in the previous position no cortical responses were obtained, even at a considerably higher intensity of stimulus.

It should be obvious from the diagram of Fig. 5 that the electrophysiological determined regions giving rise to recruiting responses cannot be identified with previously described intralaminar nuclei of the thalamus such as ventralis medialis, supra geniculatus, n. reticularis, as well as portions of the border zones of some specific nuclei, such as medialis dorsalis and lateralis posterior, as shown in frontal plane 7.5 and ventro-lateral border of n. antero medialis. (Of course the accuracy of the electrophysiological method may not be such as to make very fine distinction between these border zones.)

CORTICAL DISTRIBUTION OF UNSPECIFIC PROJECTIONS

In the original observations of Morison and Dempsey (1942a) the distribution of recruiting responses in the cat was found to be dominant in the frontal and parietal regions, with very prominent responses in the sensory and motor cortex, but to be present in all areas readily exposed. To quote from this original study (p. 289): 'It will be seen from the figures that all parts of the readily exposable cortex participated in the recruiting response but that the most striking results were recorded on the gyrus proreus, the middle supra-sylvian and a small triangular area at the lower margin of the posterior supra-sylvian gyrus'. It should be pointed out that these conclusions were based upon a rather limited series of observations and were considered only tentative by Morison and Dempsey.

In previously reported studies (Jasper and Droogleever-Fortuyn, 1947; Li *et al.*, 1953; Jasper and Li, 1953; Li and Jasper, 1953), the findings of Morison and Dempsey regarding the widespread generalized distribution of recruiting responses have been confirmed, as well as the fact that such responses are more readily obtained from the rostral cortex of the frontal and motor regions in most experiments, especially when stimulating mesial-thalamic structures.

It was pointed out also with Droogleever-Fortuyn that there

was a topographical organization within the thalamo-cortical system, the ventral mesial portions projecting forward to the frontal and motor cortex, while the dorsal-lateral portions project more posteriorly, as a general rule. This has been repeatedly confirmed in many more extensive studies. Wide variations in cortical distribution of recruiting responses are found depending upon the thalamic site stimulated.

No single map will indicate the complete distribution of the unspecific projection system. There is a definite topographical organization within the thalamus. However, we would not like to give the impression that this organization is a rigid one. We have not been able to determine a reliable series of maps for a single point in different animals and in different experiments. There was considerable variability in the distribution from time to time with different levels of anaesthesia. This was particularly true for responses in the sensory receiving areas which could be absent or very prominent, depending upon the condition of the animal and the amount of sensory stimuli he was receiving at the time of the experiment. The impression that unspecific projections occur only to association areas can be obtained only from certain points within the thalamus and under certain experimental conditions.

This is an extremely labile system. It is well known that in the unanaesthetized alert animal or with stimulation of the mesencephalic arousal system no recruiting responses can be observed from stimulation in any portion of the thalamus. In order to demonstrate them clearly, the animal must be relaxed, either naturally or artificially by a mesencephalic section of the brain stem or by barbiturate anaesthesia. Consequently, the distribution of these responses will depend to a great extent upon the activity in the main afferent systems of the brain and the general excitatory state of the brain. This does not mean that the unspecific system becomes inactive but merely that it becomes refractory to experimental demonstration by electrophysiological methods in the normal functioning of the brain. It must be set at rest by artificial means before its presence can be clearly demonstrated by these methods.

It might be mentioned also that from certain portions of the thalamic reticular system very prominent recruiting responses can

be obtained from rhinencephalic structures, including the olfactory bulb itself in confirmation of the work of Moruzzi (Jasper and Ajmone-Marsan, 1952). Certainly the limbic cortex has important connections with the thalamic reticular system, as well as with the more caudal portions of the reticular system in the brain stem.

Our conclusions regarding the cortical distribution of unspecific recruiting responses in the cat may be summarized as follows:

1. The unspecific thalamocortical projection system, which may be called the thalamic reticular system, does not necessarily respond in an all-or-none manner as a whole when stimulated in any part. It may respond in parts, selectively, and project to different areas of the cortex, depending upon the portion locally stimulated, and depending upon the competing effects from other projection systems to the same area of cortex. It is closely interconnected, however, by multisynaptic pathways.

2. The thalamic structures yielding recruiting cortical responses include only the rostral pole of centre median, n. suprageniculatus with adjacent portions of n. lateralis posterior and limitans, n. ventralis medialis and ventralis anterior, as well as the ventro-lateral borders of medialis dorsalis and anteromedialis, the intralaminar nuclei, the rostral pole of nucleus reticularis and probably a considerable portion, if not all, of the lateral and caudal extent of n. reticularis. Projection pathways pass forward in the mesial thalamus and are distributed to posterior areas of cortex, probably through n. reticularis of the thalamus. They are independent of projections from specific sensory or 'association' nuclei of the thalamus.

3. Cortical areas receiving unspecific projection fibres from the thalamus include all of the sensory receiving areas and rhinencephalic structures, as well as frontal, motor and parietal areas, though recruiting responses are more readily demonstrated under the usual experimental conditions to rostrally situated cortical regions, particularly the motor and frontal cortex and the anterior cingulate areas with visual and auditory receiving areas being the least susceptible to recruiting responses under the usual experimental conditions.

4. Unspecific projections terminate in a different manner in the cortex – are probably peri-dendritic, and exert their major effect

on spontaneous cortical rhythms and upon the elaboration of impulses arriving over specific projection systems.

We believe that the question of the mediation of all recruiting responses through the specific projections of association nuclei has adequately been ruled out as a necessary pathway by the experiments recently reported with Hanbery (Hanbery and Jasper, 1953), in which the association nuclei were completely destroyed while retaining good recruiting responses to frontal and parietal cortex; responses in somatic, visual and auditory cortex remained after destruction of their relay nuclei in the thalamus. Intrathalamic effects mediated by specific nuclei and their connections with the unspecific system may also have important functions.

AN HYPOTHESIS REGARDING THE FUNCTIONAL SIGNIFICANCE OF THE THALAMIC RETICULAR SYSTEM

Experimental observations have been reviewed in some detail in order that certain facts may be established before attempting to formulate a working hypothesis concerning the functional significance of the thalamic reticular system.

Two additional observations which we cannot discuss in detail must be considered when thinking of functional hypothesis:

1. The thalamic reticular system seems to receive collateral afferent connections from all of the principal ascending sensory pathways, and,

2. There are many important corticofugal projections into the same system.

We do not believe that one will find in the thalamus the system of neurones fulfilling the definition proposed by Penfield for a centrencephalic system with equal functional relationships with the two hemispheres. In man the two halves of the thalamus are quite separate; in about one out of four brains there is no massa intermedia and in others it would not provide a central system of neurones of importance. A system of neurones having bilateral connections would have to be sought for more caudally in the basal diencephalic and mesencephalic portions of the reticular system.

Ascending impulses from the brain stem reticular system in man probably divide at the thalamic level, pass through the

multisynaptic network of the thalamic reticular system on one side on their way to the cortex of one hemisphere. Functional integration of activities of the two hemispheres in conscious mental processes must occur, therefore, either by means of the corpus callosum and other commissural systems or by cortico-subcortical projection systems below the thalamic level. The latter seems to be the more important as judged by the lack of significant functional deficits following section of the corpus callosum.

The thalamic reticular system does seem to play a unique role in the regulation of whatever functional significance we may attribute to the alpha rhythm. In no other portion of the reticular system is it possible to obtain timing of the alpha rhythms of the cortex in a general manner. Due to the close thalamic interconnections within this system widespread areas of cortex may be caused to beat in rhythmic synchrony while stimulating directly only 2 or 3 square millimetres in the central portion of the system. Such a central regulating mechanism must have an important function in the inter-areal co-ordination of the various specific functions represented in different regions of the cortex.

Perhaps even the little knowledge we have regarding the functional correlates of the alpha rhythm may give us a clue. Among the first observations made of the alpha rhythm was its relationship to processes of attention, and its sensitivity to variations in the level of consciousness.

It has been shown also with Shagass (Jasper and Shagass, 1941a, b) that blocking of the alpha rhythm is readily conditioned in even the more complex Pavlovian types of situation. It seems to respond in relation to the anticipatory set of the conditioning process.

Hans Berger (1930) was the first to suggest that the mechanisms underlying the alpha rhythm must represent the central regulatory system underlying processes of attention, capable of facilitating specific cortical areas whose activities are momentarily 'focused' in the attentive process, and inhibiting many other areas of systems of neurones which would otherwise be competing for the 'central stream of consciousness'.

It would seem that the unspecific thalamocortical projection system might well play such a role with its closely interrelated

central reticular network and separate radiating projections which seem to terminate within the layers of the cortex in a manner capable of facilitating, inhibiting, or timing conduction processes in synaptic networks of the more specific functional systems.

One would think, however, that the central mechanism of attentive processes should be equally effective on functions of the two hemispheres. The mechanism of this bilateral integration with relation to the thalamic reticular system is not clear. It may depend upon the close functional inter-relationship which is known to exist between the thalamic and more caudal portions of the reticular system which are presumed to subserve a somewhat more primitive function in relation to 'arousal' or general alerting processes.

It is a well-recognized fact that alerting processes often involve highly complex perceptual discrimination. It is often the meaning of a complex stimulus pattern, learned from past experience, which determines the arousal value of a stimulus for a sleeping person, or the attention value when awake. It would seem that such processes must involve some form of interaction between elaborate patterns in specific thalamocortical systems and brain stem or thalamic reticular systems.

Finally, our observations upon the finer structure of both the descending and ascending reticular systems in diencephalon and midbrain have convinced us that it is a highly organized system whose function is not adequately described as simple overall inhibition or facilitation, or general awakening or arousal of the nervous system as a whole, though this is one aspect of its mass action. When studied with more discretely localized stimulation, especially in the lightly anaesthetized or unanaesthetized animal, one finds a more highly differentiated patterning of responses which are quite different at different levels. Sprague (1953) has recently shown also that one does not produce simple inhibition or facilitation when stimulating the bulbar reticular system with implanted electrodes in the unanaesthetized animals; co-ordinated posturing is observed instead.

The 'arrest reaction' obtained by stimulating the thalamic recruiting system in unanaesthetized animals is quite different from the aggressive arousal obtained from the posterior hypothalamus; neither are adequately described as simple awakening. The 'arrest

reaction' probably represents an interference in the highly integrated normal functioning of the thalamic reticular system, analogous to the aphasia produced by electrical stimulation of the cortical speech areas. More refined methods may be required to discover the true functional significance, the fine structure and patterned organization of thalamic as well as more caudal portions of the reticular system.

GROUP DISCUSSION

HEBB: I am a little confused by your statement that unit firing may be quite independent of the slow waves, on the one hand, and then you show also that the slow waves exert a control over unit discharge.

JASPER: This does seem paradoxical at first but both statements are true. Units can fire independently of the field effect of the slow waves or their dendritic potentials, but when there are large slow waves present, and the tendency for the units to fire spontaneously is not excessive, they then become controlled by the slow waves. It is clear that excitability and discharge of cortical cells must be considered as a separate phenomenon, capable of independent action, but influenced by excitatory or inhibitory effects of their electrotonic environment. It is possible for the slow waves to provide rigid limits on the timing of unit cortical discharge, or even to cause them to fire in much the same manner as an externally applied electrical current may do.

MORISON: Dr. Dempsey and I would agree with the fundamental conclusions of Dr. Jasper regarding the maps of cortical distribution of recruiting responses. We would agree that this is a labile system and that it is difficult to get reproducible results. Also we agree that as one goes through the thalamus with a stimulating electrode one gets different cortical distribution of responses from different points. The cortical distribution changed also, in our experiments, according to the condition of the animal throughout the course of the experiments. In the course of many experiments in which the difference between specific and non-specific responses were being investigated we obtained many different cortical distributions of responses. If we took all of these experiments to make our maps they would be practically meaningless. We had stimulated many different points so that if you overlapped all of these you would just show that the cortex responded everywhere in about the same way. So what we did was to take 5 or 6 animals and try to stimulate in about the same spot in each one under the same conditions of anaesthesia. We selected the point where we thought we would get the maximal distribution of cortical responses.

It seemed to us that the most interesting point would be that which had the possibility of co-ordinating all the other points. The map we presented was to show only the cortical distribution of responses from stimulation of a single thalamic point which gave the maximum representation in the cortex and we did succeed in finding some responses in all areas of cortex examined. There were less clear responses in auditory and visual receiving areas than anywhere else. By and large the responses were better in frontal and parietal association areas as found later by Dr. Magoun. Certainly the distribution varies with different conditions of the animal.

MAGOUN: I would like to add to what Dr. Morison has said, that we find also one can vary his conclusions according to the interests of his approach. I think I have been remiss in always trying to emphasize the generalities rather than the variations or the more detailed specific features which Dr. Jasper and his associates have shown so clearly can be revealed in the non-specific system when one's attention is focused upon them.

To me there was a great deal of interest in Dr. Jasper's finding that recording from the different strata of the cortex sometimes yields results which are inconspicuous or not evident at all at the surface. It is interesting that you find such specific phenomena at the third or fourth layer of cortex in view of the fact that the non-specific terminals are thought to be equipotential for all layers and perhaps to exert their greatest effect on the first layer. I have often wondered whether our own method of recording recruiting responses with one electrode on the cortical surface and one in the subjacent white matter might not have been responsible for the difference in distribution of the receiving zones from that seen when recording between two electrodes on the surface.

JASPER: Mention should be made of certain difficulties with the electrophysiological methods of studying thalamo-cortical relationships, which make it hard to evaluate the results obtained. Stimulation of many specific thalamic nuclei, such as the pulvinar, lateralis posterior, or medialis dorsalis with repetitive shocks gives cortical responses which resemble very closely the recruiting responses obtained when stimulating non-specific nuclei. The details of some of the maps presented both of cortical distribution and thalamic distribution may have been confused by the occasional lack of discrimination between what Dr. Morison has called the 'augmenting response' and the true long latency recruiting responses. I am sure that we are occasionally confused by stimulating both specific and non-specific systems at the same time or by stimulating a specific system repetitively and thinking it is producing a non-specific recruiting response.

WALTER: I would like to make a few comments on your observations on the difference in phase relationships when recording from the cortical surface simultaneously with micro-electrodes at different depths beneath. In ordinary EEG work a phase shift which is neither zero nor 180 degrees is often difficult to explain. You have shown a phase relationship between the surface and micro-electrode records of evoked potentials which varies gradually from zero at the surface to 180 degrees when the micro-electrode reaches the level of the arborization of specific afferent terminals in the fourth layer. The simplest explanation seems to be that you have here two fields moving through each other rather as I suggested as an explanation of the observations I reported in human subjects during pattern stimulation. It seems to me that analysis of the geometry of these effects might give us some insight into the fine structure of the mechanisms whereby patterns are recognized in the cortex.

JASPER: I think that the conception that the non-specific system acts upon the dendritic or synaptic network regulating the capability of units to fire in the specific system is a very important conception that Chang has emphasized recently. We have to remember that the cortex is not concerned so much with direct transmission from sensory to motor but that it provides a kind of lattice network regulating the specific transmitting mechanism. The organization of function in the specific circuits may be regulated to a large extent by the activity in non-specific systems.

NAUTA: I wish to correct an impression that Dr. Jasper may have given that we do not agree with Lorente de Nó's finding of two kinds of cortical afferents. Indeed we have all sorts of proof that there is a dual set of cortical afferents, one that has a special affinity for the middle layers of the cortex, 4 and 3, and another one which seems to have no special preference for any layer of the cortex. Our only trouble is that we find non-specific as well as specific afferents degenerating when we destroy relay or association nuclei of the thalamus. There is no reason to doubt that impulses from non-specific nuclei reach the cortex in some way. Our only problem is how do they do this? The controversy between our findings and those of Dr. Jasper is merely one of degree. We do not believe that the non-specific cortical afferents categorically represent projections from the non-specific thalamic nuclei to the cortex. Our findings suggest that there are cells in the specific nuclei that emit non-specific fibres to the cortex. I would like to stress again that there is no reliable anatomical evidence of significant direct cortical projections from the non-specific thalamic cell groups, the reticular nucleus excepted. Dr. Jasper's findings nevertheless strongly suggest that non-specific cortical afferents are prominently involved in the

corticipetal mediation of the activity of non-specific thalamic nuclei If this important notion can be further substantiated, the question will raise itself once more: do these non-specific transmitters originate in the non-specific thalamic cell groups, or in other cell groups, or in both? So far, we have anatomical evidence of only the second of these possibilities. My second question is: was Dr. Jasper's statement that Lorente de Nó interpreted 'non-specific cortical afferents' as arising from non-specific thalamic nuclei based upon a personal communication or have I always misinterpreted Lorente de Nó's papers on the subject?

JASPER: I think you are quite right in raising that question. Lorente de Nó did not identify the non-specific afferents with the non-specific thalamic system. I think we are indebted to Dr. Morison for making that connection as an hypothesis rather than as a demonstrated fact. Is that true, Dr. Morison?

MORISON: That is about right. I asked Lorente de Nó where he thought they came from and he said he wasn't at all sure. I don't believe we ever said that there were direct projections from the non-specific thalamic nuclei to the cortex. We left the possibility open that they might go through another set of thalamic nuclei before reaching the cortex.

ADRIAN: I have been wondering whether you find any difference in your microelectrode recording of spikes in different areas of cortex. Some time ago, exploring with a wire electrode I had the impression that there were far more spikes to be got by exploring the receiving areas than by exploring the association areas and that these persisted in quite deep anaesthesia, so that they were presumably from some afferent terminations or in neurones in very close connection with them.

JASPER: Our studies are far from complete in this respect. We have formed the impression from a few observations that your observations are quite correct, Dr. Adrian. The sensory receiving areas do show more spontaneous unit discharge under depressed conditions of the animal, while during arousal the activity in other areas is more comparable to that in sensory and motor areas.

JUNG: For the last two years we have been studying unit discharges with microelectrodes, mainly in the visual cortex. Here we find always active neurones in all layers of the cortex but, if we try to connect their activity with slow waves we have difficulty. We have the impression that single unit discharges are only rarely related to spontaneous slow waves in the sensory receiving areas, but this may be much more common in the lower efferent layer of the motor area, as the early work of Dr. Adrian and Dr. Moruzzi has shown in the pyramidal tract. Even when a relationship is found between single unit discharges and

slow waves, this relationship may persist for only a few seconds at a time. The only consistent relation of unit discharge is to the surface positive wave of the primary response which follows stimulation of the optic nerve or a flash of light to the eye. Although there are many types of neuronal responses in the visual cortex which we classified as A, B, C, D, E, one finds a constant relation with a reciprocal kind of discharge of either activation (B) or inhibition (C, D, E) which is clearly associated with the primary afferent wave on the surface after light on (Jung, 1953). Otherwise the neuronal discharge varies a great deal and one sees only occasionally that the slow waves may condition the neuronal responses. It seems to be a labile system which, however, must be a well co-ordinated one; still we are ignorant of the controlling factors.

MORISON: Since Dr. Jasper has alluded to the rather vexed question of the 'augmenting response' I would like to raise one or two questions about it. It occurred to me in one or two of the last slides Dr. Jasper has shown when he was stimulating presumably a recruiting area that a response occurred earlier than the usual recruiting latency which was particularly marked at about the fourth layer of the cortex. I would like to raise the possibility that there might have been contamination with an augmenting response by simultaneous stimulation of a specific system. In that connection did I understand Dr. Nauta correctly: did he find two types of non-specific fibres, one going all the way to the surface and the other ending in the 3rd or 4th layer?

NAUTA: I meant that two types of thalamocortical fibres seem to arise from the specific thalamic nuclei.

MORISON: It depends whether one wants to call the augmenting system specific or non-specific. I think the term that has sometimes been applied to the non-specific system, 'the more or less specific system', would apply very nicely to the augmenting system. It is going to be terribly difficult to unravel this but I think Dr. Jasper's micro-electrode method offers great promise.

JASPER: I am convinced that in certain parts of the thalamus you arrive at a point where the intermingling of specific and non-specific fibres is so great that neither with the stimulating electrode, nor by Dr. Nauta's anatomical method, is it possible to know without great difficulty what proportion of specific and non-specific fibres one is dealing with.

BREMER: Dr. Jasper has presented us with a very interesting working hypothesis concerning the function of the core of the brain stem and related diencephalic structures which is quite different from the views developed by Dr. Magoun and myself. We have thought rather of a general dynamogenic function of that system while Dr. Jasper suggests

a rather more co-ordinating and correlating mechanism. He is fully justified in doing so from the complexity of the anatomical structure of the reticular formation which allows such a generalization. I would not think that the two conceptions are necessarily opposed. One may consider that in the reticular formation, especially in the latter's core, there are structures which yield a mass effect, essentially of a dynamogenic nature, on the telencephalon and diencephalon, with no co-ordinating function at all. In this respect arousal and sleep regulation is an indivisible function. What Dr. Olszewski and Dr. Jasper remind us is that the reticular formation (Edinger's nucleus notorius tegmente!) is certainly more complex than we sometimes figure.

JASPER: May I apologize for leading the discussion into what may have seemed to be a side track by discussing the details of specific and non-specific systems in relation to microelectrode studies of brain waves, but it seemed to me that this was the core of our problem. The interpretation of the significance of the function of the reticular system depends, perhaps, to a great extent upon what the functional significance of the electrical activity of the cortex may be, since the latter has been used so extensively to test reticular system function.

I would like to emphasize again the principal property of specific thalamocortical systems as studied electrophysiologically, namely that when stimulated they have a discreteness in localization, both thalamic and cortical, which makes them an isolated system not affecting the activity of other parts of the brain. Moving the stimulating electrode in the thalamus only a fraction of a millimetre, entering the non-specific projecting system, one suddenly sees the development of widespread recruiting responses. In a sense the non-specific system is a very 'specific system' with regard to the properties which distinguish it from other thalamo-cortical systems.

PENFIELD: But it is diffuse in its goal.

JASPER: It is diffuse in its distribution because it is projected differently from the more discrete specific systems. However, in the thalamus, it is a very particular set of closely interconnected neurones which are precisely located and not 'diffusely' distributed all through the thalamus.

HEBB: The term diffuse means that it has widespread cortical connections?

JASPER: Yes, and that they overlap the projections of what has been established anatomically as the specific projections to the same cortical areas.

MORISON: We used the term 'diffuse' for the following reasons. Our thought was partly that there are places in the system, and rather small places, from which the entire system can be activated. That is why we

emphasized somewhat more in the early explorative studies the intralaminar group of nuclei and the rostral part of the centre median because it was from that area that the whole cortex, more or less, could be activated. When stimulating the rostral pole of the thalamus we became rather defeatist, I am afraid, because of the great mixture of fibres present there which contaminated the responses. It was rare in our experience, when stimulating the n. ventralis anterior or reticularis, not to get somewhere in the cortex obvious primary responses or this very puzzling thing which we called the 'augmenting response' which we had some evidence for believing was different from the recruiting response, and could occur simultaneously with the recruiting response in localized areas of the cortex.

THE PROBLEM OF CONSCIOUSNESS AND INTROSPECTION

By

D. O. HEBB

It has not been easy to see what, exactly, should be my task in this symposium. I do not think it worth while here to elaborate on my own speculations on neurophysiology (Hebb, 1949), at least not in detail. Their purpose was to clarify and guide certain lines of experiment that are still going on. Instead, I have chosen to try to define the problem of consciousness and see what limits it must have for the scientist (as contrasted with the theologian); including particularly the question of 'introspection', using the term in a general sense. The capacity of the human being to know (and report) what is going on inside himself has seemed to some writers to put his behaviour beyond the reach of scientific explanation, and we must ask whether this is so.

Communication between disciplines is always defective. Most psychologists, like me, find it hard to keep up with both psychology and physiology. The rapid advance of neurophysiology these days makes it especially difficult. But also, too many physiologists seem unaware that psychological knowledge – equally relevant to the problems we are considering – is not still mired in doubts and difficulties of the nineteenth century. An eminent neurologist recently complained that the psychologists had made aphasia so complicated that no one could understand it. A plain man, he thought, might brush all the hair-splitting aside and treat the matter in a common-sense way. Unfortunately for the resulting discussion, it is not psychologists but God who complicated aphasia: the complexities are real, and must be taken into account if the problem is to be solved. The problem of consciousness is equally complex and no more likely to yield to a simple common-sense analysis; yet it is exactly in this area that the appeal to common sense has always seemed most cogent.

THE COMMON-SENSE VIEW OF CONSCIOUSNESS

The word *conscious* is used of course in several ways. One is simply to designate the responsiveness of the normal waking animal. In this sense 'conscious' and 'unconscious' are descriptively clear, as 'awake' and 'asleep' are clear. Our concern is with another usage that refers to something inside which is thought of as a causal agent.

For common sense, consciousness is a primary fact of existence, part of the initial data from which thought begins. It may even be regarded as *the* primary fact or datum. Eccles (1953) has put this clearly, quoting several writers to the effect that one knows the inner world of consciousness directly, the outer world only by inference from the inner data. The events of this inner world largely determine what one does; it follows therefore that a physiological explanation of human behaviour cannot be a complete one, for the redness of the morning sky, the feeling of sorrow, are by every common-sense criterion totally different in nature from any patterning of electrochemical activity in nerve cells.

Thus speaks common sense: but is it, perhaps, also non-sense and inconsistency? *Are* these things obviously true? Every scientist knows that observation is fallible, that preconceptions can blind an observer. Should we give more weight to common sense in psychology than we do in physics? It is a matter of simple observation that the sun moves from east to west while the earth stands still. Common sense will tell anyone that matter and energy are wholly different things. A great part of the success of the physical sciences has resulted from assumptions that are as preposterous, to common sense, as Newton's first law of motion (though this may no longer seem preposterous, now that we have absorbed it into everyday thinking and 'see' friction wherever we see motion).

As Ryle (1949) has shown very forcefully, the common-sense view of consciousness leads directly to absurdities. The only evidence for it, besides, is the demonstrably unreliable evidence of introspection. For some time, psychologists have had to abandon introspection as a crucial argument. The test of any theory is in what a subject *does*. Though the question of consciousness and

introspection is still an uneasy one, it has become quite clear that introspective evidence is a dangerous tool to handle carelessly, and that theory must rest mainly on a foundation of observable behaviour.

Others, less familiar with the painful steps by which this clarifying position was reached, still cite common conviction to oppose what they call 'behaviourism'. What this amounts to is (*a*) a refusal to use the scientific method (especially the scientific willingness to try out 'improbable' assumptions) and then (*b*) concluding that the problem of man's behaviour is not scientifically soluble. I do not assert that it is soluble: we have yet a long way to go before being sure that the solution will be achieved; but there is no possible basis for asserting that a problem is insoluble because we have not solved it yet.

I have recently tried to show (Hebb, 1951) that the psychologist who avoids physiological conceptions merely succeeds in avoiding modern ones, and is likely to have his thinking dominated by older ideas, vintage of 1890. But the physiologist who analyses behaviour without knowing something of modern psychology is in rather worse case. *He* is dominated by the psychology and philosophy of 1890 at the latest: and this in turn is largely the physiology of 1850, of Helmholtz and Johannes Müller, with their very limited knowledge of the nervous system. The coinage of ideas wears smooth, their minting is hard to trace, and the common-sense idea that seems to us today to be obvious and inescapable is sometimes the daring speculation of a hundred (or two hundred) years ago. We must not take for fact, nor allow theory to be dominated by, the crude hypotheses of eighteenth-century thinkers, brilliant as they were.

I propose to you accordingly that the existence of something called consciousness is a venerable *hypothesis:* not a datum, not directly observable, but an inference from other facts. I propose that your conviction that you are aware of your awareness (and aware of your awareness of your awareness?) may be illusion, and must *not* be made the basis for analysis of brain function. I grant at once that you are aware (or conscious) of your environment – in fact, I grant that I am, too – just as I grant that the world revolves on its axis, or that something known as an atom exists. The hypothesis that there is something we call consciousness is a

good one (what the something is may be another matter).

All this is not simply hair-splitting, but affects research in a practical way; for now, if we accept this, not only do century-old contradictions disappear but we regain freedom to modify this hypothesis of ours and see what the experimental consequences are. Furthermore, we can return to the proper limitations of the scientific method.

Any attempt to 'explain how nervous impulses can be translated into a mental experience' is, in the words of the preacher, an attempt to unscrew the inscrutable and to foresee the ways of the Lord. The phenomenal world (of brightness, colour, sound, sweetness, pain) is the starting-point of thought, its ultimate 'reality'. As mature theorizing individuals we can, in thought, choose other starting-points (e.g. a universe of electrons, permeable membranes, nerve impulses) and see how far we get; but when we try to have *two* starting-points we ask for trouble. Explanation is a process of reducing one set of ideas to another; it is evident that such a series of reductions must have an end point. We cannot reduce A to B, and at the same time B to A: we cannot make the world of experience the ultimate reality and then try to explain it as a set of nerve impulses, simply because this is logical nonsense.

It is intellectually respectable to assume the existence of the inner world as primary, and explain the physical world in terms of it (Berkeley's procedure); or, scientifically more productive, to assume as working hypothesis that all behaviour is determined by physiological processes; but not to have both simultaneously. Eventually the physiological hypothesis may fail, but we cannot know that yet. And may I add that no one need *believe* a hypothesis, and may if he likes accept it only as a means of disproving it?

CONSCIOUSNESS AS KNOWN FROM BEHAVIOUR

Assume then that consciousness is something within the head which determines behaviour, and which can be studied through that behaviour. One quite respectable but aged hypothesis is that consciousness is a function of another entity, the soul; we need not quarrel with this, but shall consider the alternate hypothesis that consciousness is simply a function of the brain. To do so, we must

ask what the behaviour is in which consciousness is manifested, and what kind of neural processes would produce it.

We are really asking here what the distinguishing marks of 'higher' behaviour are. It may help you to follow this part of my discussion if I summarize its gist, first, by saying that they are found in general in the behaviour that has obliged psychologists to conclude that the higher mammals are certainly capable of ideation; and secondly, in certain primate behaviour which indicates, I believe, an increasing flexibility or freedom of manipulation of ideas, culminating in human language.

Now to support this in somewhat greater detail. The least disputed criterion of consciousness is in certain verbal behaviour (introspective report) but this is not essential; for we have no real doubt that a deaf-mute is conscious, even without sign language. What are the other criteria?

Responsiveness is essential, but not sufficient; we need not endow amoeba, or the tail end of a spinal dog, with consciousness. If we put amoeba at one end of a scale, waking normal man at the other, it will be helpful to see what trends in development lead up to the typical human behaviour. No one I think can deny chimpanzees something like consciousness in the human sense; that is, except for language, their behaviour contains the same evidence by which we identify consciousness in man. It is not my purpose to ask how far down the scale this identification is possible, but only to note that behaviour is not unique to man and that its essentials may be better recognized when it can be observed in different species.

I hope I do not shock biological scientists by saying that one feature of the phylogenetic development is an increasing evidence of what is known in some circles as free will; in my student days also referred to in the Harvard Law, which asserts that any well-trained experimental animal, on controlled stimulation, will do as he damned well pleases. A more scholarly formulation is that the higher animal is less stimulus-bound (Goldstein, 1940). Brain action is less fully controlled by afferent input, behaviour therefore less fully predictable from the situation in which the animal is put. A greater role of ideational activity is recognizable in the animal's ability to 'hold' a variety of stimulations for some time before acting on them (Hebb and Bindra, 1952), and in the

phenomenon of purposive behaviour. There is more autonomous activity in the higher brain, and more selectivity as to *which* afferent activity will be integrated with the 'stream of thought', the dominant, ongoing activity in control of behaviour. Traditionally, we say that the subject is 'interested' in this part of the environment, not interested in that; in these terms, the higher animal has a wider variety of interests and the interest of the moment plays a greater part in behaviour, which means a greater unpredictability as to what stimuli will be responded to and as to the form of response.

This is not indeterminism, but does tell us much about the kind of mechanism we are dealing with. Also, the phenomenon of purposive behaviour, and the expectancy of the future which it entails, does not imply teleology but a capacity for ideation. When B has followed A repeatedly in the past, e.g., the animal on seeing A 'imagines' B (the idea of B arising by some process of learning or association). The behavioural evidence makes it clear that theory must provide somehow for foresight. Consciousness in the higher organism constantly involves ideas about the future, integrating these with ideas or memory of the immediate past. The mark of higher behaviour is not only that it is an adjustment to more of the complexities of present stimulation, but also that the temporal span covered by incidental memory of the past, and anticipation of the future, is greater.

What then of the mechanism that makes all this possible? There are two main problems: (1) about the nature of idea, image or concept – the link in the chain of thought – and (2) the nature of the linking, the temporal organization of ideas.

1. The first of these will not be discussed in detail. My earlier discussion tried to deal with it by the conception of the 'cell assembly', without attempting to be very specific about the locus of these processes. Is is now clearer than ever that the question of locus must be dealt with, especially in view of all the subsequent physiological studies that are the theme of this symposium. Penfield's (1952) work on the temporal lobe, and a number of other studies reviewed by Milner (Milner, 1953), further emphasize the problem of localization of function, but there is not time to enter on this here.

2. The second problem is that of the temporal organization of

ideas. This emerged as the central issue in Humphrey's (1951) important review and analysis of the classical psychological studies. It is significant that Lashley (1951), discussing different evidence and from a strictly behavioural point of view, arrived at what amounts to exactly the same problem, of the serial ordering of thought or behaviour. Let me represent the issue schematically, as in Fig. 1, regarding the train of thought first as a single series of discrete events (top line). We can then represent the classical

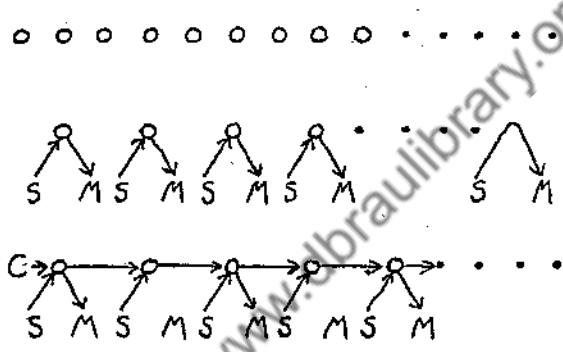


FIG. 1

Schematizing thought. Regarding the process as a series of discrete events in time, as in the top line, the motor theory of thought appears in the second line, each central event being determined by sensory input alone. A modification is presented in the bottom line, in which the central event is determined jointly by sensory and central facilitations. *S*, sensory; *M*, motor; *C*, central.

stimulus-response or motor theory of thought, which Lashley has so effectively criticized, as in the middle line: each 'idea' is fully determined by afferent input, and simply amounts to through transmission (as at the right). A significant change is made in the bottom line (if each of the central events in the diagram is a 'cell assembly', this embodies the main feature of the theory (Hebb, 1949) published elsewhere). The central event is now determined by *two* influences, one sensory, one central. The central influence is a facilitation from the preceding central activity. At each step, therefore, a selection is possible. In Fig. 2, broken circles represent potential activities, facilitated from one source only; closed circles, ones which actually occur because of facilitation from both sources. This also opens up a further possibility, shown at the right: a strong central facilitation might

by itself arouse a second series, in parallel with the sensorily guided one. This would represent pure ideation.

I do not of course try to show the real complexity of such processes, but perhaps it is worth while to present Fig. 3 also, as representing a little more adequately the sort of thing that is implied: a constant sensory influx and a complex interaction of central facilitations, with many activities in parallel which yet are more or less unified. At stage A, e.g., the organism might be thought of as having a single purpose or idea; while B and C might represent the entertaining of two ideas, or thinking of two eventualities; and so forth.

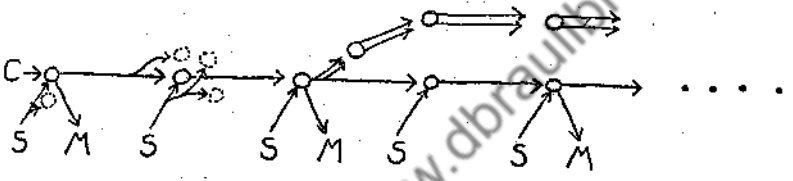


FIG. 2

Selectivity in thought. Broken circles represent central actions which might occur if facilitated both sensorily and centrally, closed circles ones that do occur. At the right, strong central facilitation arouses a second series in parallel.

SPEECH AND INTROSPECTIVE REPORT

And now let us see how this approach can be applied to the problem of speech and introspective report (in the general sense that a subject is able to tell you what he is thinking about). This certainly must be dealt with; otherwise, if the ability is left unaccounted for, it would be bound to leave some suspicion that the 'inner world' (Ryle, 1949) exists after all, and support doubts about the whole behavioural approach.

The preceding section suggested that there may be two or more series of ideas running in parallel. We may look first at some comparative data suggesting that this possibility is particularly relevant to the development of speech. Thompson and I (Hebb and Thompson, 1954) have tried to show that speech arises as the end product of a phylogenetic increase in the ability to entertain independent ideas or trains of thought at the same time. An earlier stage of development is achieving an independence of ideation

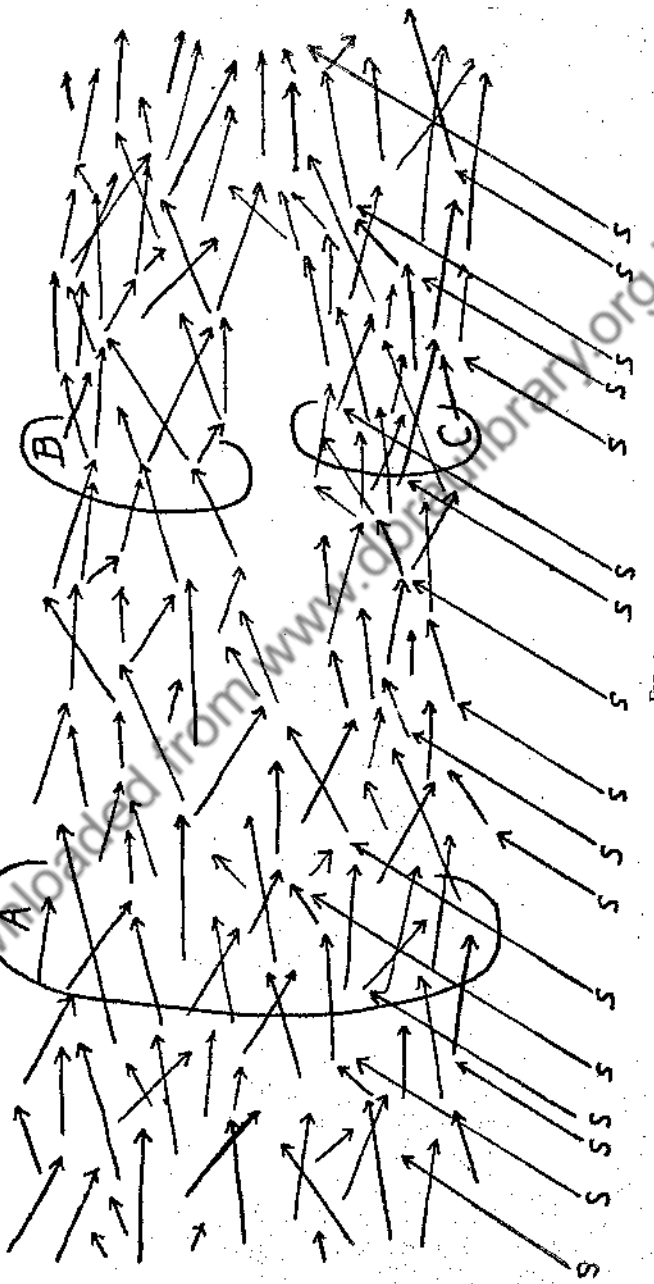


FIG. 3

The stream of thought, each arrow representing a central or sensory activity. *A*, concentration, with concurrent central activities supporting each other (and facilitating the same series of compatible motor activities, not diagrammed); *B* and *C*, divided attention, with two series in parallel.

from the environment in which the animal finds himself; subsequently, at a higher level, independence of ideas one from another so that they may be freely combined in different ways.

In the course of analysis we defined three levels of communication. The lowest (*a*) is reflexive, or stimulus-bound, exemplified in most or all insect interactions or in the emotional cries of higher animals. A higher level (*b*) is purposive communication, involving ideation but to a limited extent: as when a dog 'asks' to go out, or a chimpanzee 'begs' with his hands for an object out of reach. The highest level (*c*) is syntactic behaviour, whether verbal or manual: true language, not found in any animal but man. The essential feature of syntactic behaviour is that it shows the free combination and re-combination of two or more representative or symbolic gestures or sounds, purposefully.

The parrot of course is able to produce human words, and possibly on occasion uses these speech sounds purposefully; but neither parrot nor specially-trained chimpanzee (Hayes and Hayes, 1951) is capable of the behaviour of the two-year-old child who can use a vocabulary of four words to produce the separate propositions 'I thirsty', 'Mommy thirsty' and 'I not thirsty', and control his environment with them. Too much emphasis has been given in the past to the special problem of vocal language. The chimpanzee and lower animals are just as incapable of sign language as of spoken. The real problem of speech is not vocalization, but the capacity for manipulating ideas or symbolic acts. The behavioural evidence of phylogenetic development in this respect is fascinating – it appears, e.g., in the chimpanzee's capacity for deceitful attack, or in his empathic identification with another – but I shall just say here that though the great apes are definitely not capable of language they may still be close to a liminal level of intellect that would make language possible.

The comparative evidence, as well as much of the literature on aphasia, clearly makes thought prior to speech, not conditional on it. Now let me return to schematizing, to see what we can do in principle with the verbal behaviour that informs us about otherwise unobserved events within the organism. To emphasize that this *is* schematic, let us talk about a 'thinking machine' such as an electronic brain. Suppose that we cannot inspect its internals

while it is working, but still must be able to find out what activities occur in a given operation. That is, could we design the machine so as to report on its own activity: one that will 'introspect'?

First, it is routine that we can make a machine that when stimulated (buttons pressed, tapes fed in) will produce a given kind of behaviour. Secondly, it would be routine to build a machine that could on request repeat a given behaviour without the original stimulation. Thus there is no special problem, in principle, about the capacity of a man to respond adequately when you say to him *Repeat what you just did* – especially since it will often be found that unless he is prepared in advance for this request he will often fail. He can however be 'set' to hold the original stimulation for a repeat performance, as a machine could be. Memory will account for this, and this is not the real problem of introspection. Thirdly, there is no difficulty about having a machine with more than one kind of output, so that when it is set to multiplying or integrating, with an answer to appear on a tape, it could also have a loudspeaker system that would announce *Now I am multiplying* while multiplication goes on. Or it could announce *I have just multiplied*, after completion of the task. Here again, therefore, there is no special problem about the human being's ability to make such verbal report about other activities.

It is important to realize that I am not suggesting that there is no problem about speech, or about memory and thinking. There is, of course. What I am asking is whether 'subjective report' need be treated as a special case, a difficulty of a different order from other intelligent behaviour. So far, there is no difficulty in this sense.

But introspective report goes further. Can we find a way of asking a machine *how* it does a task? Its answer need not be complete (or perfect) to be an analogue of human introspection, for all a man really tells us is whether one of his activities involves processes related to some other activity which can be named. That is, when the subject says he uses visual imagery in mental arithmetic, what he really tells us is that his thought involves processes that characteristically occur in *seeing* things.

Thus we could ask a machine how it integrates, e.g., as follows:

We want to know perhaps whether this involves the processes that occur in addition; so we set the machine to integrating, and as soon as it is done we feed in an addition problem at a subliminal level of stimulation. If the tubes of the 'add' system (3, in Fig. 4) are still warmed up, its circuits still showing some reverberation or the switches that constituted the circuits still closed, a low-level add stimulus will produce an answer that we would not get if this system had not been active immediately before. Similarly with multiplication or subtraction.

It is clear that if system 3 (Fig. 4) is highly damped and does not have after-activity, or reverts at once to its pre-activation state,

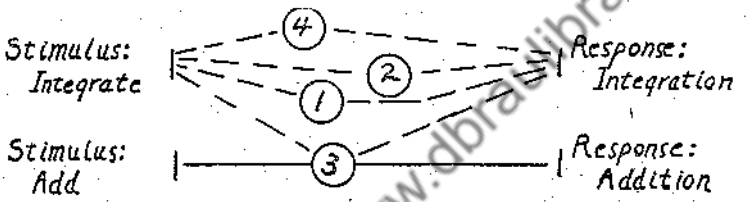


FIG. 4

'Introspection' in a calculating machine. See text.

this attempt at scanning would not work. But just such failures occur in human introspection. The 'imageless thought' problem of classical psychology was due to the discovery that something occurs in thought that the most careful introspection cannot detect (Humphrey, 1951). It is clear too that the answers we get will be completely a function of the questions we ask: the machine will not report on activities it is not asked about. But this also fits. One of the most striking features of the history of psychology is the difference between introspective reports at different stages of theoretical development. The introspections of James Mill about 1830 bear no faintest resemblance to those of William James 60 years later, but they do bear a very nice relationship to the fact that Mill had only the crudest sort of conception of sensory function to work with. The *a priori* theoretical proposal of John Stewart Mill, his son, that there might be a 'mental chemistry' among sensations and ideas, fusing the elements of thought into qualitatively different, simple compounds instead of

aggregations, appears to have permanently modified subsequent introspective reports. It seems that introspectors have always been able either to find what they were looking for or not to find it, but in general did not make observations unrelated to their theoretical conceptions of the human machine. The scanning works for the questions (explicit or implicit) that are put to the organism.

The scanning of course need not be after the event, but can also be arranged in advance. With our integrating machine (Fig. 4) we feed in a low-level add stimulation, then follow this up with the stimulus to integration. If our machine is able to hold the add stimulus (as a man could), and if integration does require the activity of the add system, the second stimulus may summate with the effects of the first. The machine will produce an answer to the addition problem at the same time as, or instead of, the integration, showing that the processes of integration are related to those of addition.

Put this in human terms: we tell the subject we want to find out whether he has coloured imagery, which sets him thinking about colours (or induces a low-level activity in the 'assemblies' involved in seeing colours); then we tell him to imagine a familiar scene. If the imagination does involve the colour systems, the two stimulations may summate, and the subject say 'red' or 'green'.

All this is worded in terms of overt stimulation and overt response; but there is no difficulty in principle about supposing that the stimuli may arise in the thought process ('I wonder if I have coloured imagery? . . . let me recall what I had for breakfast, and see whether I recall it visually, in colour . . .') nor about supposing that the answer may remain in the form of thought ('ah, no colours'), an activity which is subliminal for producing overt response directly but which could be demonstrated by the method of summation. I do not think it profitable to elaborate such mechanical schematizing further. The crudities of some of the statements above are bound to be embarrassing both to speaker and listener, they are so far removed from the richness and subtlety of the thought process; though we must employ them at present for communication, because we have no better terms or conceptions in which to convey the sort of thing I

have been talking about, there is no object in continuing to elaborate them beyond the point which shows how, *in principle*, one may see the phenomenon of introspection included within the purview of a physiological theory of thought and consciousness.

INTELLIGENCE AND ENVIRONMENTAL STIMULATION

After these general and more or less philosophical reflections, let me conclude by briefly describing some of the results of an experiment, now being carried out at McGill by W. Heron, W. H. Bexton and T. H. Scott, which seems very relevant to the subject-matter of this symposium. It appears to show that normal functioning by the human brain is much more dependent on a varied sensory input than we have suspected in the past. Even though sensory connections are intact, and the sense organ being stimulated at a level of intensity within the normal range, if this stimulation is monotonous instead of being normally varied there is soon evidence of intellectual deterioration.

The subjects are male college students, paid to stay in a quiet cubicle on a comfortable bed 24 hours a day. They wear goggles which prevent pattern vision but admit light, and cardboard cuffs extending beyond the fingertips which permit free joint movement but little tactual perception. A small speaker system provides communication with the experimenter. We have been able to induce our subjects to endure the boredom produced by these conditions for periods of two to six days. Tests of problem-solving are given before entry into the cubicle, during their stay in it, and afterwards. Control subjects are given the same tests at the same intervals.

The results show impairment in problem-solving while in the cubicle, in orally-presented problems such as mental arithmetic and anagram-type problems. Subjectively, also there are reports of inability to concentrate. On leaving the cubicle, there is apt to be some defect of sensori-motor control, and a mild state of confusion; and significant impairment is demonstrated in the Kohs-Block and Wechsler-Digit-Symbol tests of intelligence, as well as in speed of writing.

The most striking result, however, is the occurrence of hallucinatory activity, chiefly visual but also auditory and somesthetic

in a few subjects. The phenomena are quite like what is described in mescal intoxication, as well as what Dr. Grey Walter has produced by exposure to flicker. Also, there are rare cases of hallucination in aged persons without psychotic tendency, which as with our subjects does not depend on special stimulation (our method is more like a lack of stimulation) or chemical agents.

With our first subjects we did not ask about such phenomena, and we do not know how high the frequency was. The last fourteen subjects were asked to report any 'visual imagery' they observed, and our report is based on these. It appears that the activity has a rather regular course of development from simple to complex. The first symptom is that the visual field, when the eyes are closed, changes from a dark to a light colour; next there are reports of dots of light, lines, or simple geometrical patterns. All 14 subjects reported such imagery, which was a new experience to them. The next step, reported by 11 subjects, is seeing something like wallpaper patterns. Then come isolated objects, without background, reported by 7 out of 14, and finally integrated scenes usually containing dreamlike distortions, reported by 3 of the 14.

In general, the subjects were surprised by these phenomena, and then were amused or interested, waiting for what they would see next. Later, some subjects found them irritating, and complained that their vividness interfered with sleep. There was some, but not much, control over content; by 'trying', the subject might see certain objects suggested by the experimenter, but not always as he intended: thus one subject, trying to visualize a pen, saw an ink blot; or, trying to visualize a shoe, saw a ski boot. The imagery usually disappeared when the subject was doing a complex task such as multiplying three-place numbers in his head, but not if he did physical exercises or talked to the experimenter.

In addition, there have been reports of hallucinations involving other senses. One subject could hear the people in his visual hallucinations talking, and another repeatedly heard the playing of a music-box. There were also four subjects who reported kinesthetic and somesthetic phenomena. One reported seeing a miniature rocket ship discharging pellets that kept on striking his arm, and one reported reaching out to touch a doorknob he saw

before him and feeling an electric shock. The other two subjects reported a phenomenon which they found difficult to describe, but said that it was as if there were 'two of me' – two bodies side by side in the cubicle, and in one case these two bodies overlapped, partly occupying the same space.

In addition there were reports of feelings of 'otherness' and bodily 'strangeness' in which it was hard to know exactly what the subject meant. One other subject said 'my mind seemed to be a ball of cotton wool floating above my body' and another reported that his head felt detached from his body. There are familiar phenomena in certain cases of migraine, as described recently by Lippman, and earlier by Lewis Carroll in *Alice in Wonderland*. As Lippman points out, Lewis Carroll was a sufferer from migraine.

These results seem to us to bring our understanding of normal brain function close to the developing knowledge of the reticular system and the arousal reaction. We must, it seems, recognize two distinct functions of a sensory event: it may arouse or guide a specific response; but it has also a non-specific function in maintaining the normal waking organization of brain function. The cortex and Dr. Penfield's 'centrencephalic system' are not like a calculating machine operated by an electric motor, which can lie idle, without input, for indefinite periods and then respond immediately and efficiently; instead, it must be kept warmed up and working by a constantly varied input during the waking period at least, if it is to function effectively. The evidence from emotional behaviour, on the other hand, suggests strongly that the sensory input must not be too varied – that is, must not be too unfamiliar, or present too great a problem for the intracranial machinery – or emotional breakdown may occur (Hebb, 1949). Thus the higher animal continually behaves in such a way as to seek an *optimal* degree of disturbing stimulation. This is a long story, the evidence is complex and undoubtedly may be interpreted in other ways, but we feel that there is beginning to appear a convergence between the physiological and psychological evidence in this general area that constitutes a long step forward in our understanding of man and opens wide new areas for research, psychological and physiological.

GROUP DISCUSSION

JASPER: The work that Dr. Hebb has just presented is of broad interest and is of special importance to us in Canada because of the problems of men isolated in our northern outposts.

PENFIELD: I would suggest that the occurrence of spontaneous discharges in the temporal cortex might explain the two types of abnormality Dr. Hebb has reported. First of all the illusion in regard to his own position in space is like the illusion one gets with stimulation or local epileptic discharge in the temporal lobe. The hallucinations are not somaesthetic and must have to do with the temporal cortex which is the only place where formed hallucinations are possible. This is what I assume happens in dreaming. There may well be spontaneous discharges in the temporal lobe which formulate the beginning of the dream.

JASPER: Would you describe the patient we studied together, Dr. Hebb?

HEBB: One subject who had particularly vivid somaesthetic and visual hallucinations, suddenly reported over the microphone that he felt hands on his throat, choking him. He made some throaty noises and the observers promptly entered the cubicle, to find him sitting up but unresponsive. He remained unresponsive for 4 to 5 minutes. His EEG showed slow waves during the unresponsiveness and there was complete amnesia for the event. Dr. MacIntosh suggested that the subject might have undergone a period of hyperventilation as one feature of his disturbed behaviour. The subject was not electrically abnormal at other times as judged by his resting EEG.

GASTAUT: Since it is a question of defining consciousness in terms of behaviour, I should like to stress the striking dissociations which can exist between behaviour and the state of consciousness in certain pathological conditions in man and in certain experimental conditions in animals.

Most so-called 'temporal' epileptic attacks begin with a change in the attitude of the subject who appears suddenly to have his attention arrested by something not evident to those around him. He assumes an attitude of close attentiveness, leans forward and inclines his head in the direction in which he seems to see or hear something. If his head is displaced, he immediately turns it again in the original direction; this behaviour is apparently very well adapted and recalls the orientation and investigation reaction in dogs, described by Pavlov. During this time the subject's awareness is diminished. He reacts only to extremely forceful commands and has no recollection of the incident.

Similar phenomena are observed in animals when the amygdalae or

other rhinencephalic structures are stimulated; orientation and investigation reactions are produced, and the animal is confused and unresponsive.

Under certain conditions it is possible to create in animals such marked contradictions between the psychic state and the motor behaviour that even those reactions which are normally the best adapted become absurd. For example, if a light is suddenly switched on at the right of a cat at rest in a dark and quiet room, his orientation reaction is in the direction of the new stimulus, whereas if the same experiment is performed on a cat whose sub-thalamic contralateral structures have been destroyed on the left side, the orientation reaction is in the wrong direction. Under different experimental conditions a cat can be made to fight a dog, turning his back on the enemy.

BRAZIER: What is the earliest interval of time, Dr. Hebb, before you get a bizarre report from the subject?

HEBB: I cannot be very accurate about this, but it is my recollection that bizarre phenomena appear about the third day.

BRAZIER: Have you found a difference among subjects with regard to their attitude to solitude?

HEBB: The person who cannot bear to be alone looks at the cubicle and refuses to accept the job. We have no found a good correlation between the result of personality tests and the degree to which the subject can endure solitude.

BRAZIER: How are you using the word 'hallucination'? Have the people insight into what is happening to them?

HEBB: Yes. The subjects have insight, they are aware that this is not real, but it is nevertheless extremely vivid to them.

RIOCH: Dr. Hebb's experiments emphasize the importance of the nature of the interaction of the human with his environment on the inferred phenomena called 'consciousness'. Certain of the delusions and hallucinations Dr. Hebb's subjects described resemble those Dr. Edwin Weinstein has studied in brain-injured patients. Dr. Weinstein found that these occurred only in certain personality types and also only during the period when slow waves were still present in the EEG.

PENFIELD: From the point of view of the symposium are we to leave the definition of consciousness at this; that 'consciousness is what accounts for behaviour?'

HEBB: I should say it is the state of the brain of the waking, alert, normal human adult. It is without sharply definable characteristics; they are not unitary. And they undoubtedly change from one state of consciousness to another. Consciousness is a state of the brain in which ideation occurs, in which processes are going on that are not sensorily dominated, and in which there is interaction among these processes.

WALTER: My comment on your physiological model for learning is only that it is rather vague. In my opinion, specifications for such a model should be very explicit, literally specific and, if possible, quantitative, in order to compare with the quantitative aspects of behaviour. With regard to the illusions your subjects reported, in our experience, the liability of normal individuals to particular illusory experiences, and the relation of those to personality are both reflected in the EEG pattern. It would be very interesting to get an EEG check on the personality types of your subjects. Under the influence of flicker the illusion of displacement in time and space of the body-image, is quite common. One of our normal subjects felt himself displaced sideways in time, during which experience a peculiar discharge appeared in the temporal lobe.

HEBB: My reaction is the opposite to that of Dr. Walter with regard to my model: I am uncomfortable with it because it is not vague enough, because it seems ridiculous to be quite so specific. But my original task in 1945 and 1946 was to demonstrate to psychologists that such a model was conceivable, however improbable. Otherwise, I should have preferred to be vaguer, and run less risk of being wrong.

FESSARD: I do not quite agree with Dr. Hebb's definition of consciousness in terms of behaviour. I am quite sure I can accomplish complicated mental operations with the same behavioural manifestations as Dr. Hebb has associated with consciousness but without being aware of their being performed. At least a special mention should be made of a kind of behaviour that is characterized by its power of evoking more or less similar states of consciousness in minds of others, that is *language*. Verbal reports by the subject of his having just been aware of some percept, memory or any other mental operation of his own, seems to me the really useful criterion for consciousness, if at times unsafe.

BREMER: When one tries to suggest a behavioural definition of consciousness, memory is difficult to account for. Critical reactivity may be possible in psychomotor epilepsy without consciousness or memory for the event.

JUNG: These experiments remind me of my own experiences after taking mescaline. It started the same way, first with hallucinations of geometrical forms, then of objects, then of scenes. During all this, introspection showed an amazing inability to direct any active attention, or to concentrate voluntarily. It was an essentially passive state with a narrowing of consciousness. You could watch the hallucinations, in fact you had to, because you were fascinated by them. But you were not able to concentrate actively on anything else. The epileptics during their aura have the same experience. They have many

things going on in their minds, but they are unable to exercise control; if they can succeed in doing some overt act, it may avert the attack (Weber and Jung, 1940). The relations of different states of narrowed consciousness with visual hallucinations have been worked out by Mayer in 1952. For me, the main condition for consciousness is selection and simplification. The worst for conscious thinking is trying to be conscious of too many things at the same time. Confusion is the outcome. Dr. Walter said things going on in consciousness were very complicated: I may say just the opposite, they are very simple. They have to be simplified by the preceding unconscious physiological processes of integration to become conscious. These physiological preliminaries may be very complicated but what comes out at the end has to be simple and clear as an integrated abstraction which represents the very few things we can have only at one time in this narrow stream of consciousness.

KUBIE: This is remarkably close to work in which we have attempted to induce hypnoidal and hypnagogic states, semi-sleep states, states of induced communicative sleep, a whole variety of partially dissociated states which nonethelessre main under control without verbal suggestions or directions. In all of these, some degree of immobilization is essential. This is not new. For a long time psychiatric institutions have used wet packs to reduce psychotic tension and over-activity. The sheep-shearer does the same thing when he induces 'catalepsy' by immobilizing the sheep's head during the shearing operation. Similar results can be achieved by holding a hen's beak to a chalk line — or by fixing a lobster's feelers by standing it on its head. In the human one can immobilize all of him except his eyes. These cannot be immobilized without consent of the subject; and since the eyes provide one essential avenue of afferent input, the fixation of the eyes becomes an essential ingredient in almost all techniques of hypnotic induction. As soon as this immobilization is accomplished, a reduction of all kinds of afferent intake results. Only the primitive visual component of experience remains, which accounts for the visual predominance in the pseudo-hallucinations of hypnagogic reveries. Finally, I do not believe that any such studies will be complete until we develop a method for determining precisely what goes on in the respiratory apparatus without interfering with the respiratory process itself.

HEBB: I would like to make it clear that I am not saying that consciousness is behaviour. I am only saying that behaviour is our main source of information. Because processes that go on in the cerebrum may cause movement does not mean that they always cause movements which are observable. Consciousness is a complex inference from what movement is eventually observed, of the speech organs or otherwise.

DYNAMIC PROCESSES IN PERCEPTION

By

K. S. LASHLEY

As the study of the nervous system progresses from nerve conduction and reflexes to the analysis of the role of the cephalic system in more complex behaviour, neurologists are increasingly confronted with the questions that have been puzzling psychologists for generations. The nature of perception, of memory, and of the materials and organization of thought are problems which must eventually be faced in the formulation of any complete account of the physiology of the brain. Since the neurologist is dealing directly with the material structures of the nervous system and accepts as a working hypothesis the possibility of explaining all behaviour in terms of its physicochemical activities, he is even more directly concerned with the problem of the relation of body and mind than is the psychologist, who can and often does close his eyes to the events between the stimulating situation and the correlated behaviour.

During the past fifty years psychologists have largely turned from the mind-body problem, regarding it variously as unimportant, meaningless, or insoluble. Watson (1920) maintained that the student of behaviour can construct a science, disregarding consciousness, just as does the physicist in dealing with other phenomena of the physical world. The role of the observer in studying other human beings need be no different from that which he plays in the physical sciences.

Even if one adopts this point of view, however, there remains the question of how the phenomena, described by the subjectivists as conscious, come into existence. Whether the mind-body relation is regarded as a genuine metaphysical issue or as a systematized delusion, it remains a problem for the psychologist (and for the neurologist when he deals with human problems) as it is not for the physicist.[1] How can the brain, as a physico-

[1] Dr. Hebb has pointed out that we may start with the basic assumptions of either an idealism or a materialism but that the two systems are mutually exclusive. With this I agree but I would add that, whichever system is chosen, it must find a place for and deal adequately with the phenomena from which the concepts of the other system have been derived.

chemical system perceive or know anything; or develop the delusion that it does so?

I once (1923) reviewed the literature of philosophy and psychology to discover what phenomena have been thought to differentiate conscious processes, perceiving or knowing, from material events. What are the phenomena from which concepts of consciousness have been derived? In what ways have they been held to differ from those which the physicist describes in the space-time-number system? Different metaphysical systems have differed greatly in the emphasis placed on various characteristics but the following classification includes the ones most often specified as distinguishing conscious states or processes.

1. The subject-object relation. It is held that perception implies a perceiving agent, an I or self which does the perceiving.

2. The process of awareness implied in this relation achieves results for which there is no parallel in the physical world.

(*a*) It selects and unifies elements into a unique single field of consciousness.

(*b*) It transcends time and space. Memory brings into immediate relation events remote in time and space.

(*c*) It creates aesthetic and ethical values, held to be absolute.

3. The objects of awareness have esoteric character.

(*a*) Qualitative diversity. Sensory quality is held to be different in essence from the quantitative diversity of physical events.

(*b*) Awareness of the self. This is held by some to be identical with the self of the subject-object relation.

(*c*) Meanings or reference. The objects of experience have meaning which goes beyond and includes more than the immediate content.

(*d*) Purpose. Of especial importance among references is that to the future.

In discussion of these characteristics of consciousness there is rarely a distinction between psychological observation and logical inference. The subject-object relation belongs to the latter class. It is based upon a false analogy with the relation of the body, as agent, to the environment. As James (1890) pointed out many years ago, there is no direct knowledge of an experiencing self.

The self, as known, reduces to the physical self, largely kinesthetic sensations from the head and throat. The knower as an entity is an unnecessary postulate. Any process which will account for the characteristics of the content of experience fulfils all the requirements of the process of awareness.

A point of fundamental importance for a theory of the neural basis of perception is that there is never awareness of the integrative activity of the brain while it is in progress. The perceived items are always the product of preceding and complex integrative processes. Visual distance is a good illustration of this. Things are seen as near or far, yet this distance is actually determined by a number of variables, binocular parallax, estimates of relative size, texture, etc., which are not separately perceived but are only revealed by experimental isolation. Our thoughts come in syntactical form, without effort and without knowledge of how that form is achieved. So in every case, that of which we are aware is an organized structure; the organizing is never experienced.

Consideration of the role of summation in neural activity reveals a similar characteristic. Even at spinal levels summation of excitations is essential for reaction. Summation combines a multiplicity of excitations into a single effective unit which the resultant reaction cannot analyse into the separate elements. So also we must conceive of higher level integration as a sequence of excitations, individually incapable of exciting further activity, but continually summating to arouse the succeeding neural patterns. Such a sequence has the characteristics of the flow of consciousness. At each step in the process the relation between the integrative activity and the immediately preceding activity is the same as that between the process of awareness and the content; summated effects of the preceding organization determine the next step but the activities which summate are separately subthreshold and are not differentiated or distinguished in subsequent activities. Such a system fulfils all the discoverable requirements of the subject-object relation. Can it also account for the characteristics of the content of experience?

The existence of sensory qualities has formed one of the main arguments against the derivation of awareness from the physicochemical activity of the brain. It is held that transmitted excitations are qualitatively identical, whereas sensations have qualities

which cannot be discovered either in the physical stimuli or in the brain's activity. When, however, we seek to examine sensory qualities, they turn out to have only two characteristics; they are recognizable and are irreducibly different. But these are also exactly the characteristics of summated excitations. They produce a constant and differentiated reaction and therefore are distinguished and identified. They are individually subthreshold and therefore the resultant sum is unanalysably different for subsequent activity. The same relation of sequences of activity which meets the requirement of the subject-object relation also accounts for the only known characteristics of sensory quality.

I shall not attempt now to develop this idea in relation to all the other supposed unique attributes of consciousness. The task of psychology here is to sort out the facts of experience from the logical fallacies of metaphysical speculation. We must ask, what are the actual facts of experience and can these be stated as problems of neurophysiology? Some progress has been made towards such a formulation (Stevens, 1935; Boring, 1946). The important general conception is that awareness, as we know it, is not a state distinguished by any single specific character, but is a sequence of events which may be organized in various ways and which do not necessarily have any character in common. An attempt to describe the range of experience from the semi-stupor on first arousal from deep sleep to the emergency reactions of extreme fright would find few if any common elements. The definition of consciousness must be a very general one, rather like the definition of social organization. In the latter the elements, whether bees or men, do not define it; neither does the family, the government nor any other specific institution. Only some coherence and mutual interaction of individuals in a group is implied. The definition and identification of consciousness can be no more specific. There is no one criterion of consciousness. Events in the most alert waking conditions can be enumerated and other states specified as lacking this or that item, but no item defines the process.

CENTRAL DETERMINANTS OF PERCEPTUAL ATTENTION

Accumulating evidence on the facilitative action of the reticular system has suggested that it may be specifically related to

the selection of the content of experience and to the control of the direction of thought; to attention and set. I shall try to analyse these functions in some detail, to show their actual complexity and dependence upon organization which is almost certainly cortical.

The problem of attention is the problem of the selective dominance of some group of related neural activities with the simultaneous suppression of others. The animal which possesses a number of sense organs, as do all the vertebrates, is continually acted upon by a variety of stimuli. However, only a small proportion of these elicit observable responses. Further, in man but little of the total mass of excitation to which he is subjected ever comes to consciousness and there is not a constant relation between observable reaction at the time of stimulation and the evidence of conscious perception that can be elicited by later appeal to verbal report.

Data from evoked potentials in anaesthetized animals show that the excitation of any sense organ results in firing to the corresponding cerebral sensory area. In anaesthesia these excitations apparently do not spread through the cortex from their place of entry and do not activate other systems. In the waking animal, too, the effects of most afferent excitation must be blocked, either at precortical levels or at some point beyond the arrival at the cortex. There is no direct evidence as to where this blocking occurs but the facts of attention indicate that it is not at any low level of integration. A sleeper may be aroused by some relatively faint sound that has associative meaning, though unaffected by other, much louder noises; in listening to a musical composition, one can follow the melodic line of one voice and, to a greater or lesser extent, suppress attention to the sounds of other instruments. Such facts indicate that the direction and degree of attention is determined only after a considerable degree of organization has been imposed upon the afferent excitations and that this organization may vary in amount.

What are the mechanisms which determine whether or not a given stimulus is perceived? What determines its dominance over other stimuli? Very intense stimuli generally dominate, and certin sensory modalities seem generally to be prepotent. This is particularly true of pain, perhaps of movement in the peripheral

retina, of high pitched sounds, of some odours. In birds and higher primates vision is prepotent but probably not in other mammalian orders, though the evidence is uncertain. However, for man, and probably for most animals, the characteristics of the stimulus are generally of secondary importance in determining what is perceived.

Internal factors, characterized as voluntary attention, play the major role in selecting stimuli for perception. Sometimes such attention involves chiefly giving prepotence to a sensory modality, as when one looks at pictures or listens to music. Even in such cases, however, there is a further selection of the items perceived, in terms of organization which is somehow inherent in the neural processes.

Psychological studies of perception have been chiefly concerned with analysis of such organization. The laws of figure-ground structure, formulated by Wertheimer and other members of the *Gestalt* school (Koffka, 1935), describe what are probably the most primitive, innate modes of perceptual organization. Contrast, continuity of surface, or lines, reduplication of elements and the like determine the perception of 'objects' against a less definite background.

No satisfactory theory to account for this type of organization has as yet been proposed. Köhler's electrical field theory (Köhler and Wallach, 1944) is the only one that has been worked out in any detail and that has shown competence to explain any of the facts of perceptual organization in vision. However, our placing of metallic conductors over the visual cortex (Lashley *et al.*, 1951), and Sperry's insertion of insulating strips within the area (personal communication), in both cases without measurable disturbance of visual organization, seems to rule out the macroscopic distribution of electric currents as a possible mechanism of the organization. Nevertheless, there can be little question, I believe, that the organization is somehow dependent upon the spatial distribution of excitations in an extended cortical field. The projection of the retina upon a relatively thin layer of ganglion cells seems characteristic of all animals with true image-forming eyes; to the optic lobes or cerebral cortex of all vertebrates and even to somewhat corresponding structures of such invertebrates as the squid. The facts of figure organization imply some interaction of neural

elements according to their spatial position in the extended sheet of tissue.

The problem of interaction of the parts of the receptive field is complicated by the apparent fact that conduction and integration within it are not destroyed by rather extensive penetrating lesions. Experiments with animals are not altogether conclusive on this point because our means of mapping the visual fields and measuring the extent of scotomata are unsatisfactory. However, some clinical material indicates that cortical damage in the visual areas may produce a scotoma without destroying figure organization around it. Anatomic data in such cases are not satisfactory but I know that organization of form around the scotomata of ophthalmic migraine is undisturbed, and this is almost certainly a localized disturbance of cortical activity. A small foveal scotoma may blot out letters in the middle of a word, yet leave the word undistorted and legible as a whole.

There are two alternative possibilities of integration under such conditions; that the integration is subcortical, in some structure supplied by independent paths from the different parts of the cerebral area; that the integrative process can somehow spread effectively through the nerve net around a partial block. The first of these possibilities is difficult to test, since we have no certain evidence concerning the descending paths from the visual cortex. Efferent fibres to the lateral geniculate have been described from Marchi material but I regard this technique as unreliable for distinguishing the direction of fibres. (I have seen disintegration of cells in retrograde degeneration within the Marchi inverval.) Moreover, if the structuring of visual patterns occurs in the lateral geniculate, the elaborate cortical mechanism would seem to be superfluous.

The most probable subcortical regions for visual integration are the pulvinar and colliculi. There is evidence of severe visual disturbance from temporal lobe lesions and the only known afferents to the temporal lobes are from the pulvinar (Chow, 1950). Chow has now succeeded in producing massive bilateral lesions in the pulvinars, however, without any demonstrable visual disturbance (personal communication). In the rat I have evidence or normal visual perception after total destruction of the colliculi. There is no evidence of a direct path from the striate areas to the

reticular formation. Interaction in the structuring of percepts would imply relay through other thalamic structures which have been shown to be unnecessary for visual attention and organization.

To account for the passage of integrative patterns around a block in the cortex and to meet some of the problems of stimulus equivalence, I have proposed a theory of reduplication in the spread of excitations through a nerve net, on the assumption that reverberatory circuits of given frequency and space distribution tend to activate similar circuits in adjacent tissue. The on and off discharges of the retina combined with tremor of the eyes, as emphasized by Marshall and Talbot (1942), might give the intensity of excitations at lines of contrast necessary to establish the dominance of figure in the total pattern. I consider this theory very improbable, yet can think of no more satisfactory alternative. The theory of Pitts and McCulloch (1947) postulates an arrangement of horizontal fibres which certainly does not exist in the visual cortex, and in any case, would not account for the transmission of integrative processes around a block.

The problem of the nervous mechanism of figure-ground organization cannot be solved on the basis of existing evidence. A more detailed knowledge of the finer structure of the cortex and of the projection of the visual area on lower centres is a necessary prerequisite to the further development of theory. There is need also for more precise analysis of the defects produced by various lesions in the visual areas of animals and the collection of clinical material with damage restricted to the cortex. Let me emphasize again that such structuring is often, perhaps always, a major factor in directing attention. The selective character of attention is a result, not a cause of the organization of percepts.

THE SCOPE OF PERCEPTION

The number of items that can be perceived at any one moment is extremely small. For simple number of dots the average maximum for different individuals has been determined as about 11, for objects of which both form and colour must be reported it is 3.3 (Glenville and Dallenbach, 1929). Such limitation of perception cannot be separated from similar limitations in memory and,

in fact, perceptual span and memory span are not distinguished in psychological experiments. One can hold in immediate memory and manipulate, as in mental arithmetic, only a certain number of items, whether these are derived by perception or by recall. Experience consists of a succession of such groups of items. It is as if the brain produces 'quanta' of activity and experience consists of a sequence of such groups or 'quanta'.

What determines such limits? Why ten rather than a hundred items perceived simultaneously? Each item is, of course, not a neural impulse. Excitation, even by a single dot on a white ground, involves hundreds, probably thousands of neurons. Are the limits set by the available number of neurons? The problem is complicated by figure-structure. A dot may be an item in the group perceived, or a triangle outlined by many dots may constitute an item. It is not the number of excitations but the number of foci of organization that is limited in perception. I have suggested an analogy between brain organization and the organization of tissue in regeneration and differentiation. The number of tentacles that a regenerating piece of hydroid polyp can produce is limited by the size of the piece, foci of differentiation must have a certain separation or there is mutual interference. So, foci of neural activity might require similar spatial separation in order not to fuse. I have spent some years in trying to analyse the rat's visual perception (1938). The rat has about one-half of one per cent as many cells in the visual cortex as does the monkey and probably a still smaller proportion in relation to man. Except for acuity, however, the rat's visual organization scarcely differs from my own. There is a little evidence that he may perceive a smaller number of items simultaneously, but the ratio is at most 2 to 10. The analogy with growth differentiation therefore does not appear to hold, at least in terms of any simple spatial ratios. I do not know of any other attempt to account for the limitation of perceptual experience or of the memory span. About all that can be said with any confidence is that it is somehow related to the structuring or organization of percepts. In the limits of attention, as in its selective action, complex organization, of the sort that we usually ascribe to cortical levels, plays an important part. Six or eight pure tones of a melody or the same number of polysyllabic words including scores of tones are equally near the limit of the

attention span. The units of measurement may be neurologically very complex and the limits of attention span cannot be related to cell number in any simple way.

INTERACTION OF FUNCTIONAL SYSTEMS IN PERCEPTION

Thus far I have discussed only the most primitive and perhaps the simplest of the integrations which underlie perception. Most visual perception is complicated by integration with excitations from other sense modalities, particularly somesthetic, by habitual modes of perceiving, and by the integration of temporal sequences. The interdependence of different sense modalities appears most clearly in vision where the problems of depth perception have excited especial interest. I need not review here the evidence of the role of binocular parallax but another illustration may be less familiar. The moon on the horizon appears much larger than at the zenith. Hathaway and Boring (1940) have shown that this illusion is solely a function of the position of the eyes in the orbit; the somesthetic impulses determine the immediate perception of the size of the object. Where and in what way this integration occurs is impossible to say on the basis of existing evidence.

Habit plays an important part in the determining of figure-ground organization in vision. A hidden figure in a puzzle picture, when once located, may stand out against the rest of the picture, although its organization violates all the laws of contrast and continuity in the primitive structuring of figures. We do not know the nature or location of the memory trace (Lashley, 1950) which determines the selective organization and makes the outline of a human profile, for example, stand out from the maze of lines of the puzzle picture. A very similar or identical problem is raised by all recognition, for in recognition the stimulus pattern is identified with a memory trace. Our experiments with animals show that no part of the neopallium except the area striata is essential for the visual recognition of familiar objects and that the colliculi and at least the greater part of the pulvinars are also not essential. I have also one case of a monkey with combined destruction of the motor cortex and the greater part of the corpora striata, with continued visual recognition of food objects. On the other hand, there may be apparently normal perception of bright-

ness differences and some vague appreciation of visual patterns after removal of all striate cortex. Beyond this there is no certainty, but it seems probable that the assimilation of the stimulus with the memory trace in the perception of visual form is a function of the striate cortex, either alone or in combination with some unknown subcortical mechanism.

There is, however, a further complication which makes this conclusion uncertain. That is the role of scanning in the perception of visual objects. I became interested in the mechanism of scanning through its importance in the development of mechanical aids for the blind, but have come to feel that the problem of scanning underlines many other problems of neuropsychology. Visual perceptions are rarely based upon a momentary stimulation of the fixed retina. One perceives very little with an exposure too brief to permit of eye-movements and most of our perception of objects is derived from a succession of scanning movements, the succession of retinal images being translated into a single impression of form. It is also possible, with a little practice, to scan an object with a finger tip or with a sensitive probing device and to translate the successive tactile and muscular impressions into something very like a visual image of the object.

Such close interrelations of visual and kinesthetic space suggest that the perceptual processes in vision may be far more dependent upon integration with the postural-kinesthetic system than we ordinarily assume. It is obvious that the orientation of the visual field is dependent on vestibular functions; after images of movement can make the visual field spin or rock violently. It is not impossible that all of the spatial chracteristics of vision are similarly dependent upon integration with the postural system. It may be that we shall have to seek the source of visual percepts in the integraton of these two systems, but evidence for a specific locus of such integration is still entirely negative. I know of no established instance of disturbance of the basic space co-ordinates by lesions which do not directly affect the input from the vestibular system or the cerebellum, either in animals or man.[1]

[1] The behaviour of animals with damage to the reticular system has not been reported in detail and I have not had opportunity to observe it. However, descriptions of their activities, when awakened, do not suggest that they are in any way disoriented.

'SET' IN PERCEPTION

The search for a definite object in the visual field, as in the examination of a puzzle picture, raises the question of the nature of the set which predetermines the organization of the percept. Since the exact form of the object to be found is unknown beforehand (the instructions with such a picture may be only 'find the hunter in the woods') the set must have a very generalized form. In my own case this seems to be a readiness to identify a motor sequence. Some line or angle in the picture is taken as a starting point and adjacent lines are scanned. When their sequence of directions fits the generalized motor pattern, the figure suddenly emerges.

I have elsewhere (1951) discussed the problem of such motor sets with special reference to grammatical structure. The problem seems to be essentially similar for the set to perceive a visual form. A characteristic of such organizations for sequences of action is that prior to the initiation of the action, all parts of the organization seem to be co-temporal; that is, the thought may be expressed in a variety of word orders. Similarly in the set to find the hidden man it makes little difference what part of the figure is first discovered, the identification and figure formation follows any scanning sequence.

Such phenomena as this and others that I have reviewed in the earlier paper indicate that the set must involve a very complex organization of nervous elements, primed to respond in a predetermined pattern to certain cue stimuli. The nature of such priming is completely obscure. It may be related to the phenomenon of potentiation described by Larrabee and Bronk (1947). Such persistent effects require some specific modification of excitability beyond that of the familiar facilitation and inhibition of neurophysiology.

I have chosen my illustrations from vision because perception in that modality has been most thoroughly studied, but the same principles of organization hold for other sensory systems. In audition, particularly, the temporal summation is conspicuous. The span for temporal sequences is not greatly different from that of spatial distribution in vision and the items may be clicks, words, or word-group meanings. What is perceived depends upon a

structuring of elements, which must be neurologically extremely complex and which may consume a considerable period of time.

A basic problem is the neural representation of these preparatory adjustments. Are they condensed and stored in some neurologically simple form; a sort of neurological shorthand or symbolism? I believe that such a possibility is ruled out by evidence that I have cited for the co-temporal existence of the elements in a set for motor activity. In the manipulation of items within the memory span, one may scan them in many ways. This would be impossible, if they were represented only by a single cue item. Whether it be by reverberatory circuits or by some sort of potentiaton the 'quanta' must be represented neurologically *in extenso*, all the items present and available.

THE RECTICULAR SYSTEM IN PERCEPTION

What role, if any, can the reticular system play in these complicated dynamic functions of perception? I have tried to point out some of the complexities of the selective action of attention in determining perceptual organization, the interplay of habit systems and of different sensory modalities. It seems to me that a system, as diffuse and poorly organized for limited, patterned activity as the reticular system appears to be, is unlikely to contribute anything more than a general, undifferentiated facilitation in these processes. There is, however, a more direct test of its functions in perception. Starzl and Whitlock (1952) have presented evidence that the cortical potentials following excitation of the reticular system are largely or entirely confined to the associative cortex and suggest that it does not act upon the primary sensory areas. Analysis of the effects of removal of associative areas should therefore throw some light upon the relations of the system to perceptual processes. My fellow workers and I have now explored the greater part of the associative cortex of the monkey by extirpation and tested for disturbances of visual and tactile perception. There seems to be no permanent interference with any primary perceptual process following removal of any part of the associative cortex. Removal of the prestriate region, roughly the position of Brodmann's Areas 18 and 19, leaves the animal with normal capacity for form and colour perception, with

normal capacity for visual learning, and showing the usual equivalence of stimuli, transposition, and the like (Evarts, 1952; Lashley, 1948). Bilateral parietal removal has no more permanent effect upon tactile perception (Blum, 1951; Blum *et al.*, 1950). Bilateral temporal lobectomy produces some peculiar symptoms which we cannot yet interpret, especially disturbances of visual performance, yet visual perception seems normal; the monkeys may form habits based on colour or form discrimination at normal rate (Chow, 1952). Removal of the prefrontal granular cortex produces hyperactivity but the animals quickly settle down to learning tasks and show no evidence of perceptual disturbance (Wade, 1952).

We have not yet succeeded in total removal of all associative cortex, but Chow, Blum and Blum (1951) have removed almost all of Brodmann's Areas 5, 7, 18, 19, 20, 21, 22 of the dorsal and lateral surfaces together with the prefrontal granular cortex. Such animals show disturbances of more complex functions, conditional reactions and delayed reactions with some temporary amnesias, but visual and tactile recognition of objects seems to remain intact; there is no demonstrable disturbance of immediate perception in any sensory field.

The clinical literature contains a few reports of imperception or reduced attention following cerebral lesions. Typical is the recent report by Denny-Brown (1952) of a patient who was generally unaware of her left side, including the left half of the visual field. Because of accompanying sensory defects such symptoms have been ascribed to parietal lobe lesions. In the clinical material anatomic controls are inadequate or lacking and the primary sensory deficits may be sufficient in themselves to account for the imperception. In experimental work with monkeys similar defects have been observed only after frontal lesions. Kennard (1939) reported a visual imperception after destruction of the frontal eye fields. The symptoms lasted for only a few days and were followed by an apparently complete recovery. We have obtained a similar syndrome, but only by lesions which include parts of Areas 6, 8, 9 and 10. I have also one case of a unilateral imperception persisting for several months and involving both touch and vision (1948). This monkey had first a bilateral removal of Areas 18 and 19, which produced no demonstrable disturbance of visual or tactile perception. In a

second operation the frontal eye fields were removed. After this she showed for some months a defective attention to her left side. When she was prevented from using her right hand she would feed herself with the left. But as soon as the right hand was freed, she seemed to forget the left; food grasped in the left hand would be held and finally dropped while she searched eagerly for food with the right hand. She showed also a persistent visual field defect which was not apparent after the first operation.

There is one further bit of evidence for an influence of this frontal field on attention. A monkey with a visual field defect from an occipital lesion shows an apparent rapid recovery. After a few months it becomes almost impossible to demonstrate even an hemianopia with our usual crude methods. The animals learn to survey their surroundings continually with the intact field and become so sensitive to slight sounds that the usual tests are ineffective. Chow, Blum and Blum (1951) have found that a subsequent frontal operation reinstates the visual defect and apparent recovery is much slower.

These are the only cases of imperception or disturbances of attention that have come to my notice in experimental work with animals. So far as I know, the cortical areas involved are not *especially* associated with the reticular system. There is one observation which indicates that the mechanism of reinforcement is transcortial. George Clark (personal communication) cut the occipito-frontal fibres by a transverse incision through the corpus callosum at the level of the motor cortex. He obtained the same temporary visual imperception as is produced by the frontal lesions. If the observation is correct, it rules out subcortical participation in the frontal lobe influence on this phase of visual attention.

There has been time to touch only superficially on a single one of the problems of perception, selective dominance. The concept of pure sensation is now generally recognized as an abstraction from the structure of perceptual experience. What is perceived, the dominance of one neural system over others, is determined by the interaction of a number of variables; the character of the stimulus, the organization of the excitations in the central nervous system and the flow of central associative processes under the guidance of more general preparatory adjustments or 'sets'. The

selection or dominance of objects in perception is evidently dependent upon some of the most complex organizing processes of which the brain is capable. Almost all percepts include a spatial element, at least of general orientation, and there is reason to believe that the topological representation of sensory surfaces is essential for this spatial element in perception. The reticular system may contribute to the general level of activity of cerebral fields but there is no evidence that it exerts any such localized and selective function as appears in the dominance of specific perceptual processes, nor does it provide the structural diversity necessary for such control.

GROUP DISCUSSION

PENFIELD: Did I understand from your discussion that the 'process of awareness' comes as close to expressing what you mean by consciousness as any other phrase?

LASHLEY: That is just a substitute word for consciousness. The process is an active one, of continually becoming in a sequence of events. The attributes of mind, the attributes of consciousness, are the attributes of the activities of the brain. We can find an exact identity of process in the two sequences of events, as reported subjectively and as observed objectively.

RIOCH: Do I gather correctly that in your formulation it is necessary to have a function of memory in order to have consciousness?

LASHLEY: That is a difficult problem. I think that is true. There must be memory for at least the duration of the memory span. There seems to be a necessity for what I have referred to here as conscious 'quanta'. I want to emphasize the lack of absolute difference between conscious and unconscious processes, even in this respect. A single reflex, if it is maintained momentarily has that attribute of consciousness. When we speak of consciousness we usually mean human, awake condition and we can describe what is going on. But we find states which are borderline, which we cannot clearly describe, as in the partial anaesthesia which was called 'twilight sleep', where the patient could talk, but without subsequent memory.

ADRIAN: I was just wondering how far some of these models could be conscious.

LASHLEY: It is, of course, the question of how far they would correspond to the various attributes. I think it is impossible to define consciousness as a unit. All we can say is that conscious states differ from certain unconscious states in certain characteristics. What we may

find is that any one of these characteristics may be present without the others, and we are dealing with a synthesis or a complex.

WALTER: Would Dr. Lashley accept, in attempting to formulate diagnostic characters of consciousness, the existence in the brain of some statistical operator which could be of aid in recognizing experimentally the selective mechanisms which he outlined?

LASHLEY: As I understand the question, it is: Can consciousness be defined by some percentage of the total number of diverse characteristics? I think that people in the clinical field are interested primarily in the states of coma, and in getting a definition for the presence or absence of consciousness. My interests have been entirely in the structure of consciousness and how to explain it. The kind of definition you are asking for may be practically useful, but I would not know where to draw the line.

HEBB: I may be able to make clear what I was trying to say earlier about logical inconsistency in relating it to Dr. Lashley's point about quality. The inconsistency occurs when you attempt to discover the determinants of quality and still insist that the quality be included among them. 'Explanation' in such cases can only be reference to another universe of discourse, and establishment of correspondences, as Dr. Lashley has said. But when you move into the other universe you cannot retain the characteristics of the one you have left. In its own psychological universe 'redness' or 'pain' is irreducible, elemental; in another universe it becomes, hypothetically, a particular kind or locus of neural action. But when you try to explain one system by reference to another you must not beg the question by trying to carry over to the next system the qualities that you are trying to explain. You cannot ask for, so to speak, psychological identity, you cannot ask that the nerve impulse have the characteristic of redness.

LASHLEY: I do not agree in this matter. Nerve impulses may have all the known characteristics of redness. I think that the development of the operational critique gives the answer here: the meaning of colour is given only by the kind of operational definition which we can formulate, and that is irreducible difference. We can say that red is 'warm', but that is adding an emotional factor. It is not describing the 'red'. The statement that red and green are undefinably different says everything that we know, that is meaningful. Consequently, if we can say that two neurological events are unanalysibly different by subsequent events we will have conveyed precisely the same meaning and all of the meaning that there is, in any statement concerning the qualities of redness or greenness.

JASPER: I think Dr. Lashley has given certain attributes of what he is willing to define as conscious behaviour and has pointed to certain

aspects of it which he refers to neurologists as real problems. Naturally we do not intend to deal with all the problems listed above, some of which are rather metaphysical. There were at least two items which might be considered in a neurophysiological discussion. One of them is the problem of the limits of conscious awareness. Why does conscious awareness have this particular property of being so very limited in view of the multiple simultaneously active networks in the receiving systems of the brain which are all, presumably, functioning at the same time. What is the neurophysiological mechanism of the limitation of awareness? This is a concrete problem.

LASHLEY: I have tried to answer this problem in physiological terms. My first attack was by analogy with the foci of the growth in regenerating tissue. That was not satisfactory. An alternative is the span of memory, in which there is a limited number of things that can be held, possibly because there can be only so many counted before they are lost. Again that does not seem to be satisfactory. Five or six digits may be remembered for several minutes, provided there is not interference by other digits. So that the time-span does not seem to offer a possibility.

PENFIELD: A man is fully conscious when he is aware of his present experience and sets it in perspective with his past experience. At such a time he is capable of voluntary mental activity. Those are elements in the state of consciousness. When it comes to defining consciousness as a noun, it is difficult to improve on Dr. Lashley's expression — 'the process of awareness'. Dr. Bremer described a patient with a temporal seizure, who behaved in an automatic manner and yet who showed evidence that he had some hold on memory however imperfect. It was a kind of modification of consciousness. There are many types of modification of consciousness. But as long as it exists there is a continuing acceptance of information and a continuing decision either for or against action.

LASHLEY: In one sense memory is always present but I am not sure that in the sense of comparison of the present and the past this is necessarily so. When one is acting in an extreme emergency there is consciousness confined almost entirely to the environment. You are performing a lot of habitual movements but memory comparison, as I understand you, really does not intervene. Or perhaps there is really only a difference in terminology here.

PENFIELD: In such cases you set up your experience of the moment against your past experience. It is in the light of that comparison that you go into action.

LASHLEY: That involves the problem of recognition. Koffka has suggested that memory and perception must have separate localization

but be capable of superposition or coincidence for recognition to occur. But neurologically I do not know what that means.

WALTER: It is in just that part of the neurological mechanism that I suggest that a system capable of statistical evaluation may be essential, and signs of such a system could be looked for from an experimental standpoint.

ADRIAN: We can only do one thing at a time. At the motor end we are limited to one course of action. There has to be some kind of selection between the incoming and outgoing stimuli. Where and how is another matter.

JASPER: The second limited problem of consciousness which may be referred to neurophysiologists is the problem of why we are not conscious of the specific mechanisms of sensory perception but only of the 'distillation' of their meaning. The machinery of the process is not conscious. Only the product of the multiple activities of these networks enters our awareness. This is a basic statement which has physiological meaning as a problem. It has been concerning us a good deal in our consideration of the significance of corticofugal projections, to the brain stem. It must be that, in view of the possibility of multiple corticofugal projections to what seems to be a common pool of neurones, the one of these various projections which is selected must have a particular pattern, since the significance of a stimulus pattern is critical in determining its arousal value or its potency in attention. Patterning must be, therefore, one of the attributes which determine signals which get through to the hypothetical centrencephalic system. Intensity of stimulation must be a factor as well. We know that when we are attending to meaningful situations such as the one here, in this room, I am not noticing the clattering of glasses, but would certainly hear a gun fired. Obviously, the intensity of the stimulus must be taken into consideration, as well as the pattern. What it is in neurophysiology that allows a certain pattern to be a signal to the whole system, this is the real essence of our problem. Our working hypothesis is that the signalling actually does take place in this centrencephalic system and that the reason why it is essentially limited is because of the occlusive characters of the common pool. This pool will only receive a limited input, and competing impulses cannot reach it. That applies to both of the qualities of consciousness that Dr. Lashley referred to neurophysiology, the attribute of selective limitation and the problem of why we are not conscious of the mechanism but only of its result.

LASHLEY: I have one comment to make: I cannot see a real advantage in referring this function to a limited space, because there are still many thousands of neurones there and we have no knowledge as to what it

is that produces limitation. Why should 10,000 be more limited than 100,000? This does not really answer the question of limitation because there would seem to be still room for a great deal more than there actually is in, say, recognition of five or seven digits. For an anatomic analogy, I can find an even better coincidence: the range of identifiable or visible layers of the cerebral cortex is from 5 to 13, just about the range of items included in the span of attention. This is nonsense, of course. It just shows that such anatomic guesses are not particularly helpful.

I should like to suggest a problem with respect to the centrencephalic system. The possibility of integrated behaviour after cutting of association fibres of the cortex has been urged as an argument against a unifying function of the cortex. In doing many hundreds of operations on rat brains I have occasionally damaged lower centres. Such cases were usually discarded but I am rather sure that I have sometimes cut through the midline nuclei without producing serious disturbances of behaviour, I suspect that inter-connections within the reticular formation may be interrupted without producing more disorganization of behaviour than follows knife cuts through the cortex. Such experiments should be tried before we ascribe the unification of consciousness to the reticular formation.

PENFIELD: If you make a horizontal cut between any functional area of the cortex and the centrencephalic system you will inactivate that cortical area, but not the centrencephalic system. You may modify but you will not inactivate the centrencephalic system by such a procedure.

LASHLEY: I am not talking about any separation of the cortex from the centrencephalic system, but the cutting up of the centrencephalic system itself, without damaging its input or output, only to preclude integrative action between its different parts.

BREMER: At this stage of the discussion, one should remember that one section, at least, abolishes all consciousness; it is the section of the brain stem at the mesencephalic level; if we are to deal with a general, dynamic activation, even if intracortical connections, and those to the centrencephalic system are intact, when this general, dynamic factor is lacking, there is an absolute and definite unconsciousness. This conclusion is inevitable in view of the work of many of us here.

PENFIELD: In man, if you approach this particular area, with all the care and deftness of which you are capable, to take out a tumour, even an encapsulated tumour, you may be dismayed by the result. The mere act of approaching it may cause the patient to be unconscious, and probably in three or four days, dead.

LASHLEY: This is not necessarily relevant to the discussion. As I

pointed out yesterday, you can get a loss of consciousness in various ways. The essential organization may be destroyed either by too great activity, as in convulsive discharges, or by cessation of activity. The reticular formation may be necessary for keeping up an essential level of cortical tonus, without directly participating in the specific integrations which constitute the conscious organization. Stopping the heart also produces unconsciousness, yet one does not therefore ascribe consciousness to the heart.

JUNG: I was as glad as Dr. Jasper in hearing Dr. Lashley say that only the final states came into the consciousness and that the eleboration processes were unconscious. I would like to ask if Dr. Lashley also thinks that this elaboration is not only selection but also simplification, in having only the meaningful parts coming through.

LASHLEY: If I understand the question, there is continuous simplification, in that complex processes are continually summating to serve as activators for the next step in the process.

MORISON: I was just wondering if Dr. Walter has not presented us with a beautiful analogy to this concept of consciousness, in the way his camera works when it takes pictures of his cathode ray tubes. Dr. Penfield has said that he regards consciousness as a result of congruence between past experience and the present. Dr. Walter's camera waits, as I understand it, until there is a congruence between the phase of the incoming stimuli and the phase of the things happening in the brain. One might entertain oneself by thinking of the centrencephalic system which waits, like the camera, until a more complicated type of congruence occurs. The shutter goes, and it takes a picture.

JASPER: The unwillingness of Dr. Lashley to give no more than a general undifferentiated awakening function to the centrencephalic system merits further discussion. I think it is the core of our problem, but Dr. Lashley does not give us any alternative hypothesis to account for the unity of this process. I would like to know whether he might suggest one.

LASHLEY: I conceive of the cortex itself, primarily as a continuous network, and except in its extent I see no fundamental difference in constitution between the cortex as a whole and the centrencephalic system as a whole. They both are networks of cells within which patterns of activity can spread. I see no advantage in ascribing to the more limited system functions which seem to be at the highest level of complexity of which the brain is capable. Further, the evidence for this centrencephalic system seems to point to a diffuse function. It is the pattern of neural activity which is the determining thing in producing behaviour or conscious states. I, therefore, do not see what is gained by projecting these processes into a more limited system, unless

some special characteristics of that system can be demonstrated (and I think they have not yet been demonstrated) which give it special adaptation for such functions.

FESSARD: What is gained essentially is the possibility that a selection of messages from different sources can meet and interact at any instant in a small space, that is in a space of a few cubic millimetres where we know that electric forces, chemical and osmotic gradients are present and are determinant factors of the excitatory states. The same mechanisms of interaction between the auditory and visual areas would be almost inconceivable on account of the distance that separates them. Apparently they only communicate through long transcortical association pathways, but Dr. Lashley and Dr. Sperry have sufficiently shown us that destruction of these pathways and knife cuts through the mentioned cortical areas do not change much their functional properties.

LASHLEY: Dr. Fessard is speaking of electrical fields of small magnitude. I might point out that Köhler has recently demonstrated direct current fields of very large extent in the cortex. Whether or not they have any functional significance is uncertain. In my paper I sketched briefly the transmission of reduplicated patterns through a neural network. There is much evidence which implies reduplication of activity throughout extensive cerebral areas. It is characteristic of the long intercortical pathways, and perhaps of loopcircuits through subcortical centres that their arrangement is topological. They would therefore tend to transmit to other areas the same patterns of excitation which are present in their areas of origin. There are thus alternative modes of transmission around partial blocks.

MAGOUN: I am not at all sure that this is relevant to your concept of the nerve-net but in many ways it seems to me that our conscious awareness is simpler than the neuronal processes which subserve it.

LASHLEY: This is precisely what I tried to emphasize, in my concept of summation of input. When consciousness occurs, in depth perception for instance, there are a number of inputs, each involving hundreds and thousands of nerve impulses, but they are effective only in giving a single unit, visual depth, which we cannot analyse or break down.

BREMER: It has been implied by Dr. Lashley that he did not believe that section of intracortical pathways had any influence on consciousness. May I say to Dr. Lashley that in his own laboratory sections of the occipto-frontal long association tracts produced in the animal a kind of unawareness of the contralateral visual field.

LASHLEY: This unawareness lasts only about three days, after which visual functions seem normal.

PSYCHIATRIC AND PSYCHOANALYTIC CONSIDERATIONS OF THE PROBLEM OF CONSCIOUSNESS

By

LAWRENCE S. KUBIE

INTRODUCTION

The holding of this conference is an indication of the advances which make it possible for neurophysiology to attempt to explain the highest psychological functions. It is not so many years ago that Pavlov would exact fines of any student in his laboratory who used such words as 'voluntary' or 'consciousness'. Yet before Pavlov died he used those very words himself; and assembled experimental evidence that 'unconscious chains of associative connections can be set up in an inhibited field' and of the further fact that 'under favourable conditions, the unconscious synthesis may enter the field of consciousness' (Pavlov, 1927, 1941). It is evident, therefore, that over the years Pavlov's personal development covered a long distance. Neurophysiology today has come even further.

At every stage medical science learns almost simultaneously from the experimental laboratory and from those tragic experiments of nature which constitute organic disease. In serving the experimental laboratory, the clinic has always had a double purpose. It has provided data on the functions of organs and on the interrelations of their component parts; and it has also reminded the experimentalist how complex are the phenomena which must be described, isolated, explained, predicted and ultimately controlled. Without the nagging clinician, the temptation for the experimentalist to over-simplify his problem has sometimes proved irresistible; and as the neurophysiologist now turns his attention to psychological levels of organization, this temptation becomes even greater. Therefore, at this point in the development of scientific knowledge of the physiology of psychology, the role of the psychoanalytic psychiatrist is to provide provocative and

challenging problems, plus a certain amount of evidence, and always and constantly to serve as a check to the tendency to oversimplify which is inherent in the enthusiasm of the experimentalist.

This sententious aphorism has a special relevance to the problem of consciousness, because this aspect of psychological functioning is its most subtle and complex variable; and the experimentalist dares not turn his back on the complex data which are available to him through psychoanalytic psychiatry. These data come not only from the waking state, but also from sleep, from the sleep-dream of the so-called normal, from the waking dreams of the psychotic, from the neuroses, from hypnoidal and hypnagogic dissociations, from delirious conditions, from multiple personalities, from fugue-states (both hysterical and epileptic), from the automatisms of psychomotor epilepsy, etc. etc. These are all variants among the phenomenology of consciousness, which must be included in the ultimate scope of such studies as these.

The phenomena of consciousness are themselves so manifold and so complex, that it is not surprising that medical scientists have tended to shrink from tackling them. I made no statistical survey of this significant omission; but as I paged through a random sampling of the literature I was amazed to note how rarely the word 'Consciousness' is listed in the tables of contents or in the indices of classical textbooks and monographs in the fields of neurology, neurophysiology, and psychiatry. This omission leads me to hope that a preponderantly logical and psychological formulation of the phenomena of consciousness, buttressed by a small amount of new experimental data, may aid our joint efforts to organize a mature experimental attack, perhaps by eliminating some of the confusions which appear regularly in most discussions of the problem. If my paper serves this modest purpose, it will be my small repayment of the indebtedness which I feel at the privilege of participating in this symposium.

I will begin by saying that it is truly impossible to deal with psychological problems without a working concept of consciousness. Sometimes we are explicit and frank about this. Sometimes we fool ourselves about it. Many workers have attempted to avoid using the word because of its traditional connotations, which have had a somewhat mystical, imponderable, non-

scientific, philosophical and/or theological flavour. As we have seen, Pavlov in his early years was one of these, although in the end he had to give in and use the banned words. John B. Watson held out obstinately; but found that he had to characterize, although quite inadequately, certain limited aspects of the same phenomena, by using a pair of verbal equivalents, e.g. 'verbalized and unverbalized'. Furthermore, no one who has dealt effectively and usefully with the problem of consciousness has been able to avoid considering its many variants, including its opposites. Just as we cannot understand white without understanding every shade of grey to black; so we cannot understand consciousness without understanding not only its total absence but also all intermediate modulations. I will return to these later.

I realize, of course, that this confronts the experimentalist, whether he is an electroencephalographer, a neurophysiologist, a neuroanatomist, a neurosurgeon, a clinical neurologist, or a neuropathologist, with many complexities which are alien to his usual intellectual habitat. However, we cannot help this. No one of you would investigate 'Sensation' as such. As experimentalists, you would attempt to explore some specific modality of sensory experience, with all of its individual qualities and intensities. You would not lump together the sensory processes of vision and audition, of taste and of smell, of pain, touch, and temperature; but you would study each in its own right. This would add to the complexity of your task: but it is a complexity which arises out of the nature of sensory experience. The psychologist and psychiatrist must challenge the neurophysiologist with the necessity of undertaking to explain not 'Consciousness' but the multiple phenomenology of varied conscious states.

Therefore at this point it is relevant to emphasize the seemingly paradoxical but basic fact that although we cannot get along without the concept of consciousness, actually there is no such thing. Consciousness is an abstraction, one facet of psychological processes which are repeated millions of times in the course of every human life, processes which are infinitely variable, yet all of which have in common this one trait, namely, *the experience of being aware of something* . . . Note please that this is always an *awareness of something*. Awareness-consciousness does not exist alone. It is an abstraction for which we have coined a name. Just

as there is no such thing as redness, only red objects, i.e., objects which reflect or give off or transmit wave lengths which produce an experience to which we attach the word red. Red objects exist but redness is an abstraction. Similarly, *consciousness of something* exists; but *consciousness* is merely an abstraction. Therefore, what the neurologists and the physiologists and the psychiatrists are called upon to understand, to describe, to explain, to predict, and ultimately to control is not the abstraction, but the concrete and varied phenomena of being aware of concrete experiences in specific situations. Integral to this scientific challenge are the many problems arising out of the many variations which occur from the full state of consciousness to partial and altered states, of many degrees and kinds.

I suppose that some philosophers will object to this, and will say that it is a summary and superficial dismissal of a venerable philosophical quandary. I believe, however, that it satisfies in some measure at least the needs of the scientist for a pragmatic delimitation of the problem for experimental purposes. . . .

Furthermore, I am saved from being overawed by these hypothetical philosophers by some august support. Indeed, even as I wrote, my own words had a quality of familiarity, which led me to think back over the years to my first teacher in psychology, the late Dr. Edwin B. Holt, with whom I studied at Harvard in 1913. I turned back to his two remarkable books, *The Freudian Wish* (1915) and *The Concept of Consciousness* (1941) which in turn carried me back still further to Holt's great teacher, William James, and his pathfinding and brilliant essay, 'Does "Consciousness" Exist?' from his *Essays in Radical Empiricism* (1912). A careful study of these three essays would provide a clear basis for our deliberations in this symposium, and would likewise have saved the participants in the recent series of Macy Foundation conferences on problems of consciousness from much philosophical floundering and confusion (1950, 1951, 1952).

It is almost impossible to select for quotation any section of James' brilliant essay, because all of it is relevant to our thesis. At one point, however (page 3), he states the issue succinctly in the following words: 'To deny plumply that "consciousness" exists seems too absurd on the face of it – for undeniably "thoughts" do exist – and I fear some readers will follow me no further. Let

me then immediately explain that I mean only to deny that the word stands for an entity, but to insist most emphatically that it does stand for a function . . . That function is *knowing*. "Consciousness" is necessary to explain the fact that things not only are, but get reported, are known. Whoever blots out the notion of consciousness from his list of first principles must still provide in some way for that function's being carried on.' From this point on, carrying his erudition as always with an unequalled lightness and simplicity, he correlates this clarifying statement with the laboured and intricate erudition of the classical philosophy and philosophers. In an illuminating study of James, Knox (1914) shows how the treatment of the concept of consciousness by James is an essential addendum to the Darwinian theory of survival: i.e. that the process of consciousness performs an essential survival function. The very words that James uses in this connection are interesting premonitions of our current concern with self-steering mechanisms. He writes (Knox, page 18), 'The study of the distribution of consciousness shows it to be exactly such as we might expect in an organ, added for the sake of steering a nervous system grown too complex to regulate itself.'

Another generalization may be helpful to us in our effort to understand one another; namely, that it is not the experimentalist alone who has this impulse to oversimplify. This tendency exists in every scientist as soon as his scientific problems carry him beyond the borders of his own special empire. In his own domain he can accept complexity with comfort; yet he views the subtle distinctions and differentiations in other areas of scientific work almost as superfluous annoyances. He wants to simplify them, so that it will seem possible to apply his own data with confidence.[1] For instance, the experimental physiologist wants to simplify

[1] As an example allow me a personal confession: early in this conference I leaped at the data presented by Dr. Magoun and Dr. Moruzzi which suggest that dissociations may occur between levels of activity in the cortex and in the reticular substance. This brought to my mind at once the possibility that varied states of consciousness may correlate with the different combinations which such dissociations make possible, e.g., (*a*) both augmenting together; (*b*) both diminishing together; (*c*) the cortex augmenting and the reticular substance diminishing; and (*d*) the reticular substance augmenting and the cortex diminishing. The idea occurred that in such combinations one might find some of the neurological substrata for the many puzzling variations in the phenomenology of consciousness. I leaped at this possibility: yet even as I did so I recognized that my leap was scientifically premature guesswork. This is justifiable only if we do not forget that it is speculative; since out of such a speculation much valuable scientific ferment can come.

psychological data; whereas the psychologist in his turn wants to simplify the physiological, anatomical and experimental data. Give each an opening and he will accuse the other of not being able to see the woods for the trees.

What makes it additionally difficult to bridge the gap between the psychological disciplines and the 'organic' disciplines is the fact that psychologists, psychiatrists and analysts do not agree among themselves about what data can be simplified and what must always be treated in full complexity. The experimental psychologist simplifies one group of psychological data, the animal behaviourist another group, the neuropsychiatrist another, and the psychoanalytic psychiatrist still another. This is why you do not find the four of us (to wit, Drs. Rioch, Hebb, Lashley and myself) in full agreement as to which complexities in the phenomenology of consciousness are important and relevant. From your point of view and that of the conference as a whole, it is unfortunate that we do not present a more nearly united front. It would surely make your task easier if we could challenge you with a uniform picture of the nature of the phenomenology of consciousness; and the lack of this must be for all of you a frustrating experience. Yet actually our disagreements give a truer version of the present state of our knowledge than would any artificial unanimity.

This has a bearing on the problem of definition. Many of our confrères have been troubled at the fact that no wholly satisfactory definition of consciousness has been forthcoming. This does not bother me at all; because I believe that definitions should come at the end and not at the beginning of such a research as this. Indeed is this not precisely where the semanticist goes astray? A premature definition is always a bed of Procrustes, into which one can never fit the complex facts of life without lopping off the hands or the feet or even the head. Hence, my favourite semanticist is Humpty Dumpty, who reminded us that when we pay words extra we can make them mean whatever we want them to mean. Clearly Humpty Dumpty had in mind the only useful definition, to wit, the operational definition, which changes with our evolving knowledge of the phenomena for whose definition our researches are the search. Therefore it is my conviction that we will be able to define conscious states, as contrasted with unconscious

states and/or states of altered consciousness, only at the end of the many years of researches which this conference aims to initiate.

With these general reflections, I will end what might be called my philosophical introduction, and turn my attention to the concrete challenge with which this symposium confronts me.

WHAT MAKES CONSCIOUSNESS POSSIBLE?

I want to say with frank humility that I have taken seriously the assignment which you have given me, that I have found it very difficult (which is why my lecture reached you so late), that I have often felt that I was not competent to meet your needs, and that it had been a presumption on my part to accept this invitation. I have thought of the enormous enrichment which the laboratory has brought in recent years to our knowledge of this whole problem. Not so many years ago, when we thought of consciousness we thought only of the cortex and largely of the prefrontal cortex. Now we think of the elaborate structures of the periventricular system, the ascending reticular apparatus, its higher representation in the centrencephalic system, the reverberating circuits of varying complexities, the special role of the perceptual apparatus, the archipallial contributions from the visceral brain, and from outside of the central nervous system itself the play of endocrine factors, of biochemical processes, of oxidation and reduction potentials, of vitamin and enzyme systems (Milbank Fund, 1952), and the special role of all rhythmical functions in the body, and specifically the rhythmical function of the respiratory apparatus which leads us back through the recent work of Barach (1946, 1951), of Kubie and Margolin (1942, 1944), through Kleitman (1939), to Sidis (1909), and all the way back to the early semi-mystical and semi-scientific observations of the Yogis (Rele, 1929).

This is a fantastically rich fare. When I felt most overwhelmed at the prospect of trying to understand and digest it all, my only comfort was the realization that if any one person in this room really could understand it all, then there would not have had to be this gathering of minds, in search of the clarification and simplification which all of us seek here in this symposium.

To match this exciting display of organic wares, what do we as

psychiatrists and psychoanalysts bring to you as clinical phenomena which we are asking you to help us to solve? Here I hope that we can be of some value in ways which I have already indicated, i.e., by posing the problems, and then by being nasty enough to make sure that you do not turn your back on the more complicated ones just because they are so difficult. You have every right to ask us to accept the infinitely subtle complexity of the body; and I am sure that you grant us the same right and duty to ask you to face the equally subtle complexity of the physiological levels of organization.

The first question that we bring to the neurophysiologist is what makes possible a level of integration of psychological functions at which there can be an awareness of things? and conversely, of course, what can interfere or obliterate all function on that high level?

The essential fact to explain is that the human brain can function, to a limited degree, in spite of a total absence of the type of process which we speak of as the conscious processes. Yet just as the word 'consciousness' is poorly represented in our textbooks, so we lack a clearly defined name for its total obliteration or absence. We speak of coma, stupor, torpor, of being unconscious, of dulling of consciousness, of unconscious cerebration, of decorticate behaviour. None of these is either precise or inclusive or even accurate. We have no single word with which to characterize a basic condition of cerebral activity which is devoid both of consciousness of anything and of the capacity to become aware of anything, whether external or internal. This is the state in which the neurophysiological apparatus functions as a machine, devoid of any capacity for awareness of that which is going on around it, of that in which it is participating, or of its own participation. This is the total absence of any process of consciousness: a state of Being without Thinking. Just as we cannot fully understand white without understanding black, we cannot be clear in our characterization of consciousness if we cannot be clear in our characterization of its absence. Therefore our first problem with respect to conscious processes is to characterize more precisely and clearly that which is the neurophysiological *sine qua non* for a capacity to become aware of anything at all. If we can isolate these physiological mechanisms, and if we can determine to what

extent variables on the level of psychological experience as well as physiological variables enter into its determination, we will have established a base of essential operational understanding of the fact of consciousness, its presence or absence, and of its variations.

Here I must introduce a word of warning. It is possible, of course, that the presence or absence of this basic capacity depends solely on organic variables. This is certainly a legitimate working hypothesis. Yet it would be dangerous to assume that this must necessarily be true; because there is much fragmentary evidence to the contrary. For instance, the amount of anaesthetic which an individual requires to achieve deep anaesthesia depends not alone on the mass of active protoplasm, or on the level of tissue metabolism, but also upon the state of tension and anxiety under which the individual labours, and on the play of fantasies, both conscious and unconscious, with which he may be dealing. The same is true of analgesics and of hypoglycaemic states. In experimental work with intravenous narcosis, Dr. Margolin and I presented much experimental data on this phenomenon (1945 a, b). Thus it may be that the capacity or the lack of capacity to become conscious of anything at all may be influenced not alone by anatomical, pharmacological, and toxic processes, but also and simultaneously by emotional processes. In experimental work on the process of consciousness, this possibility must be kept in mind. Furthermore, I believe that the experiments of Magoun *et al.* (1952), and of Barach (1946), to which I will refer below, give hints as to the nature of some of the physiological mechanisms which may transform psychological experiences into psychophysiological influences on the capacity to be aware.

A further warning against an absolutist point of view that the presence or absence of consciousness must depend either exclusively on organic or exclusively on emotional and psychological influences, is found in the work of Dr. Howard Fabing during World War II on the disturbances of consciousness which followed shell blasts (1947). I was privileged to observe some of this work in 1945 at the neurosis treatment centre which the American Army had established in Ciney, Belgium. Here were individuals who had been thrown into states of unconsciousness by the blast effects from a shell which had exploded nearby.

Usually they had been hurled through space. It was not clear whether this was the result of a sudden pressure wave, or whether they had been lifted by the sudden wave of negative pressure behind the pressure wave and momentarily and abruptly decompressed, and whether the initial unconsciousness was due less to concussion than to a sudden syncope from the general decompression and a sudden loss of blood into the abdominal lake. Perhaps all of these factors were at work in some individuals, and perhaps in others one or another preponderated. However that may be, all had in common a period of unconsciousness, and a retrospective amnesia covering memory gaps for certain aspects of the experience. This looked like an organically induced disturbance of consciousness and memory. Nevertheless with abreaction under pentothal followed by coramine the memory gap could be penetrated in a large percentage of these individuals. If we consider that these individuals were subject to enormous emotional pressure in addition to the organic forces, this should not be entirely perplexing (1947). It is of special interest that the one symptom which was resistant was the sensitivity to noise, and that the one thing which never was recaptured was the memory of the sound of the explosion. Since visual impressions must have reached the individual before the pressure wave and the pressure wave before the sound waves, it may be that the individual had become organically incapable of consciousness of anything before the sound had reached him. This, however, is speculative: and it is introduced here only as a reminder of the fact that even this basic issue 'what makes consciousness possible?' cannot be approached from a purely organic standpoint.

At the least it is clear that states of diffuse underlying affective tension, as well as affects which are focused on some particular group of problems, will influence the effects of such organic variables as operations on the brain, drugs, hypoglycemia, or even concussion.

ESSENTIAL COMPONENTS AND VARIABLES IN THE PHENOMENA OF CONSCIOUSNESS

We ask what are the essential ingredients of any psychological process in which awareness of something is the central phenomenon. There must, of course, be an organism capable of receiv-

ing signals simultaneously from many sources both outside and inside the boundaries of its own body, and also from the interface between the outer and the inner world. I base this emphasis on the multiplicity of incoming excitatory processes on everyday observations of the deaf and blind, on experiments in the induction of hypnagogic and hypnotic states, as well as much other neurophysiological experimental work which I will not review here since others will present it fully.

To summarize briefly, my own data make it clear that consciousness of anything implies and depends on an ability to differentiate an 'I' from a 'non-I' world, which in turn depends upon an incessant inflow of multiple afferent excitatory processes, and their continuous sorting, organizing and patterning into perceptual units with their symbolic coding. There is no single sensory modality which is essential for the maintenance of those ego boundaries, which are inherent in the processes of consciousness. For instance, with respect to the two dominant distance receptors, blindness and deafness may be either acquired or congenital without preventing the development of conscious processes or the maintenance of a differentiated ego with the capacity to be conscious. Under all such conditions, however, multiple exteroceptive, proprioceptive, and enteroceptive impulses must be active; and the ego which develops in spite of a lack of one or more of these afferent tools or which persists in spite of their loss is altered, with consequent alterations in its conscious processes. The most familiar example of this is sleep with its intrinsic shift from a preponderance of exteroceptive to a proprioceptive and enteroceptive influx. A pathological example of altered consciousness processes is found in the paranoia of the deaf and the submissiveness of the blind, a subtler 'normal' manifestation of which is the difference between visual and auditory types.

Many years ago the French philosopher, Etienne Bonnot de Condillac (1715-80) recognized that an individual who had only one active sensory modality would not be able to differentiate himself from his environment. In his treatise on sensation (1754) he presents his fantasy of a statue of a man endowed with a sense of smell alone. De Condillac described how such an individual would be incapable of recognizing objects as things which had an existence outside of himself, and how each olfactory sensation

would seem to him *to be himself.* The statue would actually *be* each new odour that reached it; because without multiple, simultaneous, afferent stimuli it would be unable to distinguish between sources within itself and sources outside of itself. De Condillac noted further that, within the limits to which such a statue could 'remember' such experiences, his activity or passivity towards past and present experience would vary: the statue being relatively passive towards a present experience and relatively active in the evocation of its symbol out of the past. (It will be shown below that this multiplicity of perceptual processes and its role in the differentiation of the 'I' and 'non-I' is closely related to the bipolarity of the symbolic process, which is another essential element in a rounded understanding of the process of consciousness.)

Here, however, it is important merely to indicate that these multiple perceptual signals set off in the central nervous system chain reactions with differentiating characteristics, which are of such a nature that gradually during infancy and early childhood afferents arising from without the soma of the individual become distinguishable from those which arise from within that soma, including those arising from the individual's responses to exogenous and endogenous stimuli. It is this which makes it possible for an individual who is equipped with multiple receiving and responding apparatus gradually to differentiate between an 'I' world and a 'non-I' world; i.e., between a somatically and psychologically internal world and a somatically and psychologically external world. Out of this learning process comes the *self-aware component which is always either latent or explicit in the process of consciousness.* Note that all of these consist of perceptual processes, perceptions of concrete signals from both worlds: and that these perceptual processes are essential units in the stream of conscious processes. Note again that consciousness is always of something, never an abstraction; awareness of perceptual experiences and of the concepts built around these perceptual experiences. (A concept is only a percept once, or twice, or thrice removed.) Consciousness itself still remains an abstraction, just as the concept of movement is an abstraction, although every actual movement is a concrete phenomenon.

I have already stated that a moment of conscious process may

have many varied attributes. It is a colloquial short cut to say that consciousness itself has varied attributes: a short cut in which we attribute to the *abstraction* variations which actually occur only in the concrete experience of being conscious of something. The short cut will not lead us into trouble as long as we keep clearly in mind that it is an economizing device for communicating our thoughts about the problem. There is danger in it only when we forget this and treat the verbal short cut as though it had an independent existence, speaking anthropomorphically of consciousness as an entity or process in its own right.

CONSCIOUSNESS IN RELATION TO SLEEPING AND WAKING: ALERTNESS: ATTENTION: HYPNOSIS, INTUITION AND CREATIVITY

I hope that by now I have established three propositions as legitimate working hypotheses: (*a*) that consciousness itself is merely an abstraction, while consciousness of actual things is a definite functioning process; (*b*) that the first task that we as psychiatrists assign to you as neurophysiologists is to explain why consciousness of things can occur at all, what are its essential neurophysiological and biochemical ingredients, and requirements, and how it can be obliterated; (*c*) that consciousness implies and requires a differentiation between an 'I' and a 'non-I' world, with a parallel evolution of consciousness of self and of things outside of the self. This in turn depends upon a multiplicity of simultaneous perceptual processes, and their complex organization and representation through a series of perceptual units, present and past, from which generalizations and abstractions are made, which in turn are represented in the form of concepts with their symbolic signals. All of these steps constitute essential stages in the development and evolution of the consciousness process, both philogenetically and ontogenetically. In turn these steps must ultimately be correlated with stages in neurophysiological development.

In this section of my paper, however, I have thrown together what will seem to be a heterogeneous mass of clinical phenomenology, as indicated by the chapter heading. I have done this deliberately because from each of these comes some aspect of the same lesson, namely that within the level of that type of psycho-

logical process which implies a capacity for consciousness, there can be infinite variety. Therefore, we have to challenge you to join with us in explaining more than its presence or absence *in toto*, on an all-or-none basis. The explanation of the consciousness process must comprehend the states of alteration and reduction in consciousness which we call sleep, in contrast to that state of relative alertness which we call the waking state, and every intermediate state. Certainly sleep is not the same as the obliteration of consciousness which occurs in profound concussion or with deep and prolonged hypoglycaemia, or with decortication, to mention only a few examples. It is probably more accurate to say that we are never either totally asleep or totally awake, and that part of the human organism is asleep when he is at his most vigilantly alert and wakeful, and that part of him is awake and actively aware when he is most deeply asleep. The tacit assumption of an absolute polarity between sleeping and waking has had misleading effects upon much of the experimental work which has been done on these two states. It has already been suggested that the major difference may depend on a shift from the preponderant role of exteroceptive perceptual units in the waking state to a preponderance of proprioceptive and enteroceptive perceptual units in the sleep state.

Perhaps the easiest way to open our minds to some of the problems that centre around these subtle variations in the phenomena and processes of consciousness is to consider some of the interrelated phenomena of attention, of artistic and scientific creativeness, and of hypnosis.

Pavlov emphasized the fact that in the adult as opposed to the foetus, central excitatory processes do not become diffuse but are surrounded and circumscribed by areas of 'inhibition'. From this experimental fact he concluded that the state of hypnosis is nothing more than a physiological extension of any state of maximal attention, i.e. of maximally focused activity, just as sleep itself appeared to him to be merely a physiological extension of a state of sharply focused inhibition around an active excitatory nucleus. Hypnosis loses its mystery thereby and becomes the inevitable physiological by-product of any state of complete concentration. (Kubie, 1941; p. 336). (These issues are developed further in the article by Kubie and Margolin (1944) on hypnotism, q.v., and in

the author's study of 'A Physiological Approach to the Concept of Anxiety' (1941).

The essential characteristic of the processes by which hypnotism is induced were described in the paper referred to above (Kubie and Margolin, 1944) (the psychological aspects on pp. 611-13; the physiological factors on pp. 613-16; the emotional factors on pp. 616-17). These descriptions are directly relevant to the problem under discussion. They pointed out that the essential physiological prerequisite for the induction of a hypnotic state is the creation of a focus of central excitation with surrounding areas of inhibition (or non-excitation), which in turn depends upon: (*a*) relative immobilization; and (*b*) a monotonous stimulus of low intensity (either continuous or rhythmical), to make sensory adaptation possible. Dr. Warren McCulloch made the interesting suggestion (personal communication) that there is a close relationship between sensory adaptation at the periphery, and central extinction of response. As he put it, these two are 'spacially separated but functionally like processes, to be accounted for principally by the factors for extinction already known in the central nervous system'. Controlled psychological experiments with hypnosis as well as daily experience make it clear that many psychological and emotional processes determine which aspect of mentation becomes the central focus of conscious awareness, and which aspects remain on the outer 'fringe of consciousness' (as William James called it), or 'preconscious' (as Freud called it, to indicate that it is in an antechamber to consciousness, where it remains available on need).

Thus within the whole phenomena of conscious functions are two accessible sub-divisions: the Conscious and Preconscious. There is still a third area of 'conscious' psychological process which remains behind an iron curtain, inaccessible and unavailable even on need except through the application of some special procedure of search. It is *conscious* in the same sense that a bell-buoy on an empty ocean is giving off sound-producing waves even if there is no one around to hear, except perhaps a few deaf mermaids. This area of 'conscious' process is that dynamically charged but buried area of mentation, which Freud called 'The Unconscious'. It is not in the focus of awareness; nor does it remain in reserve yet accessible to consciousness, as does the Preconscious.

On the other hand, it is not *unconscious in the sense which I described in an earlier section, as something which is devoid of any potentiality of conscious experience.* To this problem of *Unconscious processes within the area of potential conscious mentation* I will return below. Here I want only to emphasize the fact that in the total phenomenology of those aspects of mentation which carry the potential of conscious awareness, we must recognize three broad spectral bands of mentation: the *Conscious*, the *Preconscious*, and the dynamic *Unconscious.*

At this point I want to single out the *Preconscious* functions for emphasis. 'Preconscious processes drop out of the central focus of consciousness through repetition. Thus all simple activities of life such as breathing, sucking, excreting, moving, crying, are originally random and often explosive acts. Early in life their purposeful execution is learned through repetition, by which they become economically organized into synergistic, goal-directed patterns. As any such act is fully learned, it can be initiated simply by a contemplation of its goal; and as this happens we gradually become unaware of the intermediate steps which make up the act. This great economy is achieved in the process of learning by repetition. It is in this way that we become able to walk without pondering each step, to talk without working out the movements by which we enunciate each word. It is in this way that the violinist and the juggler and the athlete learn complex trains of synergistic movements. It is in this way that our thinking processes acquire seven league boots; i.e. the ability to leap over countless myriads of intervening steps as we perform complex arithmetical processes, for instance. This is the mechanism of intuitive thinking, whether in science or the arts. In each case the intermediate steps drop into the background and disappear from consciousness. Yet they remain accessible to conscious self-examination.'

The importance of this 'preconscious' system of conscious function cannot be overestimated. As has been pointed out by Kris (1952), by Rosen (in press), and by Rapaport (1951), as well as many others, it is inconceivable that we could have any scientific, artistic, literary, mathematical, or indeed any creative functions without the capacity for enormous economies which preconscious processes possess.

Yet preconscious functions pose some of the most difficult questions concerning conscious functions in general. All of these centre around the issue of what happens to the co-ordination among all of the areas within the brain and to their co-ordination with those extra-cerebral processes which together influence the processes of consciousness. Such preconscious phenomena as the following are a few random examples of the problems which demand explanation:

1. An individual sits at his desk working with complete absorption, hearing nothing. Then he walks away whistling a tune that he has not known that he has been listening to, but which a friend had been whistling for a full half hour in an effort to attract his attention.

2. A young patient meets his analyst out dancing on a Saturday night, fails to give any sign of recognition, but on Monday comes in with a dream that they have met dancing; and refuses to believe that this had actually occurred.

3. Many phenomena of somnambulism.

4. A gynaecologist in a dream finds out how to tie a certain type of knot with his left hand deep in a wound. Poincaré solves a difficult mathematical problem in his sleep. Otto Loewe formulates the neurohumeral mechanisms out of a dream. Kekule describes the structure of the benzene ring after a famous dream of six snakes each swallowing the tail of the one in front.

5. The fantastic hypermnesic phenomena that occur under hypnosis, and the many other evidences that the hypnotic state has at its centre a sharp focus of activity, with a surrounding area of maximal extinction, which obliterates everything else except the central focus. Directly related to this are the phenomena of creative thought in mathematics, science, literature, and the arts, the lightning calculators, the idiot savants, etc. (cf. Rosen – loc. cit.)

6. The multiple structuring of the consciousness processes, when there are more than one 'I' centres in a personality, as in multiple personalities, both those in which there is free access between the various 'I' structures, and those in which the different ego-structures are unknown to one another.

7. The altered structure of the consciousness process in states of psychomotor automatism.

These clinical examples challenge the neurophysiologist to characterize accurately the physiological and anatomical substrates of the preconscious as well as conscious systems of consciousness.

In many fundamental ways such preconscious functions form a contrast to the dynamic unconscious . . . Elsewhere it has been pointed out that the dynamic unconscious is no mere limbo of shadow. It is an area of hidden force or rather of whole constellations of force in psychic life. Such unconscious processes are constantly at work in our lives, yet we cannot become aware of them by ordinary methods of self-observation, because they are hidden from us by vigorous opposing forces within ourselves. Throughout life these processes exercise a powerful influence on human behaviour; and it is out of their influence that everything that is neurotic in human affairs has its origin. In this sense everything that we say and do and think and feel serves multiple functions and represents symbolically and simultaneously the conscious, preconscious, and unconscious levels of psychological organization.

In repeated experiments it has been demonstrated that every psychological process, perceptual, conceptual, and executive, can be experienced on levels which are *conscious*, *preconscious*, or *unconscious*, that in varied mixtures we are always operating on all three levels simultaneously, and that any clarification of the interrelations and interactions between organic and psychological variables in the determination of these levels must wait upon the development of instruments for their clearer delimitation. (This problem has been discussed more fully in the recent Hixon Fund Lectures) (q.v.). At this point it is important chiefly to remind ourselves that as far as we know there is no single psychological process, from the simplest to the most complex, which cannot occur on all three levels – from the fullest alert awareness to the most deeply disguised processes of unconsciousness and of sleep. Yet all fall within the general area of conscious processes.

THE RELATIONSHIP OF THE SYMBOLIC PROCESS TO THE CONSCIOUS PROCESS

Fifteen years ago Penfield (1938) indicated that even extensive cortical lesions do not obliterate consciousness. In the intervening

fifteen years much additional information has accumulated to substantiate this, and to indicate that the area around the third ventricle and at the cephalic end of the brain stem is essential to this process.

In 1951 Penfield (1951) described what he called the 'Centrencephalic' system as a diffuse neuronal network, linked equally to the cortices of both hemispheres, high in the brain stem and including the cell masses of the thalamus, and probably constituting the cephalic end of the ascending reticular activator system, which Magoun and his co-workers (1952) have described in the lower brain stem. The evidence is becoming increasingly clear that the activity of this system is indispensable for the consciousness process.

This work is further supported by the experiments of Barach. Barach developed a pressure chamber in which it was possible to maintain gas exchange across the capillaries of the pulmonary alveoli in spite of an essentially complete arrest of respiratory movements. In the course of this work he noted that those patients who reached the most complete state of respiratory rest automatically went into some degree of hypnagogic or hypnoidal dissociation. Similarly Kubie and Margolin (1942, 1944) found that a subject's breath sounds, when conducted through an amplifier to his own ears, often exercise a strikingly hypnagogic effect. This is also linked to the experiences of the Yogis, as described by Rele (1929). This is only a small fraction of the evidence which indicates that the respiratory system and its nuclei and connections in the hind brain have a special relation to the mechanism of the consciousness process as such.

As we go beyond this, however, to a consideration of the variations within the area of the consciousness process it is essential to include a consideration of the variations in the symbolic process, since it is this which mediates our awareness of things. Paralleling precisely the distinction which has already been made between conscious, preconscious, and unconscious psychological processes, there are three types of symbolic representation. And like the levels of conscious organization, these three types of symbolic process form a continuum.

1. At the one end is the symbolic function by means of which we represent abstractions from experience, and by means of which

we communicate to one another our ideas, thoughts, feelings, memories and purposes. This is the conscious symbolic process.

2. There is another symbolic function with which we are familiar in figures of speech, metaphors, and allegory, as well as slang and poetry, puns and jokes. In this symbolic function the concept behind the symbol is translated into a form which is once removed from direct representation, but in which the relationship between the underlying concept and its symbol remains transparent. Literature, art and humour, as well as science and mathematics are built upon this type of allegorical or figurative symbol. This is the type of symbolic function which plays a predominant role in that preconscious functioning which is most highly developed in the intuitive processes of the creative artist and scientist. (cf. Kris, Rosen, etc., loc. cit.)

3. Finally there is the symbolic function in which the expressed symbol is the manifest representation of a latent idea which remains not only unconscious, but also inaccessible to conscious self-inspection even on need.

The function of the symbol in the first type of symbolic representation is to communicate the bare bones of the central idea. In its preconscious form the function of the symbolic process is to communicate not only the central idea but an enormous amount of accessory ideas and feelings which are condensed around and linked to the central idea. The function of the symbol in the unconscious form of symbolic function is to hide something, i.e. to render the central idea impenetrable.

It is a fact which has been demonstrated in many studies of the evolution of the symbolic function, Kubie (1953), that every symbol is anchored simultaneously both in the 'I' world of internal perceptual processes, and in the 'non-I' world of external perceptions. This is true of a literal symbol which is predominantly *conscious*, of the metaphorical symbol which is predominantly *preconscious*, and of the obscure symbol whose roots are predominantly *unconscious*. It was pointed out that as a consequence every symbolic unit 'hangs like a hammock between these two poles, one internal or bodily, the other external', and that the processes of consciousness always involve simultaneously and with varying degrees of clarity, an awareness of internal and of external percepts. Whenever we consciously think and speak

of an outer world we are wittingly or unwittingly thinking and speaking with reference to an inner world at the same time: and similarly when we are consciously thinking and speaking of that inner world, then whether we are aware of it or not we are simultaneously referring to elements in the outer world. Experiments which bear this out were recently conducted in the operating room of the Montreal Neurological Institute through the generous hospitality of Dr. Wilder Penfield (Kubie, 1953 b, c).

In turn all of this links to the problems of memory and especially the various kinds of memory, which also challenge the neurophysiologist, to wit:

1. The memory which depends solely upon verbal clues with a minimal evocation of vivid sensory imagery.

2. The memory which evokes the past with something more than purely verbal representation, i.e. with participation by those sensory components which are predominantly exteroceptive, plus some proprioceptive components of tactile and kinesthetic sensations (in other words the afferents that orient us to the external world).

3. Finally there are those rare memory experiences which evoke the past with such vividness that there is some measure of actual reliving. These involve enteroceptive components, i.e. the 'gut' components of memory, which can evoke a full affective re-experiencing of the past almost as though it were the present, sometimes to the point even of obscuring the clear differentiation between the past and the present. The same article (Kubie, 1953b) discussed in detail the significance of Penfield's work and of other recent investigations for these three categories of memory. For our present purposes it is sufficient to indicate that all of these variations involve changes in the quality and quantity of the phenomenology of consciousness; and that these too must be comprehended in any rounded investigation of the problem of consciousness from the electrophysiological and neurophysiological point of view.

On this difficult note I will close my discussion by quoting from that same paper the following description of a personal experience (p. 29):

'Not long ago I watched words at work busily screening and denaturing a full-bodied psychological experience. I was return-

ing to New York by plane, dozing fitfully, in and out of half-waking, half-sleeping reveries which were essentially hypnagogic in quality. Finally there was one of great complexity, multiplicity of action, vivid, and highly emotional – sufficiently emotional in fact to stir me to full wakefulness. As I wakened, the dreamlike imagery passed through a swift series of transformations, each simpler than the last, each losing some of the emotional charge and sensory vividness of its predecessor, until finally I found myself fully aroused with nothing remaining in my mind but a dry and dusty packet of words. All of the blood and guts were out of the experience. Words had served their customary purpose.'

SUMMARY

Let me briefly summarize my general thesis as follows:

1. Consciousness is an abstraction, and cannot as such be the object of scientific investigation. There are however concrete experiences of being conscious of something which may be investigated with respect to (*a*) the presence or absence of consciousness of anything; (*b*) the factors determining whether or not consciousness of something is possible; (*c*) the many vicissitudes and variations to which the process of being conscious of something is subject.

2. Consciousness of anything implies a capacity to differentiate between perceptual processes which pertain to the self (the 'I'), and those pertaining to the rest of the world (the 'non-I'). The development of this differentiation between an 'I' and a 'non-I' world is intrinsic to an understanding of the development of the process of consciousness, and must be considered and explained in relationship to it.

3. Concurrently with the development of the awareness of these two fundamental worlds arises an awareness of moments of perceptual experience, both past and present. Then comes the awareness of elisions and condensations among these multiple perceptual experiences, awareness of generalizations from multiple experiences, awareness of conceptual abstractions of such generalizations, and finally an awareness of the symbolic units by which such concepts are represented. This is the hierarchy from the simplest perceptual components of experience, both past and

present, through stages of condensation, generalization, abstraction and conceptual representation in symbols which comprise the total complex paraphernalia of the process of consciousness.

4. The neurophysiologist must ask at what point in ontogeny and in phylogeny the capacity emerges to become aware of perceptual experience.

This can be broken down into certain sub-questions:

(*a*) At what stage in phylogenetic development does awareness of each of these levels become possible: from the simplest perceptual to the most complex symbolic representation of abstract concepts?

(*b*) At what stage in the ontogenetic evolution of each human being does this become possible?

(*c*) What types of disorganization of the central nervous apparatus can occur so as to limit the development of this capacity, or to obliterate any pre-existing consciousness potential?

5. Assuming that the consciousness potential has developed and has remained unimpaired, then what variations can and do occur within the consciousness processes themselves, confronting the neurophysiologist and the electrophysiologist with phenomena to explain?

I have tried to make it clear that the consciousness process must be understood on three general levels of organization: (*a*) the full conscious awareness of things; (*b*) the level which has been called the 'fringe of consciousness' or the 'preconscious'; and (*c*) the level of dynamic unconscious, i.e., of inaccessibility even on need. All psychological processes, including all symbolic processes, function simultaneously on all three of these levels.

6. Finally, as is clearest in the dream, all processes of consciousness have both manifest and latent components, and all have both 'I' and 'non-I' components. This makes inevitable a simultaneous awareness of subjective and objective data, which is characteristic of and essential to the processes of consciousness; but which again is most clearly and naively observed in those dreams in which as onlookers we see ourselves in action. Closely related to this is the bipolar anchorage of the symbolic process, on conscious, preconscious and unconscious levels, to both the 'I' and the 'non-I' worlds. When all of these aspects of the process of being conscious of something are understood in neurophysiological terms

we will indeed be well on our way towards a mature understanding of the physiology of psychology.

GROUP DISCUSSION

JASPER: I am very grateful to Dr. Kubie for giving us the breadth of our problem. There are many ramifications which eventually must be incorporated into our thinking, though perhaps we may not be able to achieve this at the present time.

HEBB: I wonder whether Dr. Kubie feels that there are only very few items in consciousness; I was thinking of the preceding discussion as Dr. Kubie was speaking, and it seemed to me that what he has said implied not a small number but a great diversity, more or less clearly present at the same time.

KUBIE: I can answer this only through a diagrammatic figure of speech. If we think of a large area of data on an equipotential plane, and out of that area gather all that is accessible to those processes by which we became aware, then the moment of awareness is like a beam of light which scans the total area constantly. That which is the centre of the beam, at any given moment, is just a small fragment of the whole field. At the same moment, there are also elements which exist behind what I call an 'iron curtain' in that they are not accessible to us without special exploratory instruments.

PENFIELD: You referred to the phenomena of the dynamic unconscious. Can you give us a hint as to what you think the neurological mechanisms are which are responsible for that kind of unconsciousness?

KUBIE: I have never been able even to imagine any satisfactory neurological mechanism for this phenomenon before this conference. I do not think that there are any moments in our life in which our behaviour is not being concurrently guided by an admixture of conscious, preconscious and unconscious processes. All of them are always operating together, in varying admixtures. We have not known the mechanism by which unconscious dynamic mechanism operate, nor the mechanism by which they are blocked. It is probable, however, that when we understand how conscious and preconscious processes operate we will understand how unconscious processes operate; because there is much evidence that they operate in exactly the same way, except that they are separated by a wall, the nature of which we do not know. At least, I think that this is a reasonable working hypothesis.

JASPER: It is interesting how Berger was speculating about this in his first work on brain waves, when he concluded that brain waves were chiefly representations of attentive mechanisms and that attention was

chiefly an inhibitory process, blocking everything but a small portion of the activity of the brain.

WALTER: When one talks about this wall, which is a little worrying from the neurophysiological standpoint, I would suggest again that the mechanisms of conscious awareness might depend upon a statistical sorting based on some built-in or earlier acquired criteria. It is just conceivable that the wall you are speaking of might be the lack of a statistical criterion; that signals have entered the nervous system, have gone through a process of selection but cannot fire the spot of insight because there is no criterion established as to whether they are significant or not. If in later life a criterion of significance *is* established, then suddenly a whole field of experience which has been stored in an unprocessed form becomes available for significant assembly.

KUBIE: When you say significant, you mean statistically significant?

WALTER: Yes.

KUBIE: It is a word which carries many connotations. When you speak of statistical significance you mean one thing. Emotional significance is another.

JUNG: On a similar line, I would like to ask Dr. Kubie about amnesia of early childhood. Is it not easier to explain it, by a lack of background and of a framework collecting the data than by dynamic psychoanalytic processes?

KUBIE: I have many doubts about details of the problem of infantile amnesia, but no doubt that it occurs. There are sufficient experimental and clinical data which show the existence of these lacunae in memory. I had, as a patient, a very bright woman, who had many precise memories from her early childhood. She could remember very well the log cabin in which she lived, but only the outside of it, never the inside. Yet we later discovered that many important events occurred inside. With hypnagogic and pharmacological devices, the shutters suddenly opened, and she was able to remember the inside of the cabin in great detail. A process seems to operate which scotomatizes often those details which are emotionally most important. Assuming that the child withdrew from painful experiences by thinking about them less and less, would it not be possible that in the course of time the number of signalling channels which were established will become fewer and fewer?

MAGOUN: There is a trend, in recent neurophysiological writings, to attribute emotional activities to the rhinencephalic part of the brain. MacLean has recently reviewed the data and I would only point out now that the work which Green and Arduini have been doing in the past year has shown that the hippocampal component of this brain area is accessible to afferent excitation of all modalities and that, upon

arrival there, such incoming stimuli induce a series of large slow waves, from 3 to 7 a second. They have also shown that this slow wave activity which, as Dr. Walter could tell us better than anybody else, may be related to the theta rhythm, is reflected back into the diencephalic portion of the brain stem by way of the fornix. I hesitate to propose any more generalities at this gathering, but nonetheless the question comes to my mind as to whether there might be some kind of interference or interaction between discharge conducted to the hippocampus, elaborated there and thrown back into the remainder of the brain, with activity proceeding between thalamus and neocortex. Whether there is any relation between these observed or proposed electrophysiological events and the psychological phenomena which Dr. Kubie has been discussing remains to be seen.

KUBIE: The reason why I was impressed by the work of MacLean and by what Dr. Penfield and others have said in this symposium, is because it seemed that there we have an apparatus in the brain which makes it possible to see how all interoceptive, exteroceptive and proprioceptive experiences, emotionally charged or not, can be brought to one meeting ground, through the deeper structures of the temperoral lobe, and what MacLean calls the 'visceral brain'.

PSYCHOPATHOLOGICAL AND NEUROPATHOLOGICAL ASPECTS OF CONSCIOUSNESS

By

DAVID McK. RIOCH

The phenomena referred to by the term 'consciousness' – including sensations, feelings, emotions, motives, and so forth – cannot be directly communicated and must therefore be inferred. For most purposes in the past it has been sufficient to use the subjective conclusions of the observer with regard to the characteristics of the observed subject. In other words, it has been sufficient to use the hypothesis derived by the observer and to regard this hypothesis as a property of the subject. Thus, when an amputee in an orthopaedic ward says that he feels his hand is attached to the stump of the upper arm and that the hand is painful, different observers project different properties into the subject. The range of properties projected into the subject depends on the school of thought to which the observer adheres and to his anticipation of his technical competence to modify the performance and verbalization of the subject. One observer projects a 'pathophysiological state' in the neurinoma and/or in the 'body schema' of the subject. Another observer concludes there is a 'libidinal investment' of the stump due to a 'castration complex'. Recently Captain Douglas Price, M.C. (Noble, Roudebush and Price, 1952) found that a very high percentage of amputees who developed painful stumps were patients who did not have visitors, and that the pain stopped with change in the social *milieu*.

Since the pioneer work of Georg Simmel (Wolff, 1950) and of George Mead (1934), a considerable number of investigators have emphasized the necessity for including observations on several different classes of data and for taking longer time intervals into account for the purpose of deriving generalizations concerning 'consciousness'. (cf. Spiro (1951), Sullivan (1940, 1950), Ruesch (Ruesch and Bateson, 1951), Riezler (1939).) That

many current concepts of 'conscious' processes may need radical revision has been discussed at some length by Glover (1952) and will not be further considered here. Recent studies on the physiology of somatic sensation (cf. Cohn, 1953) indicate that attention has to be paid not only to data on the anatomy and physiology of the nervous system and end-organs, but also to the subject's *perception* of his body as extended in time and space, and to his *conceptions* of his potential capacities for functioning in the environment, and of his status in his social *milieu*.

The study of 'consciousness' thus involves the explicit operational formulation of the patterns of interaction between the subject and his environment, recognizing that the observer is a participant. Rather than further discussing this theoretical proposition, it is proposed to present in this paper, first, some notes on certain characteristics of the patterns of interaction of patients in schizophrenic states and, second, some generalized formulations of the characteristics of the patterns of interaction between the organism and the environment mediated by phylogenetically determined divisions of the central nervous system.

CERTAIN CHARACTERISTICS OF 'CONSCIOUSNESS' IN SCHIZOPHRENIC STATES

I have been interested in the question as to whether patients in schizophrenic states are 'conscious' or 'aware' of differences between hallucinations and delusions on the one hand and what is ordinarily termed 'reality' on the other.

If the investigator discusses the hallucination or delusion either in terms of questioning, agreeing, or negating such concepts, the patient tends to become more and more concrete in his formulation and affirmation. This 'concretization' has been widely recognized as a characteristic of what is called schizophrenic thinking. On the other hand, if the investigator responds in terms of the needs of the patient, which are tangentially referred to by hallucination or delusion, or if the investigator treats the hallucination or delusion as a symptom and looks into the questions of the precipitating events and of the purposes served, the response of the patient is frequently very different. In many instances it may then

be determined (sometimes with extraordinary rapidity) that the concrete hallucination or delusion is in fact a highly condensed symbol referring to acute problems in the patient's interpersonal transactions. Thus, the pattern of interaction between the patient and the investigator is quite different, depending on the approach and attitude of the investigator.

It is further to be noted that when a patient in a schizophrenic state describes the significance of some symbolic or ritualistic act, his formulation varies, depending on the observer to whom he is talking. Thus, a self-mutilating act (such as amputation of an ear) may be formulated in one situation as an experiment to demonstrate the power of mind over matter and that the amputation can be performed without pain. On another occasion the act may be formulated as 'trying to get mother out of me'. (In passing it may be noted that the concept 'mother in me' is frequently met with in male schizophrenic patients.) With another interviewer the same act may be described as part of a frustrated love affair, or a number of other 'explanations' may be given. In general, the explanation used with any particular observer seems to be designed to fit the interests of the observer and to assure continuity of communication.

Data in this field are still to a large extent in the form of anecdotal descriptions and hence do not justify any firm conclusions. It is suggestive, however, that schizophrenic patients either are in some way aware of the difference between their projected symbolic formulations and operationally verifiable events or that schizophrenic states are frequently interrupted by brief intervals of 'clarity and insight' (Harry Stack Sullivan, personal communication). Analogous differences in many 'average normal' people between their reactions to *opinions* and their reactions to *events* are of everyday occurrence. Whether the differences between the average normal and the schizophrenic are qualitative or quantitative still has to be determined.

One patient offered the following explanation for the concretization of the symbol. He said that one '*has* to be concrete, specific'. 'It is too dangerous to be general or abstract. You never know what implications the person you are talking to will draw from what you say unless you are concrete.' In this respect, as in many others, the chief problem in the psychopathology seems to

lie in the anticipation of and preparation for the probable responses of the environment. It seems as though, with the anticipation of increasing difficulties in the interpersonal transactions, the patient in a schizophrenic state attempts to simplify the situation by becoming more concrete. Unfortunately the result is to increase obscurity.

In talking with schizophrenic patients I have been impressed with the extent to which other people in the environment are ignored. If I pay attention to someone else nearby, the patient is very likely to indicate that he feels hurt and slighted. During the course of the conversation the patient's references to other people are in the form of fixed definitions, without expectation of these people being influenced by what is said or done at the time. When the patient turns from me to someone else he similarly ignores me in turn. However, when the patient deals with the 'staff of the hospital' or with the 'doctors and nurses', the group is dealt with as a unit, not as a group consisting of several variables. It is as if there were a reduction in the number of interacting variables which can be dealt with at a time. The interaction with the separate persons, however, shows great finesse when observed sequentially.

In a somewhat analogous manner problems are discussed as though they were separately all important and as though existence as a human person depended on the answer, yes or no. Decisions are between black and white. There are no shades of grey, unless by verbal definition, and the average normal-neurotic 'compromise' is intolerable.

I have also had the impression that consciousness of the sense of continuity of time is modified. Schizophrenic patients refer to episodes as isolated events, not related in temporal sequence to preceding and succeeding events. It is as though 'that which is *now*, is *always*; and that which is *not now*, is *never*'. (This is in striking contrast with the disturbed neurotic patient for whom *now*, *always*, and *never* seem to be practically non-existent and are replaced by *soon*, *perhaps*, and *maybe*.)

In line with the interests of this symposium I should like to call attention to a series of studies on psychiatric symptomatology accompanying disturbance of brain function (produced by physical or chemical agents) which have been carried out by Dr.

Edwin Weinstein and his collaborators at the Mt. Sinai Hospital and the Walter Reed Army Hospital. (For the bibliography on this work, reference should be made to Weinstein *et al.*, 1953). Certain, though not all, patients with diffuse abnormalities of the forebrain or with small, bilaterally symmetrical lesions of the midbrain show psychiatric changes during the period in which the EEG is abnormal. The type of symptomatology correlates with the premorbid personality of the patient. Of particular interest are the symptoms of delusions – e.g. denial of illness, denial of parts of the body, reduplication of time and place – disorientation, and paraphasia. In the premorbid state these patients were usually obsessive and perfectionistic or showed paranoid types of attitudes. Such symptoms have in the past been commonly considered as 'confusion'. It is found, however, that the changes fit an organized pattern and that the mode of communication is one in which the symbols used are 'experiential', in contrast with the conventional normal 'referential' symbols, to use the terms introduced by Sapir. In other words the symbolic communication of these patients includes factors of personal needs, rather than reference with conventionally normal precision to objects, events, places, etc. The symptoms clear when the EEG becomes normal.

Whether or not abnormalities in the EEG are *necessary* for the appearance of this symptomatology under all circumstances is not yet clear. Similar syndromes have been described in seriously ill patients without head injury, such as in patients with extensive burns (Hamburg *et al.*, 1953). Also, frontal lobotomized patients deny the operation for years later. Indeed, occasionally their parents also deny that anything was 'done to the patient's brain' (Dr. Oscar Legault, personal communication). This condensed symbolic form of communication would appear to be a not uncommon defence against further disorganization of function on anticipation of threat to personal integrity.

CERTAIN ASPECTS OF THE NEUROPATHOLOGY AND FUNCTIONAL NEUROANATOMY OF 'CONSCIOUSNESS'

In the second section of this presentation I wish to offer a skeleton outline of a general hypothesis concerning the roles of sub-

divisions of the central nervous system in patterns of interaction ordinarily classified as 'conscious'.

The various functions of those structures which Adolf Meyer referred to as the 'segmental apparatus' have in general a common characteristic of 'local sign', as pointed out by Sherrington. This refers to the fact that the stimulus evokes more intense activity close to the level of input with decreasing activity with distance from this level. There is no total organization of the segmental apparatus. (Partial exception to this statement may be represented by the scratch reflex and by alternating walking movements.) The central nervous apparatus characterized by the phenomenon of 'local sign' may, in the case of the hindbrain, show sequential activity, such as in righting reflexes, swallowing, etc. These more complex patterns would appear to be in the nature of chain reactions. In contrast with this, behaviour patterns which require the integrity of the reticular nuclei of the midbrain appear as stereotyped units in which the whole organism is integrated. Such patterns include sleep and sleep postures, fighting behaviour and, in female animals, coital behaviour. When one studies preparations surviving total removal of the neocortex together with parts of the paleocortex, one finds a wide variety of patterns of behaviour, including various escape reactions, fighting behaviour, etc. Under various conditions of stimulation one or another of these patterns appears, but no mixtures are seen. It would seem as though these parts of the nervous system mediate an integration of the organism as a unit and that the response of this unit is directed towards that part of three-dimensional space in which the particular stimulus originated – as though the whole universe were concentrated in the said stimulus. Pitts and McCulloch (1947) have discussed a mathematical model of the functions of the superior colliculus from this point of view. They describe the mathematical treatment as a 'double integration'. Taking the liberty of using the term 'integration' in the Sherringtonian rather than in the mathematical sense, one may say that the neodecorticate animal integrates the organism as a unit, integrates three-dimensional space as a unit, and at the same time determines the nature of the interaction between the two. In contrast with this form of behaviour the functions of the neocortex may be best described as those of 'differentiation'. Dr. Penfield first pointed

out to me several years ago that electrical stimulation of the neocortex characteristically results in very precise, localized responses, whereas electrical stimulation of the subcortical structures evokes either patterns of behaviour or postures involving the whole organism. Pitts and McCulloch, in the same paper referred to above, also describe this contrast between the functions of the neocortex as compared with those of the brain stem. They discuss the problem in terms of responses to visual stimuli. Analogous results were obtained in two decorticate cats in response to auditory stimuli in some preliminary experiments on this problem. These preparations responded to scratching noises by pricking up their ears, opening their eyes wide, arching their necks and running towards the source of the sound. When presented simultaneously with similar noises from two different sources subtending an angle of approximately 60° at the position of the cat, the response was entirely different. The cat oriented to a point between the sources of sound, but the ears were laid back, the eyes screwed to slits, the teeth bared in a snarl, the head retracted, and the forelegs braced.

A few experiments of the reverse type – that is, with lesions in the midbrain, leaving certain cortical mechanisms intact – were also performed. These consisted of removing one occipital pole (in order to get adequate exposure of the midbrain) and both superior colliculi, together with the dorso-rostral parts of the reticular complex of the midbrain. The retino-geniculo-striate system of the contra-lateral side was intact and the cats showed strong blink-defence responses. However, when placed on a table they walked off the edge, on the floor they bumped into objects or the wall, and to all appearances they behaved as though blind. This condition lasted for some three weeks, following which it was noted that certain responses to visual input reappeared. These, however, seemed to be abnormal in that single objects were responded to as units and not in relation with other objects. Thus a cat walking on the table would stop at the edge. If a food bowl were placed on the table the cat walked straight to it and ate. If the bowl were held a foot beyond the edge of the table the cat walked straight towards it but fell off the edge of the table. Some, but not all, of these cats showed the amusia and loss of the fighting reaction described by Dr. Magoun (Kelly, Beaton

and Magoun, 1946), in cats with lesions in the same general area.

On the basis of these observations, as well as on others on the differences between normal, decorticate, and midbrain-lesion cats, it would seem useful to formulate an hypothesis somewhat as follows for the planning of further experiments. The functions of the brain stem, particularly of the reticular nuclei of the mid- and upper hindbrain, are related to the integration of the organism in three-dimensional space in one or another pattern of interaction, i.e. 'attitude' or 'psychological set'. Anticipatory behaviour may be evoked, but it is completely stereotyped. The neo-cortical functions are those of differentiation of parts of the organism and of parts of the environment, and also of temporal sequences. These highly complex differential functions can be carried out only if the brain stem integrative functions are stable.

The adequate functioning of the intact nervous system, then, depends on the transmission of information between these two major systems. One extensive mechanism for transmission of information upwards, namely, the reticulo-thalamo-cortical part of the centrencephalic system, has received considerable attention from neurologists, physiologists, and anatomists. The mechanisms for transmitting information from the cortex to the midbrain are less well known. Dr. W. J. H. Nauta in our laboratory has found numerous direct connections from the neocortex to mesencephalic and closely related centres. These include extensive diffuse projections from the cingulate and frontal (including motor) areas to the reticular nuclei; large numbers of connections from the striate cortex to the superior colliculi; and connections from Auditory I cortex to the pretectal area and the region of the zona incerta.

Another descending system consists of paleocortical-hypothalamic-mesencephalic pathways. The functions of this system apparently differ from those of the neocortical systems in a quite important respect. Whereas the neocortical systems have to do with the differentiation of more or less precisely defined spatial factors in more or less precisely defined time sequences, the paleocortical systems appear to be more concerned with feeding behaviour on the one hand and, on the other hand, with putting the organism into contact with the environment in terms of attitudes rather than in terms of precise movement. This is well

illustrated in the beautiful experiments reported during the past few years by Klüver and Bucy (1939), Bard and Mountcastle (1948), Schreiner and Kling (1953), and MacLean (1952) and Delgado (MacLean and Delgado, 1953).

In closing this discussion, I wish to call attention to two classes of behaviour patterns, both of which may be regarded as 'anticipatory' in nature. The first is well shown by cats lacking the neocortex and may be illustrated as follows. A decorticate preparation which has been starved for twenty-four hours shows considerably increased activity, walking almost continually about the cage or the laboratory. If a bowl of fish is brought into the room the activity is markedly increased, but the food is only 'found' accidentally. A normal cat similarly shows increased activity. However, it approaches the caretaker, miaows, goes to the regular feeding area, etc. When food is brought it turns head, eyes and ears towards the source and approaches the food prepared to eat, but also, if threatened in any way, prepared to resist or escape. That is to say, with the paleocortical-brainstem systems, anticipatory behaviour patterns of one class occur, directed towards *single general organismal needs*. With the neocortical differentiating mechanisms, the organism shows another class of anticipatory behaviour patterns in which there is preparation for *several probable responses from the environment*. Whether these two classes of behaviour represent different degrees of consciousness or whether a criterion defining consciousness has to be drawn somewhere between them has still to be decided.

JASPER: This is our last session together and I want to stress our two objectives in this final discussion period. The first objective is to attempt a synthesis of the various conceptions expressed by members of the group. The second, and perhaps the most important one, is to put our finger on the most important gaps in our knowledge that we shall attempt to bridge during the coming years; in other words, let us look to the future. Dr. Magoun, may we have your views?

MAGOUN: I am a little diffident at being the first to speak, but I feel that when trends in neurophysiology are considered broadly, all of us would probably agree that, in addition to the investigation of reflexes, a dominant interest in the past twenty-five or more years has been the study of the main sensory and motor systems of the brain. Just as delineation of the major, long, compact and conspicuous afferent and efferent paths and their relays was first undertaken in study of the anatomy of the brain, so also has been the investigation of their physiology. This interest is obviously a continuing one but I have been impressed, on thinking back upon the papers and discussion of this symposium, that there has been shaping during the past decade, since Morison's and Dempsey's pioneering efforts, a major parallel programme of investigation of the diffuse or non-specific central neural systems. It has been necessary to delineate the organization of these systems at the same time that their functions were being explored, or perhaps it would be franker to say that, until the current work of Nauta, Whitlock and Olszewski, their organization has been deduced very largely from functional studies, since the foundation of anatomical knowledge of the diffuse mechanisms of the brain had not previously been laid, as was the case for the classical sensory and motor mechanisms.

As a result, the temptation to cover a rather extensive territory in a relatively brief interval of time has proven irresistible to most of us, and the gaps that still exist in knowledge of the non-specific systems are enormous. The functional relations of the lower ascending reticular mechanism to the diffusely projecting

thalamic nuclei, our present ignorance of which has been emphasized at this symposium, the intimate physiology of activities at every level and particularly in the cortex, and the many ramifications that will doubtless open for study as the corticifugal influences upon the subcortical reticular mechanism are investigated further, among them the role of the basal ganglia, are areas that suggest themselves immediately as meriting further exploration. Additionally, the significance of the inverse manifestations of non-specific influences upon the electrical activity of the paleo and neocortex is of great interest. There are, therefore, many problems remaining which collectively have to do with the intrinsic physiology of the non-specific systems of the brain.

Of equivalent interest and importance are problems relating to functional interrelations between the non-specific systems and the classical sensory and motor mechanisms of the brain. Earlier study has explored some general features of descending reticular influences upon lower motor outflows and the recent extension of these studies, by Granit and his associates (1952), to influences upon the gamma-efferent supply to muscle spindles has shown the important regulatory influences upon proprioceptive input that can be effected by this means. The programme which Hagbarth and Kerr (1953) have inaugurated indicates potent influences of non-specific systems upon transmission in afferent systems at the first central relay. Initial exploration has demonstrated the manifold contributions of classical afferent paths to the non-specific system, but many features of this are still to be investigated. Almost nothing has yet been learned of the interrelations of the classical sensory relay and the non-specific systems at the thalamic level and we are, if possible, more ignorant still of the interaction of the different functional areas of the cerebral cortex, though considerable anatomical information concerning the thalamus and cortex is at hand as a foundation for such study. A broad and systematic investigation of the physiology of interrelations between the non-specific and the classical sensory and motor systems of the brain can be expected, therefore, to yield a rich harvest of new information.

Methodologically, much study will doubtless continue to be undertaken in acute experiments and to be limited to observation of records of the electrical activity of the brain. In particular

continuation of the programme of unitary analysis, with microelectrode recording, begun by Moruzzi and his associates, by Li and Jasper and by Amassian can be expected to make major contributions. Extension of study to the chronic preparation has the great advantage of being able to relate the findings to behaviour and, in this connection, interpretation of the consequences of direct stimulation of the brain of the waking, behaving subject deserves comment.

From his extensive experience with this technique in the operating room, Dr. Penfield has pointed out that such stimulation may either excite or interfere with neural processes. The latter concept may be of considerable relevance for an understanding of the puzzling arrest of behaviour briefly discussed earlier in this symposium, which is evoked by stimulation, in the waking, behaving animal, of the cingulate gyrus (Sloan and Kadda, Clark *et al.*), caudate nucleus (Akert and Anderson, Heath *et al.*) or the non-specific thalamic nuclei (Hunter and Jasper). Viewed literally, the findings would attribute a type of inhibitory function to these parts of the brain, reminiscent of the suppressor role proposed earlier for the cingulate cortex and caudate by McCulloch and Dusser de Barenne. Alternatively, from the point of view of interference with their spontaneous patterns of firing, by discharge imposed by direct stimulation, the activity of these parts of the brain could be conceived as providing an essential substratum for waking behaviour, the arrest reaction being a paralytic manifestation. If this interpretation is correct, these parts of the brain would normally serve excitatory rather than inhibitory functions and the technique of interference by stimulation might be cultivated as a valuable experimental procedure in the study of brain mechanisms involved in behaviour.

Parenthetically, conclusions from the earlier work on the suppressor mechanisms of the hemisphere might similarly be inversely interpreted. These experiments were conducted under Dial anaesthesia and demonstrated an arrest of barbiturate bursts, an alteration that can be conceived as a type of EEG desynchronization or activation. I am aware that suppression is currently identified as spreading depression, associated with DC potential changes and vascular alterations, but the cortical and subcortical regions most involved seem closely related to the non-specific

system. This matter might bear further study and certainly attention should soon be directed to the question of whether DC alterations are associated with the activity of the non-specific systems.

JASPER: Thank you, Dr. Magoun, for your statement. Would you carry on the discussion, Dr. Walter?

WALTER: In man the electrical features of brain activity which seem to depend most intimately on something like the state of consciousness are the dispersed and variegated responses to pattern stimulation, such as I showed the other evening. These are found mainly in the temporal and frontal regions. In patients with circumscribed basal lesions and also in hemispherectomized patients, evidence seems to be accumulating that, although cortex obviously contributes very largely to the variety of these responses, it is not essential for their projection. One question I wanted to ask was: What should one look for in human neuroanatomy in the way of a structure most likely to provide for the projection of these widely dispersed and variegated patterns which are related to the attitude or awareness of the subject. On theoretical grounds, and on the experimental evidence, there should be two relatively non-specific projection systems arising near the afferent channels and terminating somewhere in cortex in nearly all regions; how should one look for these systems? It does not seem likely that one could make very orderly anatomical observations on autopsy material; but in the flow-through of pathological specimens, what particular features of the case-histories and the pathology of biopsy or autopsy observations should one ask one's clinical and pathological colleagues to be on the lookout for? This is my own position in relation to this problem.

MAGOUN: It would seem to me that the field is open in clinical investigation to all of the topics which have come up in animal studies. These are not peculiar to animals. They are investigated in animals only because there are the preparations available to the anatomists and physiologists for study. I think it is the hope of all of us that any gleanings that we gain from our laboratory work may be investigated in man and their conclusions tested in man.

WALTER: What I meant more specifically is this. We receive patients for examination in whom the dispersed and variegated

responses to pattern stimulation are exaggerated in a part of one hemisphere or are absent or have some peculiar character. Later on, the patient may be operated on, or dies or in some way falls subject to pathological scrutiny. The pathologist may be anxious to help but is not necessarily aware of what method of examination he should use; what part of the brain he should look at most carefully; and what particular histological method he should use in order to tell us something about the relation between these putative projections and our experimental findings. The pathologists often ask: 'What should we do? Should we take ordinary serial sections. Which stains should we use?' And I am sorry to have to say 'I don't know.' What method is approved by the physiological anatomists in their animal preparations?

MAGOUN: We have a man here who, for a lifetime, has provided outstanding illustrations of how clinical cases can be explored physiologically and I would far prefer to hear Dr. Penfield's reply to this question rather than attempt to answer it myself.

PENFIELD: Well, one must try to think as physiologically as possible, and so be able to ask questions that are of physiological significance when the pathological material or human material presents itself. It is impossible to outline a place applicable to all situations. It seems to me that we should suggest to our pathologists that they begin to study the diencephalon and midbrain more carefully from the point of view of what portions were functionally active and what portions were obviously incapable of action during life. An occasional case will turn up that will shed a brilliant light on our problems, particularly if the patient has been well studied beforehand. The studies of Stern (1939) on the single case of a lesion of the thalamus is an example, also my own fortunate autopsy of a single patient with diencephalic epilepsy (Penfield, 1930). So many autopsies are wasted because these very areas that we have been discussing this morning were not studied and I realize that very few people are able to study this whole complex diencephalon because the anatomy is not clearly enough described yet. That is why I think the preliminary anatomical work such as Dr. Olszewski and Dr. Nauta have been describing is very important as a prelude to pathological studies.

OLSZEWSKI: I think it is needless to stress that anatomical studies present many difficulties. The purely technical but most import-

ant one is the size of the human brain, which makes it much more difficult to investigate thoroughly than the cat's brain. Some investigators feel strongly that this technical difficulty should be overcome, and that as the Vogts have always maintained, 'In no case should we abandon the preparation of complete serial sections through the entire human brain.' The preparation of such a series is not only very expensive but also time-consuming.

The second disadvantage of human material is the variability of the distribution of the lesions which only very seldom are confined to one system of cells or fibres. This applies particularly to vascular lesions and neoplasms. On the other hand, systematic degenerative diseases are perfectly suitable for the purpose of correlating clinico-physiological and anatomo-pathological observations. Most of what we know now about the function of the basal ganglia is based on such correlations. However, the basal ganglia are the site of a whole group of clear-cut systematic diseases, but to my knowledge no such diseases are known to occur in the regions of the central nervous system which we are discussing here.

Perhaps I should also mention that there exists a certain difficulty in interpreting our pathological material as we see it under the microscope. In acute conditions at least, vital, extremely important submicroscopical changes may occur in the nerve cells, and may completely escape our observation. How much easier our task would be if for instance anaesthetics left a visible mark on cells which they affect.

Some day we shall feel the need for a 'brain reference library'. This would be a laboratory to which interesting material would be sent for technical processing and for systematic organization. Such a 'library' similar to the Vogts' brain collection, would be of invaluable aid in the investigation of neurological pathophysiology of human material.

There is much important and interesting material which is now studied individually in different laboratories, most emphasis being placed on the type of the pathological process involved and not on its localization. At present a great number of cortical ablations are performed on this continent, and the individuals concerned will die, as we all do, sooner or later. It would certainly be of great interest if at least a part of this material could be concentrated in

one laboratory and studied in a systematic way, if not by this then by a future generation.

JASPER: We do not have even a very good anatomical study of a case of *petit mal* epilepsy; if we had, it might shed a great deal of light on this subject.

NAUTA: The question is, what should we do about brains where clear signs of EEG abnormality have been found? I think that the prospect of making significant contributions to the interrelation between anatomically demonstrable abnormalities in the thalamus, for example, and EEG abnormalities is at present very dim. I would like to suggest that while experimentation with animals, especially with primates, continues, clinicians, whenever they find interesting changes from the normal electrical activity of the brain should, at autopsy, apply systematically the traditional neuropathological procedures that may enable us to tell more or less exactly what systems were involved. It is possible that by the simple process of addition and subtraction we may then arrive at a conclusion concerning the overlap of observations in animal experimentation with findings in man. I would like to stress again how few chances we have of applying more refined histological techniques to the human brain for the reasons Dr. Olszewski mentioned.

GASTAUT: I would like to remind you that the two works, each of about 1000 pages published in 1900 by Dejerine, on the anatomy of the nervous centres, were based on the anatomo-clinical correlations you have in mind. In particular, the whole of the important chapter dealing with the thalamo-cortical connections and the 'cortical projection fibres' is based on data obtained from meticulous post-mortem investigations.

In what follows I shall attempt to make clear my ideas concerning the organization of the diffuse cortical projection system.

In spite of the most detailed anatomical descriptions, most of us still think of this system in terms of a simple diagram; in the minds of the vast majority of doctors, the pyramidal, extrapyramidal and lemniscal systems have never been, and probably never will be anything more than the succession of familiar lines, direct or crossed, drawn on the blackboard. This is why, in explaining the diffuse cortical projection system to my students, I always use a diagram, which varies little from year to year since

I adhere firmly to the fundamental idea that the fibres coming from the reticular formation of the brain-stem relay in the nuclei of the median line and the intra-laminar nuclei before joining the reticular thalamic nucleus which constitutes the last stage before the cortex. This conception, which I have already described in my paper and in the discussion following the paper by Nauta and Whitlock, seems to me to be confirmed to such an extent by

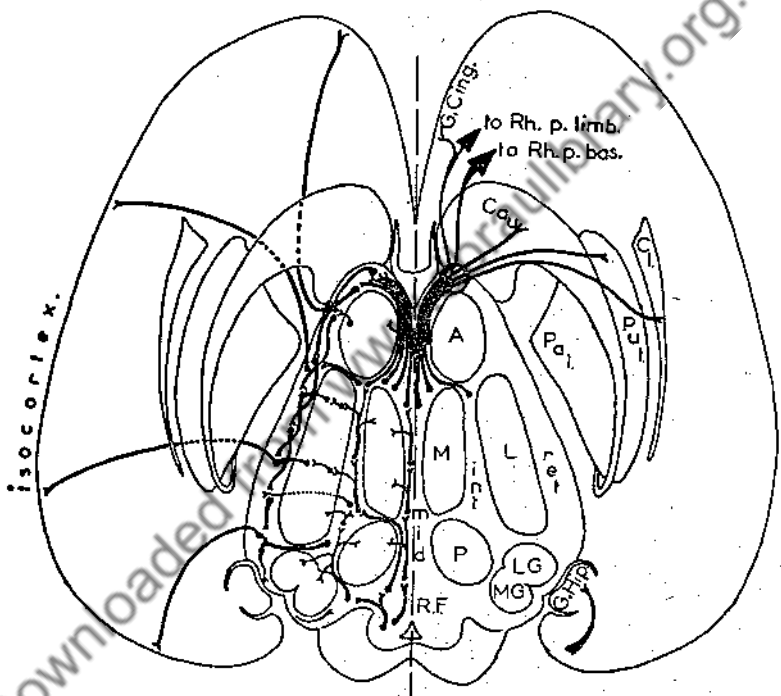


FIG. 1

certain of the opinions expressed during this symposium that I do not hesitate to put before you a diagram designed to emphasize our ideas in this connection. (Referring to the plan): On the left are shown the fibres of the reticular cerebral system which project on to the whole of the isocortex. Notice that the corticipetal fibres come from the reticular thalamic nucleus, which itself receives its afferents:

(*a*) from the intra-laminar nuclei, through the short transverse fibres;

(*b*) from the nuclei of the median line (and probably also from the intra-laminar nuclei) through the long fibres, which, following the recurrent path described by Nauta and Whitlock, pass around the anterior pole of the thalamus;

(*c*) from the specific neighbouring nuclei, through the short-axon neurones described by Ubeda Purkiss.

On the right are shown the projections of the reticular cerebral system:

(*a*) on the central grey nuclei, according to the conceptions of Gerebetzoff, Drooglever-Fortuyn and Nauta and Whitlock;

(*b*) on the rhinencephalon:

(i) on the pars basalis, and principally on the piriform lobe, to which should be added the lower orbital cortex, according to Nauta and Whitlock;

(ii) on the pars limbica and principally on the infra-limbic and anterior limbic region, but also, again according to Nauta and Whitlock, on the whole of the gyrus fornicatus as far as the presubicular and entorhinal region, from which it is easy to assume a hippocampic relay.

RIOCH: I would like to go back to the lateral reticular nucleus. Rose has been quoted in relation to its projection to the cortex. He is very careful, however, to point out that the nature of the retrograde changes is quite different from that of the retrograde changes of any of the other thalamic systems, including the central system. Retrograde change occurs much later. In fact, I have sections of decorticate cats surviving a year and a half or so with still existent cells in this lateral nucleus. Rose raises several questions as to what the explanation may be. Either this is a special type of cell, or, it may have different collaterals that modify the retrograde change, or, its final death may be due to the previous death of the specific nuclei. That is, the retrograde method is not clear-cut for study of the reticular nucleus.

PENFIELD: It seems to me that from a practical point of view the only way to achieve close collaboration is to have periodic conferences in which pathologists, physiologists, clinicians and elec-

troencephalographers give thought to special problems. If you look at what has been produced in neuropathology you will find that it has almost all been done by clinicians, whereas the general pathologist has given us little. Such men as Marie, Nissl and the rest of them, were doing clinical work along with pathological work. The same problem presents itself today. I think young men in the field must be brought up in neurophysiology, neuropathology and neuroanatomy and go on in clinical work. Men who have devoted themselves to a narrow specialization must be drawn together by conferences. The only way we will get more insight into these special problems will be through the special knowledge and experience of the pathologist, the anatomist and the basic scientist in general.

WALTER: To make the problem simpler and to make the sections of whole brains less absolutely necessary, I was hoping someone might suggest some particular region of the brain where these peculiar human effects might be generated. It is my hope, that in some of these projections, in some of these nuclei one might be able to find, through this or that section, a lesion somewhere in a particular nucleus. Well, we could just concentrate on that and look for something there, that might make the pathologists' job easier.

JASPER: Perhaps it should not be overlooked that there are transcortical mechanisms in this kind of diffusion process which might be overlooked if you only studied the brain stem and diencephalon.

KUBIE: I would like to bring up a question which arises out of several points in the discussion. I think it has specific bearing on the problem of consciousness, its relationship to the reticular apparatus and to respiration. Furthermore it leads to a suggestion of two quite specific experimental approaches. The first experiment would be designed to answer a question I raised earlier in the conference, namely whether it is the reticular apparatus which controls the respiratory oscillations, or, whether it is the activity of the respiratory apparatus, which may be biochemical in origin, which at least contributes to the psycho-electrical change in the reticular apparatus.

The second experiment I have in mind concerns the anatomical contribution of the respiratory complex to the reticular apparatus.

If one should destroy the whole respiratory complex and maintain life in the animal with an intratracheal cannula and artificial respiration for five days (i.e. long enough to allow axonal degeneration to occur) one might then be able to trace directly the contribution from the respiratory nuclei to the reticular apparatus.

That might be of importance in understanding the relationship between respiratory mechanisms, the reticular system and states of consciousness.

PENFIELD: Perhaps you will allow me to make a few remarks about consciousness after listening to these discussions. We have heard definitions and Dr. Kubie quoted the statement made by William James that consciousness stands for a function, the function of knowing. Dr. Hebb pointed out that consciousness is responsible for behaviour. Dr. Lashley began by denying the possibility of defining consciousness as a whole. But it seems to me, nevertheless, that he defined some of its aspects very well indeed.

Let me quote fragments of his talk: 'Consciousness' he said, 'is the human awake state.' He pointed out that there must be a 'set' and 'a time element'. There must be memory. The method of synthesis is unknown but the 'awareness is real'. Consciousness is the 'process of awareness'. Finally Dr. Lashley hastened to qualify all his foregoing argument by saying that he was not satisfied with it. No doubt he will be much less satisfied with my re-statement of a few of his phrases which seemed to me applicable.

This dissatisfaction, with which he accepts his own thinking, has characterized his approach to the thinking of others all through his life. That is, I suppose, why we owe so much to Dr. Lashley and his constructive criticism.

Dr. Fessard suggested that 'integrated perception of the present' is a better phrase than consciousness and Dr. Jung stated that the essential element in consciousness was the focusing of attention, a sort of selection, as by a beam of light.

The varying expressions that members of this Conference have used illustrate the great variety of points of departure from which one may approach this great sphinx, the phenomenon of consciousness.

Perhaps a part of the difficulty in definition is that consciousness

is a noun which seems inevitably to represent an abstract conception. Participles might better describe the state that we are discussing. Consciousness is a being aware, a knowing, a focusing of attention, a comparing of present with past experience and a planning of behaviour. These participles emphasize different aspects of consciousness.

Let us rehearse some of the neurone actions that must be associated with the state of consciousness, the neuronal integration that makes perception possible. It must be borne in mind that, although such a rehearsal depends upon established facts and observations of the human brain, my explanations and the conception of a centrencephalic system, of which the reticular activating system is no doubt a proven portion, are hypotheses. Such explanations may be true but they must be treated as no more than an attempt at constructive thinking.

Consciousness is made possible by the interaction of cerebral cortex and the ganglionic connections of the centrencephalic system (which has already been defined in my contribution to this symposium). In order to avoid confusion it seems better not to call it the centrencephalon for it is made up of the pathways and ganglionic connections that make central integration possible between the two hemispheres. It is not a segment that can be grossly isolated for it is located in the diencephalon, mesencephalon and probably extends down into the metencephalon. But only a portion of each of these time-honoured subdivisions of the brain can be called centrencephalic.

The sensory pathways, that bring in information of the world about a man and his body pass through the diencephalon to the cortex and then back to the centrencephalic system. An exception to this statement must be made in the case of the pathway of pain, perhaps, which seems to make no essential detour to the cortex.

Thus, afferent sensory streams of impulses reach the diencephalon from the periphery and pass on through it to make detours to the cortex on each side and back again into the centrencephalic system that connects the two cortices.

These sensory streams are largely unilateral until after they reach the centrencephalic system. For example visual impulses are from the contralateral field until they leave the calcarine fissure and pass inward to the centrencephalic system.

Thus it may be said that at any moment in a man's conscious life there is simultaneous arrival of visual, auditory and somatic information in the form of nerve impulses within the centrencephalic system. The individual is not usually aware of all of this arriving material. It is said that he turns his attention to this or to that. He usually selects what he seems to wish to observe, as though shifting a beam of light, to use Dr. Jung's expression.

These things to which his attention is turned are recorded in the cortex of both temporal lobes. I surmise that this recording must be carried out by means of streams of nerve impulses from centrencephalic grey matter to the grey matter of the temporal cortex. We may assume that an individual is conscious only of that material which has been integrated and then projected outward to temporal cortex. We may assume further that it is actually at the moment of projection that he is conscious of that sensory material. It is at that moment that he is rationalizing it and comparing it with past similar material. He is comparing this present neurone pattern, that he is forming at the moment, with the older patterns of past experience. He is determining future action according to this awareness and this comparison. He is determining it also according to other neuronal procedures which make reasoning possible, procedures which call, presumably, for utilization of other areas of the cortex such as that in the frontal lobes as well as the co-ordinating action in the brain stem.

In regard to reasoning processes, little or no light is thrown upon the locus or mechanism of the essential neurone procedure by our present study of the human cortex. All that can be said is that a large part of the resultant voluntary muscular action is produced by a stream of impulses that flows from centrencephalic grey matter outward to the precentral gyrus of each cortex and downward in the cortico-spinal pathway to the muscles. This stream of impulses that produces discriminating action originates in the zone of central integration. It is a centrencephalo-cortico-spinal stream.

Now to return to the subject of this symposium, the awareness that makes possible the discriminative nature of the stream of impulses just described is what we call consciousness. But awareness may exist still during inactivity of the motor system.

When the electrode of the surgeon is applied to certain portions

of one temporal cortex, under the conditions that I have described, the patient may be unexpectedly conscious of an experience from the distant past. He is aware of the same sensory material that the experience produced and may 'feel' the same emotion that was evoked. He may even act appropriately, for example, by crying out in fear.

Awareness of this past experience is made possible by activation of a ganglionic pattern which recorded that experience in the temporal cortex. But the centrencephalic system must also be activated with it. You may call this a recollection. But it is clear that from the point of view of a conscious individual it seems to be the same thing as the state which existed in the interval of time which originally belonged to that experience.

Selection, or the focusing of attention, depends upon action within the centrencephalic system or action between that system and other areas of the brain such as the sensory way-station of the cortex. The focusing of attention would seem to be an essential part of central integration. The material that is projected to the temporal cortex includes only those things that lie within the 'beam of light' of attention.

One may surmise that consciousness exists during the 'to and fro' activity, between the centrencephalic system and the temporal cortex. During that 'to and fro' activity other areas of cortex are doubtless employed in an elaborative manner, thanks to the functional connections which the centrencephalic system has with various parts of the brain.

Consciousness exists because of neuronal activity, and as the accompaniment of that activity, the pattern of which must be ever various. It is misleading to say that its seat is here or that it is there. But I suspect that one essential feature in all awareness is a centrencephalo-temporal back-and-forth passage of nerve impulses.

MORISON: I have been impressed many times during this conference, by the fact that consciousness has something to do with coincidence or congruence of various different patterns in the nervous system. The most obvious one to start with is the pattern of current experience streaming up over the sensory systems and I would include in that both the specific sensory system and the system of Magoun that seems like a non-specific

sensory system. When these become coincident with some pattern of past experience, one might hypothesize that consciousness appears. This is very much in accord with what Dr. Penfield has just said. Nature gives us a tool for studying this concept through the method of dissociated states. We have heard references during the past week to several such dissociated states of consciousness, for example, hypnotism, mescaline poisoning, and the peculiar situation developed by Dr. Hebb in which the subject is deprived of incoming sensory patterns by manipulation of the external environment. For completeness one might add dreams and psychotic hallucinations.

Since this is the last day of a symposium which has all along shown a proper respect for scientific data, I hope one may be allowed a few moments of fairly wild speculation. For the moment let us assume then that the reticular sensory system is the most primitive sensory system and that it makes central connections in midbrain and diencephalon with other reticular areas which can store traces, engrams or what not as a result of past experience. Coincidence or congruence between an incoming pattern of impulses and a 'filing card' of past experience results in a sense of awareness or consciousness. The more rapidly conducting classical sensory system may be thought of as a more recent arrangement for projection of precisely refined sensory pictures on cortex and lateral thalamus. Under normal conditions these may be 'looked at' by, let us say, the centrencephalic system in order to add precision to the more generalized awareness aroused by the reticular sensory system. When all these elements are working nicely together the organism is in a position for nice adjustment to external reality.

It is interesting to note that what little evidence we have suggests that disturbances like sleep or anaesthesia seem to act primarily on the reticular system leaving the precise or classical nervous system relatively untouched. Indeed the best evidence we have for precise anatomical representation within this system comes from studies on deeply anaesthetized preparations. Several times during the past week our attention has also been called to the fact that gross damage to this system ordinarily does not interfere much with generalized awareness of consciousness although it may result in errors of precision or localized field defects. Re-

latively minor upsets in the reticular or centrencephalic system, however, result in gross distortions or even complete destruction of awareness.

Now let us assume that all three systems, reticular sensory, classical sensory, and centrencephalic are capable of independent activity but that arrangements also exist for putting them in touch with one another. As mentioned before, the hypothesis is that when all three systems are locked together 'in phase' steady complete consciousness of the external world results. But one may be allowed to suppose that the system may get out of phase or partially unlocked thus leading to various sorts of distortions of consciousness. The following situations may be tentatively or perhaps wildly hypothesized.

Normal sleep or anaesthesia could be the result of simultaneous slowing down of activity predominantly in the reticular sensory system and the centrencephalic system.

Mescaline poisoning might decouple the incoming sensory patterns from the filing arrangements in the centrencephalic system, thus allowing the latter to 'free wheel'. Dreaming in light sleep might be thought of as a similar sort of decoupling perhaps because the sensory system is more asleep than the centrencephalic area. Consciousness then represents an inexact fit between inner patterns and those arriving from outside.

The hallucinations in Dr. Hebb's experiment may represent a decoupling similar to the above, but in this instance the lack of fit is a result of Dr. Hebb's ingenuity in preventing sensory patterns from being set up by the subject's end organs rather than because the sensory system is asleep.

Hypnotism or brain washing could then be thought of as a situation in which the hypnotist or brainwasher becomes able to substitute his choice of external sensory patterns for those which should be arriving over the subject's own sensory system but aren't, because of the dissociated state previously induced.

Psychotic delusions and hallucinations represent another sort of situation in which consciousness may occur without proper congruence between sensory patterns transmitted from the external world and those arising from past experience in the upper centres. These could occur either because of toxic depression of the incoming sensory system or because of heightened activity in the

centres themselves, the 'centrephalic system' becoming so satisfied by its own endogenous productions that it no longer seeks an external check.

Before closing may I return to a more realistic physiological point. As Dr. Magoun pointed out, electrical stimulation may interfere with rather than duplicate normal function. It seems quite possible that the recruiting response or the apparently analogous spontaneous barbiturate bursts may merely represent the unimportant activity of a particular set of neurones. When the brain is going about its business of perceiving, remembering, thinking and so on, this set of neurones presumably has something more significant to do than to produce synchronized bursts. And we just take that mechanism out of its normal participation in the complex play of cortical function when we synchronize it by producing the recruiting response. This helps us to study the path of the recruiting system but it does not help us much in telling what the system usually does. This view may help a little bit to answer the question that Dr. Bremer raised as to why we don't get any interference, or very little interference, between the recruiting response and an arriving sensory volley.

It seems conceivable to me that in the fully alert animal, i.e., one not showing recruiting responses or barbiturate bursts, the 'non-specific' neurones may be more rather than less free to influence activity in the sensory system and to be influenced by it. Such an interpretation fits the experiment Dr. Jasper illustrated this morning, in which the recruiting response was much bigger after he destroyed the sensory nucleus. I think it is the experience of most of us, that the recruiting response is also bigger after a section, such as in the *cerveau isolé* preparation, in which the normal play of asynchronous sensory impulses is reduced. What little evidence we have then seems to show that nice, big, easily seen synchronous responses in the specific and non-specific systems do not interact with one another, while the scattered, difficult-to-analyse, continuous twinkling does.

LASHLEY: I should like to add a word of general evaluation of this material from the standpoint of psychology. We are continually faced with the problem of variations in the general level of activity, of alertness, of mood; variations which are expressed through a wide variety of behaviour. In seeking a physiological

explanation of such variations, psychologists have seized upon each new suggestion with avidity. Head's theory of the facilitation of protopathic excitations by the thalamus seemed to provide a possible clue to a more general dynamic mechanism. The elaboration of this suggestion into a theory of thalamic function in emotion by Cannon and Bard seemed to be further advanced, but the thalamic functions demonstrated by experiments lacked just those features of persistent action and general reinforcement of behaviour required by dynamic theory. Cannon's studies of the function of the adrenals and the action of epinephrin provided an alternative chemical theory for the facilitation of behaviour, which was exploited for a time in psychological literature. Evidence for the hormonal activation of sexual behaviour contributed additional evidence for the chemical theory. But the slight effects of controlling such glandular secretions upon the general level of activity renders the chemical theories inadequate to meet problems of the dynamics of behaviour.

Now we have evidence that the reticular formation is capable of discharging diffusely to the cerebral cortex. Sleep or coma following damage to some parts of the reticular formation indicates that such facilitation may be necessary to maintain the activity of the cortex and, by inference, that variations in reticular activity may be responsible for variations in the level of behaviour. These studies, then, may provide the long-sought dynamic mechanism, the physiological explanation of what Head called the vigilance of the brain. If such should be the case, it would be, for psychology, the most important discovery of the century. However, much more work must be done before we can decide to what aspects of behaviour the facilitative action (still hypothetical) of the reticular formation applies.

I have not been convinced by any of the evidence presented that the system is more closely related to conscious processes than are other parts of the brain. It may serve as an activating agent or pace-setter for the cerebral cortex but this is certainly all that can be claimed for it at present. Conscious processes have a complexity and specificity of organization which are incompatible with the diffuse functions demonstrated for the reticular formation. Their structure is at least vaguely comprehensible in terms of the spatial distribution of activity in the cortical network of

neurones, for which no parallel has been found in lower centres.

BREMER: Concerning the whole outcome of the questions raised, can we 'locate' that abstraction called 'consciousness' in any special part of the brain. Or to express it less crudely, can we limit spatially and hodologically the neurobiological processes underlying conscious integration and locate them in a central office, acting so to speak as a state within the state, as brain within the brain? In spite of the evidence presented here, I would agree with Dr. Lashley's attitude. To me it is the dynamic integration of all cerebral processes at a single moment which makes consciousness.

Now may I make two remarks which are probably more significant, since we are all experimentalists rather than philosophers. Our Chairman has asked us to indicate what each of us thought were the most important gaps in our knowledge which needed to be filled. I feel there are two important questions.

First, what is the exact functional relationship between the diffuse or non-specific thalamic system and the brain stem reticular formation? In so far as I understood the discussion, the two main schools are not in complete agreement. In other words, is the diffuse thalamic system, also called 'reticular' by my friend Dr. Jasper, really the head ganglion of the bulbo-mesencephalic reticular system or is it not? I am not sure that we will leave this symposium with a definite conclusion on this point.

Second, what is the functional interrelation between impulses emitted by the specific sensory thalamic nuclei on the one hand and the diffuse system on the other? Dr. Morison offered us a possible explanation of his own negative findings. The tracings which Dr. Jasper has shown us today seem to me very important because they show that perhaps the technique of pairing of two stimuli may sometimes not be adequate; also that the apparent absence of recruiting responses in the auditory areas may be due to the functional state which allows these areas to be bombarded by afferent impulses since the recruiting response was decidedly greater after the specific sensory nucleus in the thalamus had been destroyed.

However it is a rather surprising fact to see the little interference of a pair of successive volleys arriving over specific and diffuse projection systems to sensory cortex, especially when one com-

pares this relative independence with the highly positive finding in other observations on the same spot of the somato-sensory cortex when using for instance tactile volley paired with a proprioceptive volley. We were struck by the complete occlusion of these two volleys on the same spot of the sensory cortex. It may be that the interaction looked for is of a more subtle type, requiring absolute lack of narcosis. Our experiments were done with narcotized brains. As I have mentioned before one sees the facilitating effect of a transcallosal volley only in the unanaesthetized brain.

ADRIAN: The point that struck me particularly is that I don't quite see how far we are to go in regard to the 'reticular system'. I don't quite see whether we are to regard the reticular system as just coming in to wake us up in the morning and to send us to sleep at night, to do non-specific activation, or whether the evidence implies that it has got something to do with the direction of attention, with the actual work of the conscious brain. Dr. Magoun has shown us that it does produce the arousal reaction, the desynchronization, or whatever causes the disappearance of the alpha waves, which is what happens when we direct our attention consciously to particular fields. That rather implies that it may be a very important thing in connection with the analytical side of consciousness, with the actual thinking processes. On the other hand the fact that it reacts equally to a very loud click and to touch, and that it has this sort of non-specific function rather implies that it is mainly concerned with just the general level of the whole brain, with whether one is asleep or awake. Regarding these things simply from the standpoint of the physiologist who is interested more in the cells and units and so on, it seems to me that one very obvious line of advance will be further understanding of the potential waves of the cortex, the alpha waves and the beta waves and all the others which I look forward to seeing very greatly elucidated by Dr. Jasper, Dr. Jung and all those who are working with microelectric techniques. At present we are in a lamentable state of ignorance about where these potential changes are being produced, what they mean, how they tie up with all the other potential changes that electrophysiologists study. Until we know more about all this it is exceedingly difficult to know whether our theories are good or bad. That is a line

of advance which is obviously going ahead and all I should say is that it seems to be the most fruitful.

HEBB: Dr. Adrian raised one question that seems to me to be of first importance. Dr. Lashley spoke of this system as filling a need, which it certainly does. There is the further question of whether the functioning of the system merely raises or lowers levels of cortical function or whether it modifies the organization, whether it is involved in changes of patterns of activity.

The problems from the psychological point of view, as I see it, are two in number; the first is the problem of what ideation consists of; of what an idea or a purpose, an intention or a set is. The second problem is the relationship between ideas. That is the problem that Dr. Lashley discussed, that of serial order and temporal organization. It seems to me most important to continue searching for the possible relationship between the brain stem structures we have been speaking about and those two problems.

I may just add one word or two concerning what Dr. Penfield said: he stressed earlier that we should think of consciousness as a function. I would think that we must be relatively modest in our attempts to attack the problem. We should not try to devise a theory that will be completely adequate to account for all of what we know that human beings know, feel and do. We should try to account for those aspects of the problem we might have some chance of accounting for and not worry if the theorizing appears to be inadequate in some respects to cover all known features of the system. Also I still think that it is well to be very wary indeed of using introspective evidence. It is very difficult indeed to interpret that kind of evidence, and we should make it our first goal to try to understand the main outlines of what human beings *do*.

PENFIELD: My use of the word 'function' in regard to consciousness was not my own, but William James's. I would just like to try to escape from the assumption in Dr. Bremer's discussion that I have a belief that consciousness resides in a separate area of brain. When a patient is aware or conscious, he is aware, for example, of a visual experience; I am willing to assume, then, that the cells of the retina, of the lateral geniculate body, of the primary visual cortex, secondary visual cortex and of the centrencephalic systems

are all involved and active in this experience. But the recording mechanisms of the experience are also active. The accompaniment of all this neurone activity is awareness or consciousness. But there *are* levels of integration. All levels are important but some enter the process of integration later than others. I would like to try to divorce myself from the idea of a localization of consciousness. Awareness is not a thing that we can localize because of its nature.

BREMER: Since I am accused of a misconception I must defend myself. I was never rash enough to think that, but nevertheless undoubtedly Dr. Penfield's conception has a tendency to overemphasize one point of view, that of the brain stem, and to under-emphasize the immensely intricate intercortical and intracortical relations. Therefore I would incorporate his ideas into the whole picture and this does not at all detract from the considerable interest of the many positive facts upon which his views are based. To me, conscious integration is an integrative process of the whole brain. When one considers the innumerable facilitatory processes which are going on within the brain, from one oculomotor centre to the other, from one homotypic area of the cortex to the other and so forth one cannot refrain from the idea that it is the participation of the whole that makes awareness and consciousness possible.

PENFIELD: As you express your conception you seem to go back to the time when the brain was called the organ of the mind, before Broca pointed out the first step in the working out of the separate parts. When you relate consciousness to the whole brain you really are carrying us back to the conception of the brain as an organ of the mind, which is an easy way but not very constructive. Consciousness is related more closely to certain integrative mechanisms than it is to other mechanisms within the brain.

JASPER: If you will pardon me for saying so, Dr. Bremer, this notion of the brain acting as a whole is, to my thinking and experimenting, rather sterile. It gives us no possible conception of a real mechanism of integration. It leaves us completely without experimental approach to these problems. Until we begin to think of mechanisms of integration which can give us unity and simplicity from the complexity which impresses us all in terms of definite mechanisms the statement that the brain acts

as a whole is retrogression and we would rather look into the future.

BREMER: The concept of the brain acting as a whole does not imply that we cannot make fruitful analytical studies of parts of that whole. We are all doing just that. We are hoping that in the very remote future the two parallel lines of psychology and neurophysiology may join. But I am afraid they will join when our present domain shall be frozen. I am not a defeatist, but of a very deterministic mind, yet I think that at the present time we are completely unable to explain accurately any state of consciousness in neurophysiological terms. Let us take for instance the fact that when a tune is perceived by the auditory area it must have, as Dr. Adrian has suggested, a topographical organization in space which someone must interpret. But who is this someone? That is, after all, the problem of perceptual consciousness.

JASPER: Dr. Eccles has attempted to meet this problem by leaving the physical and by going to the spiritual world for an explanation.

RIOCH: The concept that 'consciousness' refers to something happening in *one* person's brain is, I think, untenable. The phenomena concerned are the phenomena of interaction, and 'consciousness' is necessarily inferred and may then be projected as a characteristic of the experimental subject. Consciousness is thus necessarily a function of two or more brains, not of one. Culturally the concept of 'consciousness' or the broader concept of 'mind' has largely replaced the older concept of 'soul' and we have the phenomenon now of political movements to 'win men's minds' replacing earlier religious movements to 'win souls'. The implication is to assure group belongingness for purposes of anticipated intra- and inter-group transactions. It is my impression that anticipatory behaviour – in anticipation of one or other of several probable responses from the environment – is a necessary, though not sufficient, characteristic of those patterns of interaction which may be classed as 'conscious'. In the special case of human 'conscious' behaviour the environment is composed of other humans, except in the more or less mythical cases of 'wolf children', etc.

JASPER: Where is the second brain?

RIOCH: For purposes of operational formulation the second

brain is that of the observer, who is necessarily a participant in the investigative procedure.

WALTER: I only want to weave a little web between Dr. Morison's views and those of Dr. Adrian. Dr. Morison suggested that one aspect of consciousness might be the matching or comparison of incoming current information and stored information, and Dr. Adrian mentioned what has been done with microelectrodes. It seemed to me that in some of the records from microelectrodes – the actual records shown here – there was some evidence of a comparison, or at any rate an overlapping of information from various sources in a highly complex and mathematically rather intractable way. I think that this may represent a very serious problem of analysis but, if it is so, I would suggest that you have in the records from microelectrodes, and I think we have also in our large scale studies, evidence of a texture of electrical interweaving which might in fact be the physical representation of that matching and comparison that Dr. Morison suggested. This is one aspect at least of the consciousness problem.

KUBIE: I would like to emphasize what I believe Dr. Penfield had in mind and with which I agree fully, by asking you to think back for a moment to a time when we were just beginning to study the reception, registration and organization of afferents in the central nervous system. We would not today study sensation as though all sensations were one, as though all forms, all modalities, all kinds, no matter what their origins, were all one thing. We would recognize that was a sterile concept. This is a contribution to neurophysiology by the psychologist who came along and said: 'But look, there are a lot of different kinds of sensation? This is very complicated, sensation is not all one thing.' Naturally the experimentalist is unhappy to find that his task is more difficult than he had thought. Yet, in the end it is an essential conceptual step which he must take, if he is to adjust his experimental methods to the problems that confront him. It is in that spirit, that I have hammered away at the fact that the conscious processes and also the unconscious processes are a complex constellation of many types of experience. It would be very misleading to assume that there will be one single set of neuronal or neurophysiological dynamics for all of these processes, even if it turns out that they have certain elements in common. I would summarize the pro-

blem by stressing the fact that there is nothing at all that we can do consciously that we cannot do also unconsciously. This means that there are processes of compartmentalization or dissociation of the processes of consciousness. It does not mean that there is no difference between the two, that is between doing something with awareness and doing something without awareness; but it is important to stress that the brain can do the same things, with or without awareness of what is going on. Furthermore, there are different kinds, as well as different degrees, of compartmentalization. All of that must be comprehensively described and understood if a total explanation of the neurophysiological mechanisms of states of consciousness is to be found.

FESSARD: After having heard so many pertinent criticisms directed against the view that the nervous process underlying consciousness could be localized in some limited place of the brain, I realize that we are not all speaking of the same thing; for consciousness is an ambiguous term that lends itself to a great deal of misunderstanding. I do not want to repeat here what I have already said during the preceding discussions or considered in my paper, but only stress my feeling that experienced integration or EI, or even simply 'perception', may be better terms, provided perception is understood in its broadest sense of anything we feel, including percepts, affects, memories and intentions. Although I perfectly agree that many parts of the brain, if not all, participate at every moment in the organization of this integrative perception, I remain convinced that some regions of the brain are more important than others for the arousal of conscious experience. As has repeatedly been noted here, organization itself is an unconscious process of which we know only some end-products, and this arousal of awareness, which is our real problem, is not even a fatal consequence of a high level of organization, not a regular accompaniment of a complicated form of behaviour. I think therefore that we can conceive, without being inconsistent, of rather limited parts of the brain that would be essential for the arousal of EI and of other parts – perhaps the majority of the brain centres and connections – that would not be so. This would not mean of course that we could expect a maintenance of consciousness if the supposedly critical region was disconnected from its surrounding! But 'brain as a whole' does not seem to be a

stimulating hypothesis. You would not say for instance that retina, optic nerve or optic radiations, although necessary for normal vision, contribute essentially to the arousal of visual sensation. We must face the problem of determining what part of the brain, if any, has the property, not so much of organizing visual perception, but of giving rise to visual experience.

Reverting to the heterogeneous aspect of EI we must not forget that at every moment we are aware of a set of qualities from different origins, visual, auditory, emotional, etc. . . . Is it conceivable that cortical areas alone could integrate all these qualities? We could imagine, if not perform, an experiment in which these areas would be isolated from the subcortical centres, and nevertheless kept in normal condition of dynamogeny by appropriate artificial stimulation: would you say that they could produce an integrated field of consciousness?

BREMER: Why not, after all we know that the cortex is the seat of an intricate apparatus of interrelation of amazing complexity. That does not exclude of course the fundamental importance of thalamo-cortical and cortico-thalamic relationship as well. It is possible to conceive of integrative processes of all these types. I think confusion may arise here between the notion that when we destroy or suppress the action of the brain stem reticular formation we suppress awareness, and the fact that the same reticular formation collects in its neuronal net-works the most diverse impulses, including corticofugal ones. That does not give us the right to assume that this is the mechanism for conscious integration. There is concentration of heterogeneous impulses, which often activates the same nerve cells, thus providing the tonus of that reticular mechanism. This is convergence and summation of nervous stimuli but not perceptual integration of sensory messages in the sense of which we are thinking now.

FESSARD: Usually one considers the tonic effect that comes from the reticular fields as a diffuse dynamogenic action, whereas I wonder if, in natural conditions, there is not there a more differentiated process. This would provide selective facilitation or inhibition which I am tempted to parallel with the psychological mechanism of attention. There is a familiar comparison between attention and a searchlight. Although an old one, it is all the more valid now as we can find for it a close neural analogue in the

streams of corticipetal impulses coming from the non-specific reticular structures. But the real and difficult problem is that of the selective orientation of the searchlight. What is the mechanism of this selection? We are reluctant to attribute the whole responsibility of this control to such poorly differentiated structures as are reticular systems. These must probably receive their orders which produce their instantaneous dynamic structurations from above, through those corticofugal projections recently studied by Jasper and Marsan (1952). This is why I think we have to introduce here the patterns of cortical activity, as we imagine them to organize themselves, spontaneously throughout the whole cortex. The succession of operations would then be: sensory projections to the receptive areas through the specific pathways, unconscious patterning in the cortex, projection of competitive patterns towards the centrencephalic structures, where interactions would produce a higher degree of integration, this resulting in a new orientation of the selective ascending impulses and eventually in the arousal of an integrated perceptive experience.

JASPER: May I present a slide which has been previously published in the Milbank Memorial Symposium where we discussed this problem (Fig. 2). This is a diagram to illustrate a summary of experimental findings of thalamocortical and cortico-thalamic relationships. It is based upon electrophysiological studies with interpretation very much the same as that which Dr. Fessard has just presented. It shows the specific projection systems which we know from physiological studies act independently of each other and which are obviously not representative of conscious processes. We can then trace the elaboration from sensory receiving systems into what we have called elaborative systems as a second step. We have, in addition, the elaborative systems which are parasensory, such as the para-striate areas in the occipital lobe and other areas (which have been called association areas) in the frontal and temporo-parietal regions. It is these areas which seem from physiological studies to have the strongest projection to portions of the brain stem reticular system. This would be in general agreement with the conception that Dr. Fessard has presented.

PENFIELD: I liked what Dr. Fessard said very much, the use of

the expression 'integrative perception' provides a very useful conception. I agree that we must consider also the selection or focusing of attention as one of the elements in the conscious process. I would like to ask Dr. Fessard why he assumes that the searchlight of attention should originate in the cortex rather than in subcortical areas. I am not adverse to this conception but why should we say that it originates anywhere.

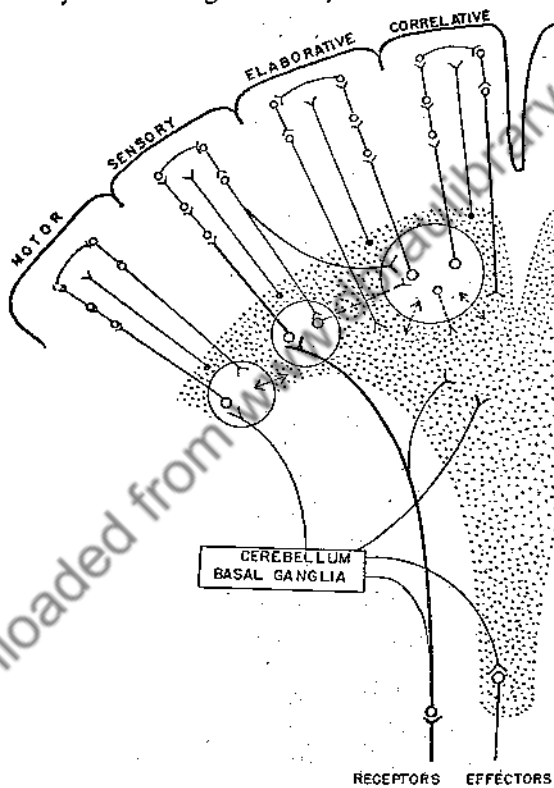


FIG. 2

Schematic diagram of thalamo-cortical and cortico-thalamic relationships. Specific nuclei are shown as open circles, the reticular system by the stippled area extending into mesencephalic areas. Each cortical area is supplied by both specific and reticular projections. Two-way connections are shown between specific nuclei and each type of cortical area. By 'elaborative' is meant such areas as the peri- and parastriate cortex of the visual system. Correlative areas are the 'association' areas in temporal parietal and frontal regions. Particularly strong connections are indicated from the latter areas back into the reticular system. 'Collateral' fibres running from ascending sensory pathways directly into the reticular system are also shown.

FESSARD: I do not exactly say that the 'searchlight' should originate in the cortex, but more precisely that the cortical patterns at any instant should exert a determining action upon the orientation that the searchlight, as represented by ascending impulses of subcortical origin, shall take at the next instant; in turn this new orientation contributes by its proper facilitatory effects to the structuration of the following cortical patterns, and so on. This 'to and fro' activity is of course strongly remindful of that invoked by Dr. Penfield himself a moment ago and generalizes it. I am all the more convinced that subcortical structures are involved as I cannot dissociate attention from motivation and affective processes, which are themselves mostly under the dependence of central activities at this level.

MORUZZI: In the present discussion we have been mainly concerned with the nature of the ascending influence of the reticular system. As Dr. Adrian pointed out a few moments ago, the issue is one between non-specific functions controlling the general level of vigilance and a reticular activity which would contribute in some way to the analytical side of consciousness.

The neurophysiological background of the first point of view is provided by our present concepts of an ascending reticular system driven 'diffusely' by all sensory modalities and projecting 'diffusely' onto the cerebrum. It is perhaps advisable to analyse briefly the experiments which support this hypothesis.

1. There is abundant evidence, already reviewed in my report, that different sensory modalities share the same neurones of the reticular formation. These findings would show that the afferent projections to the reticular system are diffuse in type.

2. 'Unilateral' high frequency stimulation of the reticular formation, performed at any brain stem level, yields 'generalized' EEG arousal. This experiment would show that the efferent paths arising within the ascending reticular system also project diffusely onto the cerebral cortex.

3. Large, acute or chronic midbrain lesions yield behavioural and EEG sleep patterns and prevent the EEG arousal which would follow otherwise any bulbo-reticular stimulation. These experiments might suggest that the tonic discharges which are responsible for wakefulness do not ascend through well-localized paths but utilize the entire core of the brain stem.

I should like to emphasize that there is no question in my mind about the opportunity of making a distinction between diffuse and specific projection systems. Clearly we have to deal here with an ascending system which is altogether different from the neuronal chains which make it possible for instance for sounds of different pitch to elicit responses in different subdivisions of the acoustic area. What we are concerned with here is merely the problem of the degree of diffusion in the afferent and efferent projections of the brain stem reticular system. To put the question in another way, we should ask ourselves if only mass activities, involving the whole of the ascending reticular system, should be contemplated or if a fractionation of the core of the brain stem will occur according to the sensory modality involved. I would not anticipate an answer which will be given eventually only by further experiments. I should like to stress, however, that the present evidence does not disprove what we may call the fractionation hypothesis.

1. Besides the fact that there are no crucial experiments showing that the potentials we are picking up with concentric electrodes from the midbrain tegmentum arise in the ascending reticular neurones (and not in the descending ones or from neighbouring sensory collaterals or extrapyramidal fibres), it is apparent that the convergence of sensory messages on a single unit, although undoubtedly conspicuous, is not unlimited, at least if iterative stimulation is avoided. Hence single shocks are followed by clear-cut effects if they are applied to the sciatic nerve, but no response occurs if a single shock is delivered to the central end of the vagus nerve. Moreover von Baumgarten and Mollica (1953) have repeatedly found single medullary units, quite easily driven by single sciatic shocks and yet completely unaffected by single acoustic clicks. These differences will be eventually levelled by temporal summation, but they are not altogether insignificant. One wonders if limited (although certainly overlapping) reticular regions might not be activated by a given sensory modality, at least whenever startling stimulations are avoided.

2. On the efferent side, cases of non-generalized cortical arousal elicited by reticular stimulation have been reported and one should never forget that repetition rates as high as 100–300 per second are

particularly suited for driving, through temporal summation, the whole of the brain stem core. Normal sensory impulses would certainly be less efficient in overcoming synaptic resistances.

3. Sleep or coma follow, undoubtedly, any decrease or interruption of the tonic discharge ascending through the core of the brain stem. There is, however, another tonic influence, which is exercised by the brain stem and the cerebrum in just the opposite direction. Its sudden interruption, following complete cervical transection, is responsible for spinal shock. Nobody would say that this descending facilitating influence is 'diffuse', although it certainly represents the sum of tonic discharges going down through multiple and scattered pathways, such as the pyramidal reticulo-spinal and vestibulo-spinal tracts. Nor would anyone of us be prepared to maintain, e.g. that the unique function of the pyramidal tract is one of facilitating, tonically, the spinal mechanisms, although its resting low frequency discharge is very likely to have such effect, at least in the primates (Tower, 1940).

It is always difficult to keep historical perspective, when dealing with recent events. But it seems to me that our present position, in so far as the mechanisms of sleep are concerned, is somewhat similar to that which confronted the nineteenth-century physiologists when they approached the problem of spinal shock. Of course the answer might eventually be altogether different, but what matters is that the issue can be tested experimentally.

If the ascending reticular system were acting only and always as a whole, the topographical patterns of its response would not change according to the sensory modality or to the cortical area which would be stimulated. Wakefulness and EEG arousal would represent the tonic and phasic aspects of the same mass activity, whose decrease would bring about sleep. The ascending reticular system might then be involved only in those functions in which mass effects are to be expected. Its tonic activity would be responsible for the 'tonus cortical' and for the variations of level of vigilance, about which we heard from Dr. Lashley. It might perhaps be added that intense phasic discharges might arise within the ascending reticular system whenever strong emotions (fear, rage) or startling sensory stimulations would occur.

If future experiments should instead support the alternative concept of a division of the ascending reticular system into many

provinces or at least into overlapping spheres of influence, then the fractionation hypothesis would be one which should be seriously reckoned with. Wakefulness might be due to the integrated influence of multiple tonic discharges arising within the different provinces of the reticular system. The concept of a centre for alertness would then appear no more justified than of a centre devoted to tonic facilitation of spinal activities. The ascending pathways would be mutually vicarious and sleep might occur whenever the reticular bombardment decreased below a critical level. The different reticular provinces might also be driven, phasically, from impulses arising in cortical areas or in sensory nuclei. Their activity would then be related to more localized processes, such as attention or the interactions between different sensory modalities (Chang, 1952). Only during startling sensory stimulation or during strong emotions of different types would a generalized involvement of the ascending reticular system occur.

I believe that one of the main tasks which will confront neurophysiologists in the coming years is investigating whether fractional activity of the reticular formation really occurs within an appreciable range of stimulation intensities. It will be a hard task, since it is obviously easier to find a reticular response to massive sensory volleys or to convulsive cortical discharges rather than detecting more localized and physiological effects, but this major problem should not remain unchallenged.

JASPER: In Montreal we have been emphasizing for years the fine structure of the system so that I am glad to hear Dr. Moruzzi re-emphasize the importance of studies of detailed topographical organization of the system rather than its mass activity which may be a function of our experimental methods.

HEBB: There is evidence in some recent work that one of our men, Sharpless is doing in Dr. Jasper's laboratories that there is as high a degree of specificity in the reticular system as there is in the cortex. This is manifested by adaptation with repeated stimulation to one particular stimulus in the reticular system and the cortex, in the cat going to sleep. The stimulus gets through but the arousal effect in the reticular system and cortex disappears with repetition. This effect is specific to one particular auditory stimulus and is not present when a different tone or a different quality of noise is presented to the animal.

JASPER: I am glad you mentioned these experiments, Dr. Hebb, since I should have mentioned them before. To complete the properties of this system which we should attempt to outline in this general summary, the property of adaptation has been overlooked. This is a very prominent property of the reticular system which is very unlike the lack of adaptation to repeated stimulation which one finds in the response of the specific afferent systems. We have been very interested by this work of Mr. Sharpless who has really shown that a portion of the system will adapt to a specific type of stimulus or stimulus pattern.

BRAZIER: I was thinking in terms of Dr. Jasper's suggestion that one of the major goals of this symposium is the design of future experiments. I think that some of the suggestions that have been made, although coming from workers approaching these problems from very different angles, contain some similarities. For example, Dr. Morison's concept that each current experience is compared to a card file of past experiences makes us, as neurophysiologists, responsible for looking for the card file. In other words, what is the neurophysiology of storage? This is also implicit in Dr. Walter's concept of attention and awareness being related to the significance of an event that is occurring in the present, in contrast with the probability of its occurrence from one's past experience. In order to predict from past history what is the most probable event in the future the brain surely needs some form of storage system. I think this overlaps with Dr. Kubie's approach. The differentiation he makes between being 'aware' of what one is doing and 'not aware' is whether or not one is referring to one's card file in a conscious way. All of these problems demand of us neurophysiologists a search for some storage system. This is perhaps not exactly the same as looking for the neurophysiology of conscious memory. We have a few clues here about the storage system. We know, for example, that it survives sleep and anaesthesia. We know that electric shock expunges the storage system of the recent past (there is a brief retrograde amnesia). Concussion sometimes does the same. Only one suggestion about the storage mechanisms has been made at all explicit and that is in Dr. Fessard's concept of neural nets (although I am not sure he wishes to make this interpretation). Dr. Jasper's scheme gives us a theory of elaboration but not a

theory for storage, so where does this lead us? Here are some problems which we might begin to design experiments for. First of all, we have to frame a working hypothesis in a form in which it can be tested. That is going to be very difficult. One route which is very familiar to the experimental scientist is to go to the paradoxes. They may give us the best leads. For example, an apparent paradox has been given us by Dr. Bremer of how the same site on the sensory cortex responds to stimulation of the specific thalamic nuclei and to stimulation of the reticular system and yet appears to do so independently. It is these queer results that perhaps may give us our best leads. Finally, I think we should never forget how bound we are by our techniques. For example, most of our records taken with condenser coupled amplifiers neglect completely the important information which Dr. O'Leary has shown is available in the slower D.C. potential changes of the cortex. Furthermore the localization, sign and form of responses of the cortex may be quite different when using the Laplacian electrode scheme rather than the methods usually employed.

JUNG: I wish only to emphasize a point I have made earlier and which we have heard from many other speakers, that consciousness represents certainly some selective process. It uses only integrated and simplified results which are worked out at lower levels. Only the end-results seem to come to consciousness. Everything else is preliminary. What we investigate as neurophysiologists are these preliminaries. Who reads the 'whole' as Dr. Adrian says, nobody knows.

WALTER: I might comment on Dr. Brazier's remarks about the effect of electro-shock. This is one of the paradoxes which we might consider for there is sufficient material for study in the hundreds of electro-shocks given every day. Many people have made studies of the effect of these shocks on memory and the results have been paradoxical. There is a slight retrograde amnesia but at most it covers only a few seconds before the shock, and it is scarcely perceptible unless there is a convulsion. This does seem to make any reverberatory theory of even immediate storage extremely difficult to hold, but it may be significant that this period of a few seconds is about the term of the persistence we find after pattern stimulation.

JASPER: Now, gentlemen, I am afraid we shall have to terminate this discussion. I want to express my personal appreciation to each and everyone of you for your intense and illuminating contributions to this Conference. Just what comes of this meeting depends upon us in our future work and upon the influence we may have upon the young men working with us.

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