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Chairman's Address

It is for us a privilege and an honour to welcome all of you to the Second Symposium of the Fulton Society on Frontal Lobe.

This is a new tribute to the memory of a man who has been for many of us a true friend, and whose stimulating personality has been a source of inspiration in our endeavours.

Our Society gathers in its midst outstanding scientists from different parts of the world, who have been, in different epochs, visiting investigators at the Yale lab. All of us keep a happy souvenir of our association with John; and his enthusiasm, friendliness and boundless energy have left in all of us an imperishable impression.

And now in this meeting outstanding scientists from France, Germany, England, Belgium, the United States, and Austria give this reunion an international flavour that is in accordance with our society's motto "Fraternity through Science". We are guests in a wonderful city: Vienna. So full of reminiscent splendor. The gates of nostalgia are fully open when one enters the magnificent palaces and seems to hear the echoes of old romantic Vienna.

From the ceilings, the mythological frescoes seem to gaze at phantoms of the past in the empty rooms. The whirling dancers, the brilliant uniforms and the glittering chandeliers, the servants in livery...

All this permeated the immortal spirit of musical Vienna. The murmur of the forest, the rhythm of the flowing Danube, the trills of the birds, the laugh of the children, all was captured by the poetic genius of its musicians Haydn, Mozart, Strauss, Mahler...

Science also has a great tradition in this country that has given its geniuses as Mendel, Boltzman, Doppler, Meitner to the world.

Neuropsychiatry owes to the Austrian school brilliant minds like Meynert, Schilder, Wagner, Jauregg, Freud, Economo, Pötzl and others.

And today this torch of enlightenment is in good hands. Our host Prof. Hoff, whom we thank for his kind hospitality, embodies in the present, along with outstanding specialists to whom we render homage in his person, the magnificent reality of to-day's neurology.

Frontal Lobe was chosen as the topic of this Symposium because studies carried on in Dr. Fulton's Laboratory culminated in the opening of a new road to psychosurgery, and to the understanding of this priceless possession of man, the site of higher intellect and the one that gives him the sceptre among the species that populate the earth.

Only man among all the species that share the earth has the faculty of autoperception. This is the landmark that separates the lower organisms from

the Homo Sapiens. This wasn't a gift, but a conquest that began in the long night of prehistory, and it is recorded in the evolution of the brain, specially in that portion in which the noble features of the mind reside: The Frontal Lobe.

Making an effort to visualize its advent and lifting the nebulous curtain of milleniums we can see emerging from the deep shadows of the remotest past an ape-like creature, thrown upon his own resources, forced to solve the most complex riddles to survive.

"Necessity is the mother of invention", says the aphorism, and the Pithecantropus or Java man of our evocation began the greatest conquest of expansion: that of his own brain. That was the first step toward humanity.

Increasing steadily his powers of adaptive reasoning, he widened the scope of his experience; he began to use his right hand and, as his inferior frontal convolution denotes, he had learned to make use of sound to communicate in verbal speech.

He used his hands as tools, giving predominance to the right one.

Studies performed on casts from his skull denote that there was a prominence of the inferior convolution of the frontal lobe, which leads to the conclusion that he had the motor resources which allowed him to invent verbal communication and to add to his conquests the supreme one of speech, even if this was a rudimentary one. His frontal lobe, with all the limitations of a recent morphological acquisition, indicates that his brain had made a definitive progress in his psychic powers, making room for such important human features as unidexterity, and language which helped to develop reason. He was the first one to elevate his trunk to the dignity of the erect position. Other areas of his brain also expanded to aid his added faculties. These came from the need for better vision to control his hands and to direct his efforts, for better hearing to detect the different inflections that make speech a source of communication. And thus the Java Man advanced toward future, in his erect position, migrating, exploring, learning, exercising this power of selection and judgement.

The dark night of irrationality was slowly receding in the chill pallor of Dawn and the Dawn Man followed the Java Man, even if the full day of human reasoning was far from coming. Vestiges of the beast were still impressed in his features and in the fan-like character of his canine teeth. This stigma is also found in the Rhodesian man, and the Heidelberg jaw shows that ape features still persisted.

Even the Neanderthal Man bore capacious orbits, heavy supraorbital torus, low receding brow, broad anterior narial openings which gave him a gorilla appearance. In spite of his brute-like aspect his brain is not altogether in accord with this low estimate of him. His brain was larger than that of modern man and he had made definitive advancement in many aspects. It was not Prometheus who gave the command of fire to man but this humble ancestor to our race. A flint worker and skilled artisan, a hunter, dwelling in the earth for almost 200.000 years. He had many of the higher attributes of man, but something failed to develop in his frontal lobe. His brain was distinctly flat even if in all its major divisions it showed expansions above that of the Java and Dawn. One important aspect of his frontal lobe is the prominence of the inferior frontal left convolution: in it could be recognized

the pars orbitalis, the pars triangularis, and the pars basalis that are found in Broca's area of Homo Sapiens in a far more complex way than in the Java and Dawn man.

He had demonstrated the use of psychic powers in mastering his environment, contesting successfully with the beasts, making use of speech in communal living, burying the dead with some ceremony that speaks of some religious feeling. But his frontal lobe failed to attain in his long permanence on earth the human standards, and another race which did it came and he was unable to cope with them, and disappeared.

The Cromagnons arrived and the breath of spirituality was really blown into their nostrils. They were not only masters of their environment, but were also creators. The long experimental process was coming to its end. Man was approaching his final form. The simian features were erased from his face and body. He was not only beautified but he developed esthetic feelings that found expression in the decoration of his dwellings, in creating ornates, in making statuettes. Thus he painted the roof and mural of his cave, carved ivory, horn and stones, and the artistic vein of his creative mind found outlet also in the dance and music even though their musical instruments were very crude.

Life provided him experience not only to survive but to enjoy living, understanding and transforming his environment. And with the enjoyment of artistic beauty, poetry entered into the scope of human mind before being captured into words.

It was a real feat of Man and Nature, in close relationship acting and reacting one upon the other. His brain had lost the marks of inferiority of the lower races, and resembled in the finesse of its structural details the final advancement of the human brain.

The parietal, temporal and occipital lobes increased their proportions, surpassing all previous features of earlier man. But the real secret of his superiority lay in his frontal portion, in which are conjugated all the highly skilled characteristics of the different areas to assume the forms of behaviour. A long journey from darkness to light was performed thanks to the brain's most important feature: its plasticity. And the hope of modern man in achieving higher gains for humanity lays in the same foundation. The human mind is always in the making. As Dewey affirms "not perfection as a final goal, but the ever enduring process of perfecting, maturing, refining, is the aim of living"...

And thus the brain still marches on, in the pursuit of new horizons, on the earth, in the sea, in the sky, and is still far away from the comprehension of its own nature.

The third eye of Siva the hindu Deity is placed on the frontal region. While one eye looks into the future and the other into the past, this third eye will look to some trascendental reality of immanent truth.

Doubtless man's frontal lobe has done so in its capacity of abstract thinking, in its creative effort to look forward, to foresee, to correct, to complete, and to solve the gift of the third eye of Siva.

Once more explorers of science confront from different angles nature's highest creation: the human brain.

They came not only from different lands but also from different realms of the neurological sciences. The neuroanatomist, neurophysiologist, neurologist, neurosurgeon, psychologist and psychiatrist bring here the fruits of their endeavours. They are merchants of light. They do not trade but exchange.

Their methods are also unlike. One faces the brain with the microscope, following the lace-like structure of colored neurons. And in this selvatic organization he tries to catch the singing bird of the mind, lost somewhere in the forest of neurons. Others work on the living matter, stimulating, cutting, recording the flashing functions witnessed by computers that control the brain.

Others operate on it and elicit thinking and behaviour with stimulating electrodes, like neurologists who use a hammer to elicit reflexes.

There are others who with pin-point exactness criss-cross the brain with needles that extract accurate references about the point of insertion. Injections of drugs plus recording, plus the psychological studies of the patient bring valuable information about the chemical influences on the brain and the resulting changes in man's personality. And thus analyzed, cut, frozen, in action, drugged, stimulated, recorded, computer controlled, remain the mysteries of the mysteries. Sherrington's enchanted loom on which mind, the greatest of nature's adventures, plays its undecipherable patterns.

VICTOR SORIANO.

John Fulton and the Frontal Lobes*

by PAUL C. BUCY

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John F. Fulton must be credited with having stimulated the resurgence of interest in the frontal lobe. He, working with Carlyle Jacobsen, demonstrated that destruction of the frontal lobes anterior to the precentral motor cortex — the so-called prefrontal area — produced a characteristic alteration in the animal's behavior. Among the changes observed were an increase in motor activity, a loss of recent memory and the development of an indifference to the animal's difficulties in the performance of certain tests and to errors in their performance. This last observation, reported at the International Neurological Congress in London, led directly to the development of prefrontal lobotomy in man. In the years since this occurred prefrontal lobotomy, which once was a commonly used therapeutic neurosurgical procedure in some patients with psychiatric and neurotic behavior, has been less frequently used. There are many reasons why this is true, including the extensive developments in psychopharmacology which have taken place. Yet the fact remains that Fulton and his collaborators established the fact that destruction of the anterior parts of the frontal lobes does result in certain specific and distinct alterations in behavior. These facts have been substantiated and clarified by many other observers since. They provide a sound basis for the further study of the relationship of the frontal lobes and other parts of the brain to behavior in man and other animals.

During this same period Fulton and his co-workers conducted extensive research as to the structure, connections and functions of the precentral region or posterior part of the frontal lobe. Years before Sherrington, Horsley, Holmes and Page May and others had conducted investigations on the precentral region both in man and animals. That this area in primates (and the corresponding sigmoid gyrus in carnivores) is that part of the cerebral cortex most concerned with the activity of the skeletal musculature, had been firmly established. But our knowledge of the organization and nature of the control exerted by the precentral area was most elementary and inadequate. In addition many erroneous concepts had become firmly established in neurological thinking. Among these were the ideas that there were two independent neurological systems concerned with muscular activity — the pyramidal and the extrapyramidal. It was believed that the pyramidal tract arose exclusively from the gigantic Betz cells of the precentral gyrus and was the sole pathway by which the precentral cortex exercised control over the skeletal musculature, that only the precentral cortex and the pyramidal tract were responsible for voluntary muscular activity

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in man and that destruction of the pyramidal tract or the precentral motor cortex resulted in the development of a "pyramidal" syndrome characterized by spastic paralysis of the contralateral extremities, increase in the tendon reflexes, absence of the abdominal reflexes, and the appearance of the sign of Babinski. The extrapyramidal system was regarded as an independent neural mechanism unrelated to and not connected with the precentral cortex. It was supposed to have as its controlling cerebral center the basal ganglia — the globus pallidus, putamen and caudate nucleus. How this extrapyramidal system functioned, what it did in the normal intact animal, how it was connected with the anterior horn cells of the spinal cord and in turn with the skeletal musculature was a mystery. An even greater mystery was how two completely independent neural mechanisms unconnected and unrelated could control the skeletal musculature simultaneously without producing complete chaos. It was generally believed that although the extrapyramidal system played little part in normal muscular activity, lesions of it resulted in muscular rigidity (a state regarded as entirely separate from spasticity), a paucity of the more spontaneous muscular movements and the development of abnormal involuntary movements. How these clinical conditions were brought about was completely unknown. Another erroneous concept common at that time was that vegetative visceral and vasomotor phenomena were controlled exclusively by subcortical mechanisms in the diencephalon and brain stem and were completely beyond the control of the cerebral cortex.

It is difficult today to realize that a short time ago this state of irrational ignorance existed and even more difficult to understand why much of this nonsense is still reflected in various publications even at the present time. It was into the period when these ideas were accepted with little question that John Fulton directed his keen intellect toward some of these problems. That John Fulton did not solve all of them

is not surprising but he did open the investigative door which has led to a much sounder understanding of the relations of the frontal lobes to normal and pathological activity. He did bring neurological surgeons, neurologists and neurophysiologists closer together. He caused neurologists and neurosurgeons to realize the importance of a fuller knowledge of neurophysiology to proper understanding of their clinical problems and to the optimum practice of their specialties. He brought the clinician into his laboratories. He taught them investigative techniques. He engendered in them a critical and skeptical attitude toward the reported results of research. He taught them to ask, in the words of that great physiologist, A. J. Carlson, "what is the evidence?". He accomplished much for the physiologist also. He related them to the clinic. He pointed out that they could not be fully effective if they concentrated their attention solely upon the laboratory and the experimental animal. He reminded them that man is an animal too; that the basic purpose of most neurophysiological research is the understanding of man and his diseases; but that experimental observation true for laboratory animals must be confirmed for man before they can be accepted as true for man.

Fulton was one of the first to point out that the muscular paralysis resulting from the destruction of the precentral cortex is not necessarily associated with spasticity and that muscular paralysis and muscular spasticity result from destruction of different neural mechanisms. The details of these mechanisms, as far as we now know them, have been worked out largely by others — some of them Fulton's collaborators and students — but it was Fulton who gave the initial impetus to our modern understanding of neuromuscular control. Von Bechterew, years before, had pointed out the relationship of the cerebral cortex to visceral and vasomotor activity but his observations had largely been ignored and forgotten. It was Fulton and his associates who again pointed out this relationship and stimulated the research which has

followed regarding the relationship of the cerebral cortex to blood pressure, cardiac activity, vasomotor phenomena, gastro-intestinal activity, etc., etc.

Neurologists have been heard to say that the work of Fulton was of little importance because none of it has remained. This, of course, is not true. Fulton, more than any other American, is responsible for the development of modern neurophysiology. It was he who laid the ground work upon which more recent research has been built. He has introduced new concepts which have revolutionized neurological thinking. He trained and stimulated many of the investigators who subsequently have further illuminated these problems.

The understanding of the neural control of the skeletal musculature has developed directly out of the ideas and the research of John Fulton. It has not stopped with his investigations, neither is it complete at this time. Great changes in our thinking and understanding have taken place. Terminology has changed. That we no longer speak of motor and pre-motor cortices, that the idea of an area 4 and an area 6 serving two different motor functions has been discarded do not mean that Fulton was wrong, but merely that he had an incomplete and imperfect concept. At that time all of the evidence now available was not available to him. As in any developing field ideas change, some are discarded. We are building now upon the work and ideas of Fulton and it is to be anticipated that some, perhaps much, of what we now believe will subsequently be altered or discarded as more is learned.

At present our understanding of the neural mechanism which controls movement may be summarized as follows:

It is now recognized that the neural mechanism is a single complex system all parts of which are related to all others. Fundamental control of this neural mechanism resides in the precentral motor cortex in primates. However, for a thorough understanding of the mechanism in primates it must be recognized that the development of this cerebral cortical control has been an

evolutionary one, and that as a result when for any reason the cortical portion of the mechanism fails the more primitive subcortical portions are capable of taking over, although in an inadequate fashion. In birds there is no cerebral cortex and control of their well coordinated, skillful movements is exercised by a neural ganglionic system comparable to the subcortical mechanism of the primate brain. In the carnivores, cat and dog, a cerebral cortex has developed and it contains a "motor area", comparable in some respects to the precentral motor cortex of primates. However, in the cat and dog this "motor area" is of far less importance than in primates. It responds to electrical stimulation by the production of movements in the skeletal musculature, as in primates, but its destruction does not produce anywhere near the impairment of function that is seen when the precentral motor cortex is destroyed in man or monkey. In fact the destruction of the "motor area", the sigmoid gyrus, in the cat (or even of the entire cerebral cortex) does not paralyze the animal, although it does abolish certain reflex activities. A cat deprived of its cerebral cortex can still sit, stand, walk and run much like a normal animal. In primates, on the other hand, destruction of the cerebral cortex, or even of the precentral motor cortex alone results in a severe impairment of motor performance. Even here a continuation of the evolutionary process is obvious. As Travis and Woolsey have shown, if the cerebral cortex is destroyed piecemeal over a considerable period of time and if the animal is given intensive care including almost continuous daily physical therapy a limited amount of awkward, stereotyped, but useful movement can be produced by the subcortical portion of the motor system alone. In man the precentral motor cortex has assumed a greater dominance and importance. Unfortunately, destruction of the precentral motor cortex in man results in a much more severe, though not complete, paralysis even though intensive care is given to the patient. In man such a destruction results in a practically

complete paralysis of the distal parts of the contralateral extremities, the hand and fingers, foot and toes. This renders the upper extremity useless but most people with such an involvement are able to walk on the affected leg. For obvious reasons no one has ever observed the results of a complete cerebral decortication in man as has been done in monkeys.

The neural motor system is an intricate one which includes the cerebral cortex, the basal ganglia (globus pallidus, putamen and caudate nucleus) the diencephalon, the brain stem, the cerebellum and the spinal cord. No one of these parts functions alone or independently. At the present time our understanding of the many intricacies of this extremely complex system is still very rudimentary. I have been concerned, primarily, with the cerebral portion of this mechanism in primates and will attempt to outline our present understanding of it. This does not imply that the brain stem, the cerebellum and the spinal cord are any less important as all are essential parts of this mechanism.

The concept that the precentral motor cortex is divisible into two parts, a "motor area" (area 4) and a "premotor area" (area 6) is obviously false. But, the basic concept which was behind this idea of Fulton's that the precentral motor cortex controls both the pyramidal and extrapyramidal portions of the motor system is sound. It is now obvious that both the pyramidal and extrapyramidal portions are represented co-extensively in the precentral motor cortex. The pyramidal is not represented exclusively in area 4 and the extrapyramidal in area 6. In fact it is doubtful if any useful purpose is served in subdividing the precentral motor cortex into different areas even though such subdivision finds support in the microscopic appearance of the precentral motor cortex. It is now well established that the pyramidal tract arises from both areas 4 and 6 (as well as from the parietal cortex), and that both areas 4 and 6 give rise to descending fibers which pass to and control extrapyramidal subcortical structures in the basal ganglia,

brain stem and cerebellum. In the intact animal these various components of the neural motor mechanism function together and simultaneously in a well coordinated fashion but, as will be pointed out below, when the pyramidal system is destroyed the remainder is capable of taking over and functioning in a useful but not perfect manner.

There can be no question now but that the precentral motor cortex is intimately concerned with the activities of the extrapyramidal system and that the latter is not an independent neural mechanism. Although it does function alone in birds and can function admirably when deprived of the cerebral cortex in cats it has lost the ability to function adequately in primates when deprived of the cerebral cortex. On the other hand, this old independence of the extrapyramidal system serves it well in primates, and enables it to function effectively when the pyramidal tract is destroyed in these higher forms.

Neurology suffers seriously under the handicap of various erroneous misconceptions which have grown up within its body of knowledge. These have arisen from inadequate and incomplete information, from the transfer of information obtained from lower animal forms (cat, dog, rabbit and at times monkey) which is not true for man and at times from "delusions by the obvious", as I have pointed out elsewhere. Observation and experimentation upon man are difficult. Prolonged observation under ideal experimental conditions, anatomical control, and repetition of observation so essential to accurate conclusions are often difficult or impossible to obtain in man, but *this does not make them any less essential for accurate interpretation in man*. One of the most serious misconceptions which has developed is that concerning the pyramidal tract. Until recently, and unfortunately still in some quarters, it has been believed that the pyramidal tract arises solely from the precentral gyrus and predominantly or exclusively from the gigantic cells of Betz to be found in that gyrus; that the py-

pyramidal tract is the only descending fiber system from the precentral motor cortex which is concerned with the activity of the skeletal musculature; that the pyramidal tract is concerned only with motor activity; and that destruction of the pyramidal tract results in a group of manifestations which have come to be known as the "pyramidal syndrome" (spastic paralysis, increase in the tendon reflexes, abolition of the abdominal reflexes and the sign of Babinski). These concepts, still to be found in many textbooks, in the minds of many neurologists, and still taught to many medical students, are wrong.

The pyramidal tract arises both from the precentral motor cortex (both areas 4 and 6) and from the parietal cortex as well. In fact there is good evidence that only 60 % arise from the precentral region and 40 % from the parietal cortex. The Betz cells give rise to only a very small percentage of the pyramidal fibers, probably no more than 3 or 4 %. The pyramidal tract is only a part of the descending fiber system from the precentral motor cortex which is concerned with the production of movement. The fibers to various subcortical centers are also so concerned.

We have a fairly good knowledge of the course and activity of the descending fibers and the mechanism concerned with the reflex activity of these muscles but even that is not complete. We know of the fibers from the precentral motor cortex to the reticular formation of the brain stem and of the control of that formation over the reflex activities of the spinal cord and of the skeletal musculature. We know that when this system is interrupted either in the cortex or the internal capsule or the brain stem or the spinal cord, spasticity and reflex hyperactivity result, and that the pyramidal tract has little or nothing to do with this reflex activity. But even this information is incomplete. One of the great gaps in our knowledge concerning reflex activity has to do with the abdominal reflexes. We know only that in many patients when some impairment of the descending motor neural system (especially in

the spinal cord) occurs, and particularly when some paresis of the muscles, spasticity and hyperactive reflexes are present, the abdominal reflexes are often absent — but not always. It is now well established that many patients who have spastic paralysis do not lose their abdominal reflexes and that impairment of muscular function by cerebral cortical lesions seldom affects the abdominal reflexes. But we do not know the neural mechanism responsible for the control of the abdominal reflexes, nor the specific lesion or lesions which will abolish them.

We now know that the pyramidal tract is not the sole descending pathway concerned with motor activity, even though there is definite evidence that it is an important one. It is now well established that in both man and monkey the pyramidal tract can be destroyed without producing a complete paralysis or spasticity or increased tendon reflexes. Destruction of the pyramidal tract does give rise to the sign of Babinski. Even though the pyramidal tract is destroyed strong, well coordinated, useful movements are still possible in all parts of the extremities. Spasticity and increased tendon reflexes do not appear. And thus the so-called "pyramidal syndrome" is a myth which must be discarded from all neurological thinking. It is obvious that the extensive and useful muscular activity which remains, both in man and in monkey, after the pyramidal tract has been destroyed must be produced by some extrapyramidal mechanism. This mechanism must be a multisynaptic one which is interrupted at one or more points in its course of descent from the cerebral cortex to the spinal cord. We know that it must pass downward through the tegmentum of the midbrain, at least in part, as it continues to function ever after the cerebral peduncles have been destroyed. However, as it appears that motor functions are less perfect after the entire cerebral peduncle has been sectioned than after the pyramidal tract alone has been destroyed, it is not unlikely that some of these extrapyramidal fibers concerned with motor ac-

tivity are to be found among the nonpyramidal fibers of the cerebral peduncle which pass to the brain stem and the cerebellum. At this time we do not know whether we are dealing with one pathway or with several, what the course of this extrapyramidal pathway is, nor in what subcortical center or centers the synapses occur.

As was pointed out above the pyramidal tract arises both from the precentral and postcentral cortices. Are both concerned with motor activity, as Woolsey believes, or is this a function of the precentral motor cortex alone? Certainly the postcentral cortex may have motor functions, but there is good reason to believe that the pyramidal tract descending from the postcentral and the precentral cortices has other functions. Kuypers has demonstrated that fibers descending from these areas terminate on sensory nuclei, such as the nucleus of the spinal root of the 5th cranial nerve and the nuclei gracilis and cuneatus in the brain stem. He has also shown that pyramidal fibers, particularly, but not exclusively, those from the parietal cortex, end upon the cells of the posterior horns of the spinal cord. The function of these fibers is still unknown but it is reasonable to assume that they subserve other than direct motor functions; that is, they do not produce movement directly. As they are descending they do not subserve sensory function directly either. As they terminate on sensory nuclei it is reasonable to assume that they are concerned with the regulation of sensory thresholds. They may control what sensory input reaches consciousness and is effective and what is not. They may also exert an important regulatory influence on the input from the muscle spindles into the spinal cord, and thus, indirectly, be an important factor in the regulation of motor activity. It must be stressed, however, that for the present such ideas are little more than speculative.

Clinical observations on patients suffering from spontaneous lesions of their neural motor mechanism as well as observations on both man and monkey in which

the pyramidal tract has been sectioned raise the very important question as to how the improvement in the control of the skeletal musculature is brought about which usually occurs following such lesions. With human disease the situation is commonly such that many factors may play a role. However, when the pyramidal tract has been sectioned, particularly bilaterally, the picture is clearer.

In man destruction of the pyramidal tract by surgical section of the cerebral peduncle results immediately in a complete paralysis of the contralateral extremities. Recovery of muscular control begins in the next few days and continues for many months before maximum recovery is achieved. In monkeys a similar situation occurs, although recovery begins somewhat earlier.

Recovery might conceivably be due to development of new pathways or to the reorganization of descending motor pathways remaining after the pyramidal tract has been destroyed. Although the gradual development of new pathways would explain nicely the gradual recovery which takes place, it seems most unlikely that this is the correct explanation. There is no evidence that new pathways do develop under these circumstances and it is most unlikely that they would do so in the adult primate central nervous system. It seems far more likely that the gradual improvement is dependent on a reorganization of existing mechanisms.

In all probability the anterior horn cells of the spinal cord respond appropriately to stimulation via a multiplicity of synapses acting simultaneously or nearly so, rather than to a stimulus arising over a single nerve fiber or a single nervous pathway. Certainly the anterior horn cell has afferents from a variety of sources making such an explanation not only reasonable but possible anatomically. If this hypothesis is accepted then it is reasonable that when such an important source of afferent impulses as the pyramidal tract is destroyed the anterior horn cells are unable to function in the production of voluntary move-

ment and a complete paralysis results, temporarily. To refer to such a state as "spinal shock" or as "diaschisis" serves no useful purpose. To do so supplies only a meaningless term without providing any understanding or worth while explanation. Instead it is essential that the physiological and anatomical facts responsible for this phenomenon be known and understood.

With unilateral cerebral lesions either of the cerebral peduncles, the internal capsule or the cerebral cortex there is good reason to believe that afferent innervation from the ipsilateral cerebral hemisphere plays some role in the restoration of function in the involved extremities. This may be via either pyramidal or extra-pyramidal fibers. However, very useful recovery occurs, at least in monkeys, following bilateral complete destruction of the pyramidal tracts, demonstrating that in the absence of these important structures other descending neural mechanisms or extra-pyramidal fibers are capable of producing strong, useful, coordinated movements of the extremities. We have also seen monkeys with useful movements who had the pyramidal tract completely destroyed on one side by section of the cerebral peduncle and both the pyramidal tract and the extra-pyramidal descending motor fibers from the cerebrum destroyed on the other side by a complete cerebral hemispherectomy. Although this experimental approach has not yet been fully investigated, the limited observations which have been made leave little doubt but that the extra-pyramidal fibers from one cerebral hemisphere and those from the brain stem are capable of producing useful movements in all four extremities in these subhuman primates. Thus although ipsilateral fibers are undoubtedly important they are not essential to the production of useful skeletal muscular activity. Furthermore, in man the degree of motor control which persists following the unilateral destruction of the pyramidal tract is far greater than that which follows a severe destructive lesion in the internal capsule. This evidence further indicates that the most important

factor in recovery after section of the pyramidal tract is the activity of the extra-pyramidal system contralateral to the involved extremities.

That the extra-pyramidal system is capable of such independent activity should not be too surprising. As was pointed out earlier lower animal forms perform extremely well with only an extra-pyramidal system. As we ascend the animal scale the cerebral cortex gradually becomes more and more dominant and the descending neural pathway peculiar to it, the pyramidal tract, more and more important. But even in man this dominance and importance are not complete. In man the cerebral cortex is apparently essential to the performance of useful movements but is capable of exercising this control over the extrapyramidal fibers which originate there and descend first to subcortical nuclei and then to the spinal cord.

The anterior horn cells of the spinal cord which initially are unable to function in the absence of the pyramidal impulses gradually readjust and become able to do so when stimulated by extra-pyramidal impulses alone. The pathways over which these impulses reach the anterior horn cells from the cerebral cortex are as yet very imperfectly understood. There are many possibilities. The cerebral cortex projects to the lenticular nucleus (globus pallidus and putamen), to the caudate nucleus, the thalamus, various nuclei in the brain stem, particularly the reticular formation, to the pontine nuclei and through it, as well as directly, to the cerebellum. It seems unlikely that any one of these possible pathways alone is responsible for the production of useful movement in the absence of the pyramidal tract. Rather it appears most likely that all or most of these neural systems function together with or without the pyramidal tract. This symphonic action of a complex descending neural motor system undoubtedly takes place both with an intact pyramidal tract or after its destruction.

The nature of the reorganization within the anterior horn cell which at first can

not function adequately when the pyramidal tract is destroyed is wholly unknown.

Over the past thirty-odd years our knowledge of the neural mechanism which controls muscular activity has increased tremendously, but much is still unknown and remains to be learned. This applies to our knowledge of the structure and function of the brain stem, cerebellum and spinal cord as well as to the cerebrum. Although I have stressed the importance which Fulton played in the renaissance of interest in neurophysiology and in the understanding of the neural motor system, this is not to deny the importance played by others. Like the neural motor system itself this has been an interrelated group of people all of whom have played a part. To mention a few — Sherrington, the teacher of Fulton, contributed much to our early understanding, probably more than any other investigator of the period, but Schaeffer, Rothman, Holmes and Page May and Otfried Foerster played important roles. Sir Francis Walshe, who disagreed with Fulton on many points and criticized him unjustly on some, also has served to bring our attention back to the problem and to emphasize errors in our thinking.

His clear, pungent use of the English language and his sharp critical attitude have served to attract attention to his remarks, but his lack of investigative approach and his adherence to authoritarianism and the traditional have detracted from his expositions. Like Fulton and all others concerned with these problems he has often been in error. This in itself is no criticism. All who do things make mistakes, but the greatest mistake of all is to do nothing. It is to be hoped that as we work, think and progress, our ideas will change and we will discover the error of some of our old concepts. In the Western Hemisphere Wilder Penfield, Dusser de Barenne, Percival Bailey, Warren McCulloch, Margaret Kennard, Sarah Tower, Marion Hines, Henry Kuypers, John Russell and William DeMyers have all made outstanding contributions to our body of knowledge.

Much remains to be done. Our understanding is still woefully incomplete and inadequate. Research in this field must be intensively pursued, but always with meticulous attention to scientific methods. We must never lose sight of the famous aphorism of that great physiologist, A. J. Carlson, "What is the evidence?"

The Architecture of the Human Frontal Lobe and the Relation to its Functional Differentiation*

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Neuroanatomical and neurophysiological approaches have revealed a new evaluation of the gyral pattern for cortical localization^{16, 24, 25, 26}. Since the great discoveries of cyto and myeloarchitecture in the first decades of this century, the gross morphology was lost sight of. It is true that the former descriptive discipline of the gyral pattern based only on formal analogies is of limited value for comparative conclusions. The study of the pattern of gyri and sulci of cerebral cortex has to be founded on exact investigations of the cortical substratum itself, i.e., the laminated cortical band, its cyto and myeloarchitecture on the one hand and its physiological properties on the other. Only in such a way can homologies be defined and functional units based reliably on morphology.

A fundamental result of such new approaches is the evidence that the majority of cortical surface indentations, including fissures and dimples, are limiting cortical areas as defined by architectonic or electrophysiological methods.

In order to arrive at a deeper understanding of the frontal lobe structure of man, we will present some common principles of organization of the primate cerebrum in the slow loris, *Nycticebus coucang*, as a specimen of the infraorder of lorisiformes of the prosimians, the prosimians being a general stage of develop-

ment which all primates have passed in evolution¹⁸. The prosimians still have the primitive sagittal gyral pattern with longitudinal sulci prevailing, as opposed to simians with a prevailing coronal pattern especially of the central region. The significance of the sulci of the latter, as well as of the coronal sulcus lunatus as limiting fundamentally different fields is well known, whereas the relationship of the sagittal sulci to the architectonic pattern was not yet known. A correlated architectonic and electrophysiological approach (Welker, Krishnamurti and Sanides, in preparation), resulted in demonstrating the medial sulcus "c" and the lateral sulcus "e" (this in its horizontal part) to be limiting sulci between the representations of hindlimb, forelimb and head in somatic sensory and motor regions (Fig. 1).

The review of the literature shows in two other prosimians, lemur and perodicticus, in which only the lateral sagittal sulcus is well developed, this sulcus was found in electrical stimulation experiments to be limiting between motor hand and head area as it is in slow loris. The experiments

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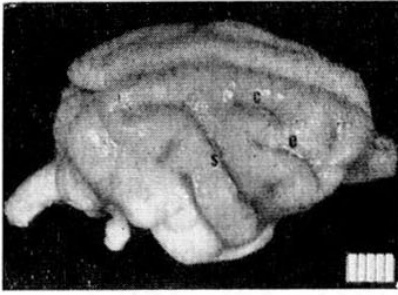


Fig. 1. — View of the right hemisphere of the prosimian slow loris. c and e sagittal sulci, s sulcus Sylvius continuing dorsally into the sagittal sulcus intraparietalis which is on the left hemisphere (dorsally) almost connected with sulcus c.

in lemur were undertaken by C. Vogt and O. Vogt²¹ and in perodicticus by Zuckerman and Fulton²⁹. Woolsey already directed the attention to the fact that there are in monkeys two little sulci, sulcus precentral superior and posterior spur of the arcuate sulcus with the same somatotopically limiting significance in precentral motor area. Thus we can recognize in these short sulci or dimples of monkeys which are rather inconspicuous compared with the coronal ones, remnants of the old *sagittal* pattern.

Corresponding evidence was presented by Dusser de Barenne in its *strychnization* experiments, and here the small *postcentral* superior sulcus plays the same role as the *anterior* one in limiting leg from hand subdivision of the "sensory cortex"⁸. However, it should be emphasized that postcentral superior sulcus varies in its form and can also be found shaped in coronal direction, in which case it separates Brodmann's postcentral fields 1 from 2. For the interpretation of sagittal and coronal pattern, we refer to Le Gros Clark, who developed the rule that sulci and gyri form vertically to the lines of stress⁶.

We prefer to speak of growth stress and could demonstrate in man's frontal lobe that such lines can be defined as *directions of architectonic differentiation*. Thus the shift from prosimian sagittal to simian coronal pattern means then a shift from prevailing *coronal* lines of growth stress to stronger *sagittal* ones in the field of force of the cerebral cortex. Eventually in man's frontal lobe we have to do with the highest degree of gyrification in the primate order. This corresponds not only to the general rule of body size-

brain size relations but also to the highest level of organization with the striking preponderance of prefrontal granular cortex as against primary motor region. This highest degree of gyrification in the primate order leads to the well known abundance of human gyri and sulci; nevertheless rules of prevailing regular sulci and gyri could be elaborated. This pattern shows beside the strong *coronal* central, precentral and postcentral sulci of the central region the *sagittal* frontal sulci and gyri in the huge prefrontal cortex.

Regular sulci mean as a rule deep sulci. The deepest sulcus, however, and by definition also the ontogenetic earliest of these sulci, is the central one. This could be interpreted as if in ontogenesis after a period of prevailing *sagittal* growth stress, which pushes the central region backward (see below), follows a period of coronal growth stress. However, the cingulate sulcus, on the mesial surface, a striking example for a longitudinal sulcus, caused by coronal growth stress*, is also a *primary* one, that means an early initiated one as the central sulcus is. Thus we ought to speak rather of a longer lasting coronal growth stress, which brings the sagittal frontal sulci of the convexity into appearance. Thus we recognize in gross morpho-

* The sulcus cinguli is just a paradigm at which Le Gros Clark developed his rule that sulci and gyri form normally to lines of stress. This sulcus can be found running parallel to the corpus callosum in all eutherian mammals. But the sulcus cinguli is lacking, giving place to radiate sulci in marsupials without an elaborated corpus callosum. Moreover this sulcus is lacking in cases of human malformations with agenesis of the corpus callosum.

logy the remarkable fact that the big human prefrontal cortex reflects in its longitudinal partitioning a high degree of the phylogenetic more ancient coronal growth stress which still prevails in prosimians. The extremely high degree of gyrification in man, however, no longer allows us to assign these sagittal sulci and gyri to a somatotopical arrangement with any security.

The *directions of architectonic differentiation* mentioned above are represented by arrows in the maps of human frontal cortex

(Fig. 2). It must be pointed out that we show here for practical reasons not the maps of the single fields, but only those of zones, i.e., belts of related fields. We begin our description with the coronal directions of differentiation, which originate in the anterior cingulate gyrus on the medial side and in the anterior insular cortex on the lateral. These spring territories are parts of old *limbic cortex sensu ampliori* including the insular cortex for ontogenetical and phylogenetical reasons as proposed by Yakovlev²⁸. At the same ti-

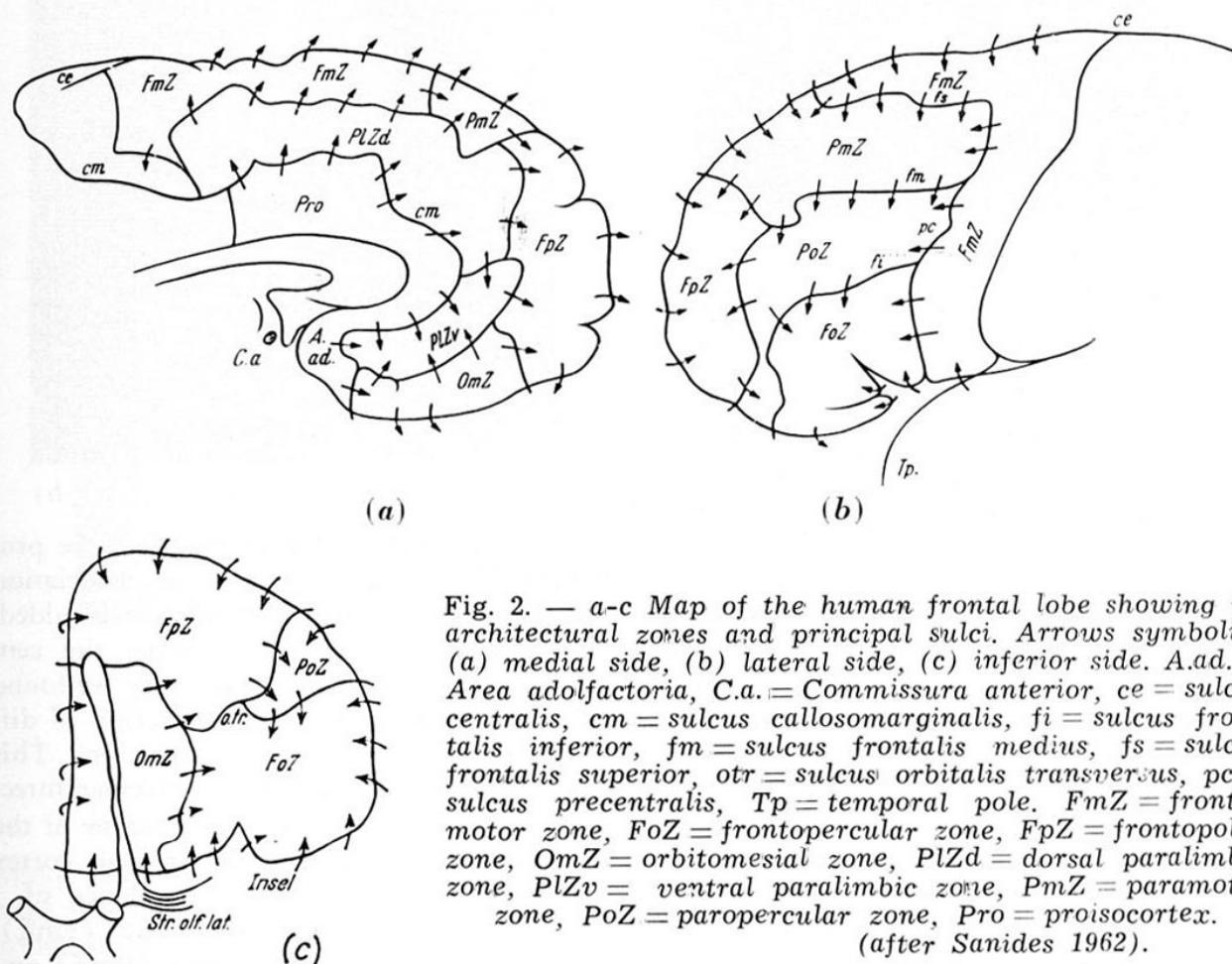
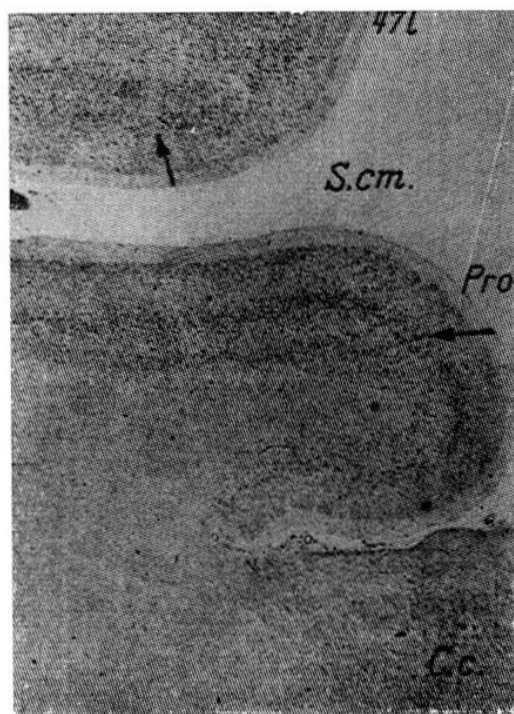


Fig. 2. — a-c Map of the human frontal lobe showing its architectural zones and principal sulci. Arrows symbolize (a) medial side, (b) lateral side, (c) inferior side. A.ad. = Area adolfactoria, C.a. = Commissura anterior, ce = sulcus centralis, cm = sulcus callosomarginalis, fi = sulcus frontalis inferior, fm = sulcus frontalis medius, fs = sulcus frontalis superior, otr = sulcus orbitalis transversus, pc = sulcus precentralis, Tp = temporal pole. FmZ = fronto-motor zone, FoZ = frontopercular zone, FpZ = frontopolar zone, OmZ = orbitomesial zone, PlZd = dorsal paralimbic zone, PlZv = ventral paralimbic zone, PmZ = paramotor zone, PoZ = paropercular zone, Pro = proisocortex. (after Sanides 1962).

me, the anterior cingulate gyrus and the anterior insula are also in architectonic terms very related, representing a *proisocortex* with a typical dense bandlike Vth layer which was also described by von Bonin as a *juxtaallocortical* feature³. As a conspicuous *limbic* feature the anterior cingulate gyrus possesses, moreover, in its layer Vb extremely slender pyramidal and

spindle cells, called rod cells (Fig. 3). These limbic signs undergo in the next grade of differentiation, in a paralimbic and parinsular belt respectively, a diminuation; at the same time a new *progressive* kind of characteristics begins, for instance increasing overall cell size and especially increasing accentuation of the IIIrd layer, still very weak in both kinds of proisocor-



a)

Fig. 3 a and b. — a) Proisocortex (Pro) of cingulate gyrus. Cresyl-violet staining 5 times. The arrows point to the bandlike Vth layer which is dorsal to the bottom of sulcus cinguli (s.cm) less accentuated. C.c. = corpus callosum. b) 1000 times, extremely slender "rod cells" left pyramidal, right spindle. (after Sanides 1962).



b)

tex. These are only two *main* cytoarchitectonic trends. After passing the first frontal gyrus the stepwise granularization is added, and the efferent V pyramids begin to *decrease* step by step. We omit here the concomitant myeloarchitectonic changes. It appears important that all these changes occur *stepwise*, i.e., in grades, thus forming a sequence of fields. This is why C. and O. Vogt, who first described these proceedings in some examples, spoke of "gradation". Summarizing, we can say that the stepwise architectonic differentiation of the frontal lobe in coronal directions originates primarily in the phylogenetically oldest limbic parts of the neocortex. Therefore these directions of differentiation may be looked upon as *evolutionary* ones and are called by us "*Urgradationen*", i.e., "*proto-gradations*"^{16, 17}.

The *sagittal* direction of growth stress

was considered by LeGros Clark to be produced by the growing *frontal* association cortex; the growing *parietal* one is added, forming counterpressure against the central region. In human frontal lobe we found a corresponding poleward direction of differentiation, or "poleward gradation". This may be demonstrated by a myeloarchitectonic instance which admits a survey of the whole sagittal spread of frontal cortex (Fig. 4). We overlook a sequence of 2 fields of the frontomotor zone (FmZ), 3 fields of the paramotor zone (PmZ) and 2 fields of the frontopolar zone (FpZ). Proceeding from the area gigantopyramidalis (42) we see a stepwise rostral decrease of the overall fibrillarity. At the same time the stripes of Baillarger emerge stepwise from the lighter ground and the inner stripe gets more accentuated. These changes are paralleled in cytoarchitectonics by a stepwise granularization and stronger lamination as well as a diminishing of

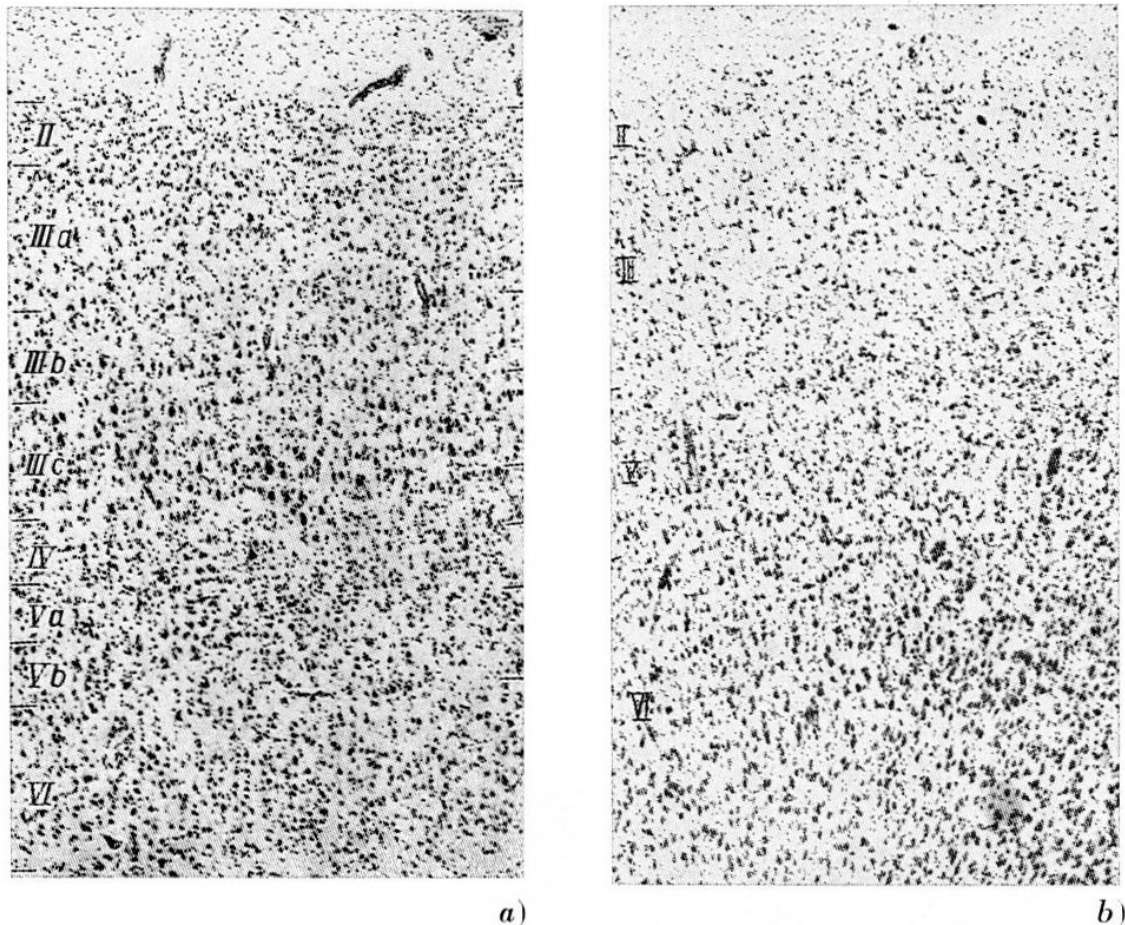


Fig. 5 a and b. — a) Central field of the orbital cortex. Cresylviolet staining, 40 times. Note the high granularization of the granular layers II and IV, the light Vb, and accentuated IIIc pyramids as a sign of parakoniocortex. b) Caudoorbital transitional field. Proisocortex with poor lamination and no clearcut granular layer. Note preponderance of the inner main layer, V and VI, over outer main layer II and III. (after Sanides 1962).

excitable site of cortex moved backward, arriving at the final position about birth-time. The concomitant change from holo-kinetic type of the elicited movements to idiokinetic type can be interpreted in our view that the latter is elicited in the area gigantopyramidalis, which differentiates last within precentral motor cortex. That the area gigantopyramidalis is the highest and most recent motor cortex elaboration was the result of its exact definition in the system of the directions of differentiation¹⁶.

Finally, a sagittal direction of differentiation originates in the frontal part of the prepiriform cortex, the basal olfactory cortex, which influences about two thirds of the orbital cortex. This orbital cortex, moreover, is subject to differentia-

tions of insular and ventral limbic origin, resulting in a special high stage of differentiation in the center of the orbital cortex, as demonstrated in Fig. 5 a. Thus the central orbital field, bound on the sulcus orbitalis transversus, presents a peculiarity within the frontal lobe, exhibiting rather parakoniocortex character. This special character can perhaps be explained by the integration of different directions of differentiation, which may mean convergent sensoric and cortico-cortical input. However, the steepest gradation, i.e. the sharpest span of differentiation, dominates between the orbital center and the caudoorbital transition field, Vogt's field 66 (Fig. 5 b), which borders caudally immediately at the primary olfactory cortex. It is still poorly laminated and shows a pre-

ponderance of the inner main layer; thus it is classified as *proisocortex*. It is important, to realize that in the central orbital field, as well as in the caudoorbital transitional field and the intermediate fields conspicuous strong tangential fibers are to be traced in the first layer, indicating further relations between the more primitive caudoorbital cortex and the highly differentiated orbital center.

It remains to be said that the sagittal direction of stepwise differentiation of the orbital cortex presents a component of the *lateral protogradation* of paleocortical origin, which proceeds here directly from the primary olfactory cortex without the detour over the insular cortex taken by the convexity component. Thus in conclusion we can speak of three sources of differentiation of frontal lobe: two main or *protogradations* of *medial* limbic and *lateral* insular limbic origin, respectively, and a more recent poleward gradation of motor cortex origin. —

These directions of architectonic differentiations in man's frontal lobe were fundamentally confirmed in the slow loris. The confirmation is noteworthy especially for one consequence which we have still to discuss. The two main directions of differentiation had led us to a classification of the additional sensory and motor areas, which present one of the most intriguing new developments in mammalian neurology. Lying in the flow of the *protogradations* from the insular cortex on the one side and from the cingulate gyrus on the other, the second sensorimotor area located at the edge of the operculum can be conceived as a phylogenetically older level of *sensorimotor* control than the classic central one, and the supplementary motor area located in paralimbic site can be conceived as a phylogenetically older level of *motor* control. Thus the parinsular area appears to be a protosensorimotor representation, and the paralimbic area appears to be a protomotor one. For the second somatic sensory representation this concept was already put forward in 1946 by Woolsey considering also neurophysiological reasons.

In the slow loris the second somatic sensory representation (SmII) was outlined electrophysiologically on the one hand and architectonically on the other resulting in congruity. The architectonically defined field (SmII) proved to be really an intermediate stage between insular cortex and classic somatic sensory cortex, corresponding to our assumption that it presents a more ancient phylogenetic level of sensorimotor elaboration than the classic one.

We have still to deal with two essential corroborations for our two main directions of differentiations of the mammalian cerebral cortex. One consists in findings of Abbie in monotremes¹ and marsupials², which we got acquainted with only after finishing our frontal lobe monograph. Primarily in monotremes Abbie found the principle of "*dual nature of neopallium*"; that means, that there are two neocortical moieties: one differentiated in stages away from the *hippocampus* and the other in stages away from the *piriform* cortex. In the marsupials *Perameles* he found this principle fully sustained, and speaks e.g. of the parahippocampal moiety of the neocortex as successive waves of circumferential differentiation away from the hippocampus in evolution.

Finally such a "cerebral watershed" (Abbie) was also found by quite another approach in the prefrontal cortex of monkeys by Nauta, presented in a preliminary note (1964). Using his silver impregnation technique he demonstrated that there is "a certain dualism in the prefrontolimbic associations", in that the principal sulcus separates two moieties of the frontal granular cortex. The dorsomedial one projects in a high degree to the cingulum bundle in the cingulate gyrus, spreading from there over the retrosplenial cortex to the juxtahippocampal region. The ventrolateral one including orbital cortex projects, by the way of the uncinat bundle, mainly to the anterior half of the *temporal* cortex. From there projections to the amygdaloid complex are known.

It should be added that a cytoarchitectonic control of monkey's frontal lobe suggests that the principal sulcus may be ho-

mologous to the sulcus frontalis inferior in man's frontal lobe. This is the same sulcus which presents by and large the limit between the two spheres of influence: the dorsomedial one related to the cingulate gyrus and the ventrolateral one related to the insular and ultimately to the prepiriform cortex.

Thus Nauta's anatomical observations indicate in his own words "a close affiliation of the anterior frontal cortex to the more primordial structures in the medial and basal walls of the telencephalon." This, however, is a very *related statement* to ours about the two main directions of differentiation of medial limbic and lateral insular origin and about the long lasting coronal growth stress originating in these bordering regions as reflected by the sagittal sulcal and gyral prefrontal pattern in man.

Thus the frontal association, or integration, cortex of higher primates including man reflects in different aspects, notwithstanding its late phylogenetic deployment deep limbic relations to and from medial and ventro lateral primordial structures of the forebrain. However, a combination of highly organized with more conservative signs appears to characterize the 6-laminated association cortex throughout (see also Sanides and Krishnamurti), in contrast to the highly specialized structure of the so-called primary motor and sensory regions which are hyperpyramidal and hypergranular, respectively. Therefore we may conclude the prefrontal cortex to be a structure of a high capacity of differentiation avoiding specialization.

Coming now to the *functional* correlations we discuss the orbital cortex first. Here we recognize in the above described special topology in the field of differentiations a possible expression of the tension between the realm of limbic reactions on the one side and the personality reactions on the other, the latter controlling the former. It appears to be significant in this connection that Fulton and co-worker demonstrated by neuronography orbital projections to the paraventricular nucleus of the hypothalamus.

After the original findings of Leonore Welt it was Karl Kleist who *differentiated the syndroms* of orbital lesions from that of the *superior frontal* ones, assigning to the first impairments of feeling and acting of personality such as tactfulness and ethical and conscience reactions. We have still to consider indications that in comparative neurology the orbitomesial zone, reaching from the ventral cingulate sulcus to the medial orbital sulcus and reflecting stronger limbic influences, might play an initial role for a somewhat lower stage of such reactions, as it is generally covered by the term inhibition. This is suggested by the experiences of Brutkowski⁵ in ablation experiments which led him to the conclusion that the anterior median prefrontal cortex of dogs corresponds in this function—and may be homologous—to the orbital cortex of monkeys.

Perhaps also ablation experiments in rats of Stamm²⁰ may cast some light on this problem. Comparing subjects with extensive median cortical ablation with subjects with lateral cortical ablation of about the same amount of cortex, he found that only in the "median group" were maternal reactions disturbed significantly. The maternal reactions examined were: constructing of nests, keeping the litter together and hovering over them, finally reconstructing of nests after destruction and protecting the litter against radiant heat. In a preliminary paper the hoarding activity of the rat was also found impaired in subjects with median lesions.

We incline to feel that in these maternal reactions we deal with the phylogenetically oldest core of the realm of reactions which aim beyond the pure ego and which in ultimate elaboration have made man peculiarly man. These are the reactions of personality and conscience which appear to be bound finally to the integrity of man's orbital cortex and its special stage in the system of cortical differentiation.

The high prefrontal cortex belonged also to the silent region of the cortex in the classic period of cerebral investigation. However, with the disclosure of the im-

pairment of the delayed-response test in frontal lesions by Jacobsen in 1936, a new research period has been entered. Considering some recent papers, we will try to correlate these experimental results with our architectural concept of frontal cortex differentiation. Moreover, we believe to find a conformity with Kleist's clinically developed term "Antrieb" as impaired in high frontal lesions in man. Evidently it is conditioned by inadequate translation as "drive" that this notion of a frontal impairment is not introduced in the English speaking realm. Actually "Antrieb" means initiative. With this we are approaching indeed the interpretation of the impairment on acquisition and retention of delayed-response tasks in monkeys by such a recent investigator as Pribram¹³: Pribram had made 7 special experiments with monkeys to examine the modality specificity of the effects of bilateral frontal injury. However, the results of the experiments demonstrated clearly that the defect in behavior that follows high frontal injury cannot be attributed either to an impaired sense of place (proprioception) or to an impaired visual performance. On the other hand, the lesions did modify behavior when the ambiguity of the test situation was increased by changes in conditions involving less reliability. Thus the delayed-response deficit can no longer be explained as an impairment of immediate memory, and Pribram results in statements which correspond verbally to Denny-Brown's⁷ experiences from human neuropathology: What is impaired may be "interest and hence sustained attention and initiative". But in such a manner Kleist's "Antrieb" is fully comprised. We still must note, that Kleist noticed within the lateral frontal cortex in a site corresponding by and large to the *oral part of our paropercular zone*, PoZ, (corresponding area 46 Brodmann) "tätige Gedanken" i.e. active thinking, that demonstrates further the conformity with the function impaired in the delayed-response test.

But we can follow Pribram's conclusions still further, when he, reflecting on the

neural nature of the process injured culminates in saying "the key to the problem may be found in the relations between the frontal eugranular isocortex and the limbic formations on the medial and basal surface of the forebrain and between these formations and the reticular core of the brain stem". Here he relies primarily on the electro-physiological findings about the diffuse thalamic projection system of Starzl and Whitlock, who, systematically plotting the cortical sites where recruiting effects occur, found a predilection of the anterior cingulate gyrus, the insula and caudoorbital region* and among the association areas special affinities to the prefrontal cortex.

However, the thalamus nucleus which projects to the frontal association cortex, the medialis dorsalis, is itself an "association nucleus"¹⁰, which developed phylogenetically in parallelism with the prefrontal cortex and is enveloped by the nuclei of the diffuse thalamic projection system, united by Hassler as "the envelope". And thus it can be said—as Pribram does—that the nucleus medialis dorsalis is "cradled" within the nonspecific thalamic nuclei. Of the latest investigations of the thalamus, especially those of Akert and al.^{14, 19} have indicated that the concentric zonation of the prefrontal cortex from the direction of the limbic cortex, insula and motor cortex is analogously reproduced in the dorsomedial nucleus of the thalamus. Thus, one could speak of common, functionally linked growth rings of the prosencephalon.

But the above dealt with architectural findings mirror quite the same relation between the frontal association cortex and its limbic boundary region including the insula. Also the prefrontal cortex appears cradled within these older surrounding cortices plus frontomotor area, from which

* This is in line with results of Rose and Woolsey¹⁵ who found the interlaminar nucleus complex, i.e., the essential part of the nonspecific thalamic nuclei, included in the degeneration of the thalamus when the ablation of the cortex was extended to the anterior rhinencephalon.

regions we pointed out concentric stepwise differentiation. And the special affinities of both, the older boundary regions and the newer prefrontal cortex, to the reticular core of the brainstem communicated by the old "envelope" of nonspecific thalamus nuclei and the nucleus medialis dorsalis suggests further, that here is a key to the

functional problem of the prefrontal cortex. In the light of these architectural and neurophysiological relations, it may be said that the "Antrieb" of the high frontal cortex has a phylogenetically old radical in the reticular activating system on which its function partly depends.

S U M M A R Y

Neuroanatomical and neurophysiological approaches of the past few years have resulted in a new evaluation of the gyral pattern for localization in primates. Since the prosimians represent a stage which has been passed by all primates in their evolution, information is given about such interdisciplinary studies in a prosimian, the slow loris.

It was possible to demonstrate the significance of the here still prevailing primitive sagittal sulcal pattern for somatotopical partitioning of the sensorimotor region.

In man's frontal lobe there exists in the central region the typical coronal gyral pattern of simians, but in the huge prefrontal cortex are to be found regular sagittal frontal sulci and gyri. The sagittal gyral pattern, unusually shared by the prosimian cerebrum and by the prefrontal cortex of man, is the result of coronal growth stress whereas the pattern of the sulci and gyri of the central region of higher primates is the result of sagittal growth stress. The evolutionary more ancient coronal growth stress is reflected by two main directions of architectonic differentiation: One originating in the anterior cingulate gyrus and the other in the insular cortex. Since the differentiations proceed stepwise away from the sites of origin, forming in this way a sequence of architectonic fields, we speak with C. and O. Vogt of "gradations". These two gradations together with two sagittal ones determine jointly all characteristic features of the frontal fields. The sagittal gradation on the convexity is directed toward

the frontal pole and originates in the precentral motor cortex. The sagittal gradation in the orbital cortex originates in the basal olfactory cortex, i.e., the paleocortex of comparative neurology. This direction of differentiation is looked upon as a component of the lateral direction of differentiation away from the insular cortex which ultimately can be traced back to the paleocortex.

The gradations originating in phylogenetically older surrounding cortices such as cingulate gyrus, basal olfactory cortex, insular and precentral motor cortex and which determine the structure of more recent prefrontal cortex represent evolutionary directions of differentiation. The two main directions of differentiation which begin in the limbic cortex (archicortex) and in the insular cortex respectively (ultimately of paleocortical origin) are designated "Urgradation", i.e., protogradations.

What is generally called supplementary motor and secondary sensorimotor representation, appears to be the protomotor and protosensorimotor representations when considered in the light of the flow of the gradations.

The classic sensorimotor representations appear contrariwise as a more recent achievement in phylogenesis.

The orbital syndrome of impairment of personality in feeling and acting is understood as being the result of the special topology of the orbital cortex which is determined by its system of gradations, including immediate influences from the paleocortex. These latter influences may be

reflected in the orbito-hypothalamic connections which were stressed by J. F. Fulton as being important for emotional life.

The main symptom of high prefrontal lesions, i.e., the impairment of "antrieb" as defined by Karl Kleist, is shown to correspond to those functions found disturbed by Denny Brown: "interest, and hence sustained attention and initiative". According to Pribram the impairment of delayed response test in monkeys is to be interpreted in the same manner.

A parallelism between the concentric zonation of the prefrontal cortex from its bordering regions and the organization of thalamic dependencies, i.e., medialis dorsalis and the enveloping nonspecific nuclei, is suggested. Since the nonspecific thalamic projection system shows special electrophysiological affinities to the older bordering cortical regions and to the prefrontal association cortex, a phylogenetically old radical of the "antrieb" in the reticular activation system is accepted.

RESUMEN

Investigaciones neuroanatómicas y neurofisiológicas efectuadas en los últimos años han dado como resultado una nueva evaluación de la configuración de las circunvoluciones en lo que se refiere a la localización funcional en el cerebro de los primates.

Dado que los prosimios representan una etapa de la evolución experimentada por todos los primates se dan algunas informaciones sobre estos estudios en un prosimio, el *Nycticebus*. Fue posible aclarar la significación de la configuración primitiva de las fisuras sagitales que aún prevalece para la división somatotópica de la región sensorimotora.

En el lóbulo frontal humano en la región central se encuentra la configuración coronal de las circunvoluciones de los simios, pero en la extensa corteza prefrontal se encuentran fisuras y circunvoluciones frontales sagitales regulares. La configuración sagital de las circunvoluciones, rara vez igual en el cerebro prosimio y la corteza frontal del hombre, es el resultado del crecimiento de la fuerza coronal mientras que la configuración de los surcos y circunvoluciones de la región central de los primates superiores es el resultado del crecimiento de la fuerza sagital. La mayor antigüedad de la fuerza de crecimiento coronal, desde el punto de vista de la evolución, es reflejada por dos direcciones de diferenciación arquitectónica: una originada en la figura anterior cingulada y la otra en la

corteza insular. Dado que la diferenciación se produce en forma gradual a partir de sus lugares de origen formando de esta manera una sucesión de áreas arquitectónicas nos referimos como C. y O. Vogt a "gradaciones". Estas dos gradaciones determinan conjuntamente con las dos sagitales todas las características de las áreas frontales. La gradación frontal de la parte convexa está orientada hacia el polo frontal y tiene su origen en la corteza motora precentral. La gradación sagital de la corteza orbital se origina en la corteza olfatoria basal, es decir el paleocortex de la neurología comparativa. Esta orientación de la diferenciación es considerada como una diferenciación que se aparta de la corteza insular y que en última instancia puede ser referida al paleocortex.

Las gradaciones que se originan en cortezas adyacentes más antiguas desde el punto de vista filogenético tales como la fisura cingulada, la corteza olfatoria basal, las cortezas motoras insular y precentral, y que determinan la estructura de cortezas prefrontales más recientes representan orientaciones evolutivas de diferenciación.

Las dos orientaciones principales de diferenciación que empiezan en la corteza límbica (archicortex) y en la corteza insular respectivamente (en última instancia de origen paleocortical) se denominan "Urgradation", es decir protogradaciones.

Lo que generalmente se llama representación motora suplementaria y sensorio-

motora secundaria, aparece como representación protomotora y protosensorimotora si se considera a la luz del curso de las gradaciones.

Contrariamente a esto la representación motora clásica aparece como una realización más reciente en la filogénesis.

El síndrome orbital de alteración de la personalidad en las emociones y los actos se entiende como resultado de la topología especial de la corteza orbital, que está determinada por su sistema de gradaciones que incluyen influencias inmediatas del paleocortex. Estas últimas pueden estar reflejadas en las conexiones orbito-hipotalámicas cuya importancia subrayó J. F. Fulton en la vida emocional.

El principal síntoma de las lesiones prefrontales superiores, es decir la alteración de "Antrieb" como fue definido por Karl

Kleist ha demostrado corresponder a las funciones que Denny Brown encontrara perturbadas: "interés, y por lo tanto atención sostenida e iniciativa". De acuerdo a Pribram la alteración del test de la respuesta demorada en los monos debe ser interpretado en este sentido.

Se sugiere un paralelismo entre la disposición de las zonas concéntricas de la corteza prefrontal a partir de sus regiones limítrofes con la organización de las dependencias talámicas, es decir medialis dorsalis y los núcleos no específicos que la rodean. Dado que el sistema no específico de proyección talámica evidencia afinidades electrofisiológicas especiales con las regiones corticales adyacentes más antiguas y con la corteza asociativa prefrontal se acepta la antigua raíz filogenética del "antrieb" (empuje) en el sistema reticular activante.

R É S U M É

Les recherches neuroanatomiques et neurophysiologiques des dernières années avaient donné comme résultat une évaluation nouvelle de la configuration des circonvolutions et scissures en ce qui concerne la localisation fonctionnelle au cerveau des Primates.

Comme les prosimiae représentent un stade de l'évolution éprouvée par tous les Primates, quelques informations essentielles dérivées de ces études dans le prosimia *Nycticebus coucang coucang* sont données. Il a été possible d'éclaircir la signification de la configuration primitive des fissures sagittales qui domine encore pour la division somatotopique de la région sensorimotrice.

Dans le lobe frontal humain la région centrale présente les circonvolutions et les fissures coronales typiques des simiae tandis que dans la grande région de l'écorce préfrontale on trouve les circonvolutions et fissures sagittales régulières.

La configuration sagittale des circonvolutions, rarement partagée par le cerveau des Prosimiae et l'écorce frontale humaine, est le résultat de la croissance de la pres-

sion coronale tandis que la configuration des fissures et des circonvolutions de la région centrale dans les Primates supérieurs est le résultat de la croissance de la pression sagittale. La pression de croissance coronale, plus ancienne du point de vue de l'évolution, est reflétée par deux directions de différenciation architectonique, dont l'une a son origine dans la fissure antérieure cingulée et l'autre dans l'écorce insulaire.

Comme la différenciation se produit graduellement en partant des lieux d'origine et donc formant une séquence d'aires architectoniques nous parlons comme C. et O. Vogt de "gradations". Ces deux gradations unies aux deux sagittales, déterminent toutes les caractéristiques des aires frontales. La gradation frontale de la partie convexe est orientée vers le pôle frontal et a son origine dans l'écorce motrice précentrale. La gradation sagittale de l'écorce orbitale a son origine cortex prépiriforme à la base, c'est-à-dire le paléocortex de la neurologie comparative. Cette orientation de la différenciation est considérée comme une différenciation qui s'écarte de l'écorce

insulaire et qui en définitive peut être rapportée au paléocortex.

Les gradations ayant leur origine aux écorces adjacentes plus anciennes du point de vue phylogénétique telles que la fissure cingulée, l'écorcepiriforme basale, les écorces motrice insulaire et précentrale, et qui déterminent la structure des écorces préfrontales plus récentes représentent des orientations de différenciation qui se produisent pendant l'évolution.

Les deux orientations principales de différenciation qui commencent à l'écorce limbique (archicortex) et à l'écorce insulaire respectivement (en définitive d'origine paléocortical) portent le nom de "Urgradation", c'est-à-dire protogradations.

Ce qui est généralement appelé représentation motrice supplémentaire et sensori-motrice secondaire, apparaît comme représentation protomotrice et protosensori-motrice si elles sont considérées à la lumière de ce sens de gradations.

La représentation motrice classique semble, au contraire, sur le plan phylogénétique, une réalisation plus récente.

Le syndrome orbital de l'altération de la personnalité dans les émotions et dans les actes se comprend comme résultat de la topologie particulière de l'écorce orbitale, qui

est déterminée par son système de gradations incluant des influences immédiates du paléocortex. Ces influences peuvent être reflétées dans les connexions hypothalamiques dont l'importance a été signalée par J. F. Fulton dans la vie émotionnelle.

Le symptôme fondamental des lésions préfrontales supérieures, c'est-à-dire l'altération de l'"Antrieb" selon la définition de Karl Kleist a démontré correspondre aux fonctions que Denny Brown trouva altérées: "l'intérêt, donc attention prolongée et initiative". Selon Pribram l'altération du test de la réponse attardée dans les singes doit être interprété dans ce sens.

On suggère un parallélisme entre la disposition concentrique des zones de l'écorce préfrontale en partant des régions qui les limitent avec l'organisation des dépendances thalamiques, c'est-à-dire medialis dorsalis et les noyaux non spécifiques qui l'entourent.

Comme le système non-spécifique de projection thalamique possède des affinités électrophysiologiques particulières avec les régions corticales adjacentes plus anciennes et avec l'écorce associative préfrontale on accepte l'ancienne racine phylogénétique de l'"Antrieb" (élan) dans le système réticulaire activant.

ZUSAMMENFASSUNG

Neuroanatomische und neurophysiologische Studien der letzten Jahre führten zu einer Neubewertung des Windungsbildes für die Lokalisation bei den Primaten. Da die Prosimier ein Stadium darstellen, das von allen Primaten während der Evolution durchlaufen wurde, werden einige angehende Angaben über solche Studien am Halbaffen *Plumpori* gemacht. So war es möglich, die Bedeutung des hier noch vorherrschenden primitiven sagittalen Windungsmusters dahingehend zu klären, dass die beiden vorderen sagittalen Sulci Bein-, Hand- und Kopfrepräsentationen der sensorischen Regionen abgrenzen.

Im Frontallappen des Menschen herrscht in der Zentralregion des typische coronale

Windungsmuster der Affen, vor, aber in der hochgradig vergrößerten Präfrontalregion befinden sich die regelmässigen sagittalen frontalen Sulci und Gyri, worin eine auffallende Übereinstimmung mit dem primitiven sagittalen Windungsmuster der Prosimier zu sehen ist.

Das sagittale Windungsmuster ist durch transversalen Wachstumsdruck bedingt, wie das coronale Windungsmuster durch sagittalen Wachstumsdruck bedingt ist. Im Frontallappen des Menschen wie des *Plumpori* sind, den Richtungen des Wachstumsdruckes entsprechend, Differenzierungsrichtungen (sog. Gradationen nach C. und O. Vogt) nachweisbar: erstens zwei ältere transversale Richtungen, eine mediale vom

vorderen Gyrus cinguli ausgehend, und eine laterale, von der vorderen Insel ausgehend; zweitens zwei sagittale, eine von der motorischen Präcentralrinde ausgehend auf der Konvexität und eine von der präpiriformen Rinde ausgehend, an der Basis.

Diese bestimmen die Architektur der präfrontalen Felder ebenso wie das Windungsbild. Da die Ursprungsgebiete der Differenzierungsrichtungen, die die Präfrontalregion ganz umgeben, phylogenetisch älter als dieselbe sind, können sie als evolutionäre Entwicklungsrichtungen angesehen werden. Die orbitale Entwicklungsrichtung, die von der präpiriformen Rinde ausgeht, kann als Komponente der lateralen von der Inselrinde ausgehenden Gradation angesehen werden, die ebenfalls bis zurück zur präpiriformen Rinde (Palaeocortex) verfolgt werden kann, während die mediane auf den Archicortex zurückgeht. Diese beiden Hauptrichtungen der Differenzierung müssen in ihrem Ursprung bis auf die Reptilien zurückgehen und werden daher von uns Urgradationen genannt.

Die sog. supplementärmotorische und sekundär sensorimotorische Repräsentationen werden, im Strom der Urgradationen gelegen, als Vertreter einer Urmotorik bzw. einer Ursensomotorik aufgefasst. Die klassische motorische Repräsentation der Zentralregion erscheint demgegenüber als

eine jüngere Leistung in der Phylogenese.

Das orbitale Syndrom der Persönlichkeitsstörungen im Gefühlsleben und Handeln wird aus der speziellen Topologie der orbitalen Rinde im System der Gradationen erklärt, wobei die unmittelbaren Einflüsse der Präpiriformen Rinde eine wesentliche Rolle spielen. Diese Einflüsse werden durch die orbitohypothalamischen Verbindungen reflektiert, deren Bedeutung für das Gefühlsleben von J. F. Fulton betont wurde.

Das Hauptsymptom der hochfrontalen Läsionen, die Störung des "Antriebs", wie ihn Karl Kleist definiert hat, entspricht den Funktionen die Denny-Brown gestört fand: "Interesse und daher nachhaltige Aufmerksamkeit und Initiative". Nach Pribrams Untersuchungen ist die Störung des "verzögerte Antwort-Test" bei Affen in der gleichen Weise zu deuten.

Es besteht eine offenbare Parallele zwischen der konzentrischen Gliederung des Präfrontalen Cortex von seinen Grenzregionen aus und der Organisation der zugehörigen Thalamuskern, des Nucleus medialis dorsalis im Verhältnis zu den ihn umgebenden unspezifischen Kernen. Da das unspezifische thalamische Projektionssystem spezielle elektrophysiologische Affinitäten zu den alten Grenzregionen und zur Präfrontalrinde selbst zeigt, wird eine phylogenetisch alte Wurzel des "Antriebes" im retikulären Aktivierungssystem angenommen.

REFERENCES

1. Abbie, A. A.: Cortical lamination in the monotremata. *J. Comp. Neurol.* 72, 428-467 (1940).
2. Abbie, A. A.: Cortical lamination in a polyodont marsupial, *perameles natusa*. *J. Comp. Neurol.* 76, 509-536 (1942).
3. Bonin, G. v.: Architecture of the precentral motor cortex and some adjacent areas. in: Bucy, P. Ch. (ed.), *The precentral motor cortex*. Urbana: Univ. Illinois Press 1949.
4. Brodmann, K.: *Vergleichende Lokalisationslehre der Grosshirnrinde*. Leipzig: Barth 1909.
5. Brutkowski, St.: Prefrontal cortex and drive inhibition. in: Warren, J. M. and K. Akert (eds.) *The frontal granular cortex and behavior*. New York: Mc Graw-Hill Book Company 1964.
6. Clark, W. E. Le Gros: Deformation patterns in the cerebral cortex. in: *Essays on growth and forms presented to d'Arcy Wentworth Thompson*. Oxford: Clarendon Press 1947.
7. Denny-Brown, D.: The frontal lobes and their functions. in: A. Feiling (ed.) *Modern trends in neurology*. New York: Hoeber 1951.
8. Dusser de Barenne, J. G.: Functional organization of sensory and adjacent cortex of the monkey. *J. Neurophysiol.* 4, 324-330 (1941).

9. *Fulton, J. F.*: The frontal lobes and human behavior. in: *The Sherrington Lectures*. Liverpool: University Press 1952.
10. *Hassler, R.*: Anatomie des Thalamus, in: G. Schaltenbrand und P. Bailey (eds.) Einführung in die stereotaktischen Operationen mit einem Atlas des menschlichen Gehirns. Stuttgart: Georg Thieme 1959.
11. *Hines, M.*: Significance of the precentral motor cortex. in: Bucy, P. Ch. (ed.) The precentral motor cortex. Urbana: Univ. Illinois Press 1949.
- 12 a. *Krieg, W. J. S.*: Connections of the frontal cortex of the monkey. Springfield, Ill. Charles C. Thomas Publish. 1954.
- 12 b. *Nauta, W. J. H.*: Some efferent connections of the prefrontal cortex in the monkey. in: Warren, J. M. and K. Akert (eds.) The frontal granular cortex and behavior. New York: Mc Graw-Hill Book Comp. 1964.
13. *Pribram, K. H.*: A further experimental analysis of the behavioral deficit that follows injury to the primate frontal cortex. *Exp. Neurol.* 3, 432-466 (1961).
14. *Roberts, Th. S.* and K. Akert: Insular and opercular cortex and its thalamic projection in macaca mulatta. *Schw. Arch. Neurol., Neurochir. Psychiatr.* 92, 1-43 (1963).
15. *Rose, J. E.* and C. N. Woolsey: Organization of the mammalian thalamus and its relationships to the cerebral cortex. *EEG clin. Neurophysiol.* 1, 391-404 (1949).
16. *Sanides, F.*: Die Architektonik des menschlichen Stirnhirns. Monograph. Gesamtgebiet Neurol. Psychiatr. 98, Berlin-Göttingen-Heidelberg: Springer 1962.
17. *Sanides, F.*: The cyto-myeloarchitecture of the human frontal lobe and its relation to phylogenetic differentiation of the cerebral cortex. *J. Hirnforsch.* 6, 269-282 (1964).
18. *Sanides, F.* and A. Krishnamurti: Cytoarchitectonic subdivisions of the sensorimotor and prefrontal regions and of the bordering insular and limbic fields in the slow loris (*nycticebus coucang coucang*). *J. Hirnforsch.* 1966 (in press.)
19. *Scollo-Lavizzari, G.* and K. Akert: Cortical area 8 and its thalamic projection in macaca mulatta. *J. Comp. Neurol.* 121, 259-270 (1963).
20. *Stamm, J. S.*: The function of the median cerebral cortex in maternal behavior of rats. *J. Comp. Physiol. Psychol.* 48, 347-56 (1955).
21. *Vogt, C.* and O. Vogt: Allgemeine Ergebnisse unserer Hirnforschung. *J. Psychol. Neurol. (Lpz.)* 25, 279-462 (1919).
22. *Vogt, O.*: Über strukturelle Hirncentra, mit besonderer Berücksichtigung der strukturellen Felder des Cortex pallii. *Anat. Anz.* 29, Erg. Bd., 74-114 (1906).
23. *Vogt, O.*: Die myeloarchitektonische Felderung des menschlichen Stirnhirns. *J. Psychol. Neurol. (Lpz.)* 15, 221 (1910).
24. *Welker, W. I.* and G. B. Campos: Physiological significance of sulci in somatic sensory cerebral cortex in mammals of the family Procyonidae. *J. Comp. Neur.* 120, 19-36 (1963).
25. *Welker, W. I.* and S. Seidenstein: Somatic sensory representations in the cerebral cortex of the racoon, *J. Comp. Neurol.* 111, 469-499 (1959).
26. *Woolsey, C. N.*: Some observations on brain fissuration in relation to cortical localization of function. In: Tower, D. B. and J. P. Schade (eds.), Structure and function of the cerebral cortex, Amsterdam-London-New York-Princeton: Elsevier Publish. Comp. 1959.
27. *Woolsey, C. N.* and D. Fairman: Contralateral, ipsilateral and bilateral representation of cutaneous receptors in somatic areas I and II of the cerebral cortex of pig, sheep, and other mammals. *Surgery*, 19, 684-702 (1946).
28. *Yakovlev, P. I.*: Pathoarchitectonic studies of cerebral malformations III. Arrhinencephalies (Holotelencephalies) *J. Neuropath. and Exp. Neur.* XVIII, 22-55 (1959).
29. *Zuckerman, S.* and J. F. Fulton: The motor cortex in Galago and Perodicticus. *J. Anat. Lond.* 75, 447-456 (1941).

The Frontal Eye Field of the Monkey

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In 1874, Hitzig and Ferrier^{8, 10} showed for the first time that it was possible in dogs and monkeys to elicit a horizontal deviation of the eyes towards the contralateral side by electrical stimulation of a certain region of the frontal lobe. Since then, study of the neural mechanisms responsible for ocular motility has occupied numerous neurologists, neuroanatomists and neurophysiologists.

Nevertheless, our knowledge of these mechanisms is still very fragmentary, and the schemas of the oculogyral pathways which are generally to be found in textbooks of neurology are not based on sufficiently well established anatomical and physiological data. Such schemas oversimplify the central oculogyral pathways and incorporate to a greater or lesser extent features of unproved hypotheses. Moreover, in man and in higher animals, the oculomotor mechanism is particularly complex, since binocular vision requires conjugate eye movements.

Under the guidance of our director, Professor P. Van Gehuchten, who has already carried out much research into the problem of the conjugate motility of the eyes, we undertook an experimental study of the functions and efferent pathways of the frontal eye field of the monkey^{3, 4}. Our first experiments were performed in 1951, under the direction of J. F. Fulton, who held the Franqui Chair at the University of Louvain.

The study was made on 49 macaque

monkeys, and is divided into three parts. The principal findings are presented below.

I. Electrical stimulation of the frontal eye field

The topography and functions of 20 different oculomotor fields were studied in 14 monkeys, using either acute methods, during the surgical intervention, or chronic, using permanent electrodes.

In the monkey, the frontal eye field resembles a horizontal V, the two branches forming the anterior lip of the arcuate sulcus. From a schema (Fig. 1) showing a total of 75 points stimulated by permanent electrodes, it is evident that each branch of the frontal eye field can be divided into three sectors, each with its *own oculomotor function*: conjugate deviation of the eyes either horizontally towards the contralateral side, or obliquely towards the contralateral side, upwards or downwards. This schema confirms and details the observations published in 1952 by Crosby et al.⁷ However, stimulation of the sectors VT and DT by permanent electrodes does not provoke ocular divergence, contrary to results obtained in the same area in acute experiments reported by Crosby et al.⁷ and ourselves³.

Furthermore, as several authors (Mott and Schäfer¹⁶, Crosby et al.⁷, Pasik and Pasik, 1961) have previously observed, simultaneous bilateral stimulation of homo-

logous regions elicits purely vertical movements, either upwards or downwards (Fig. 2).

Though each sector has its own oculomotor function, excitation at any point of the eye field also gives rise to *accessory responses*: opening of the eye-lids, dilatation of the pupils, rotation of the head and bo-

dy, and even a circling movement towards the contralateral side (Fig. 3). This demonstrates well that the eye field controls not only ocular, pupillary and eye-lid motility, but also that it has connections with the vestibular system. To use Hassler's term⁹, the frontal oculomotor cortex is part of the "adversive contraversive" sys-

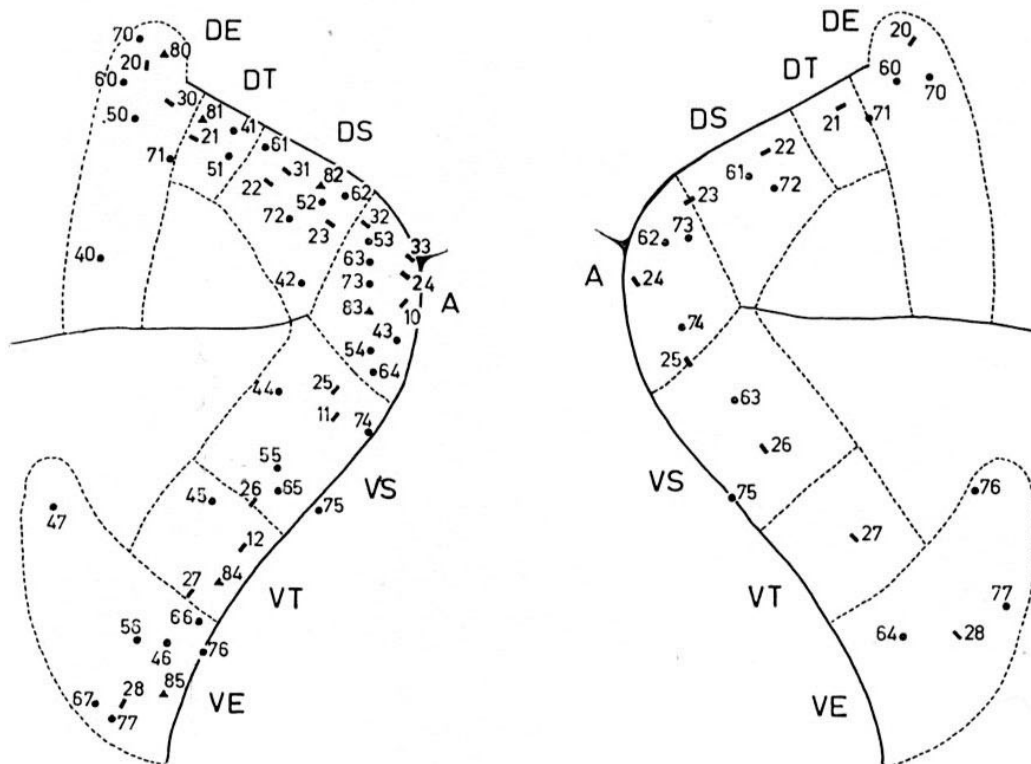


Fig. 1. — Schema of the two frontal eye fields of the monkey. All the points stimulated during the chronic experiments are represented by a circle, a rectangle or a triangle, according to the type of electrode used. The number given to each point in the motor area refers to both the monkey and the electrode. These 75 points were distributed over 11 different oculomotor fields in 8 monkeys with permanently implanted electrodes. The dotted lines encircle groups of motor points which gave identical responses to stimulation. The functional subdivisions thus delineated have been given the names proposed by Crosby et al. (1952): DE: dorsal extension of the dorsal subfield; DT: dorsal subfield; A: apex; VS: ventral subfield; VT: ventral transitional area; VE: ventral extension of the dorsal subfield.

tem responsible for movements of body rotation (Wendebewegungen).

It should be remembered, however, that these different accessory responses originate from the entire eye field and that none are especially connected with any particular site, contrary to the old charts published by Mott and Schäfer¹⁶, Vogt and Vogt^{25, 26}

and Smith^{18, 19}. Neither have we been able to find the centres responsible for dilatation or constriction of the pupils, which Jampel¹³ believed he was observing when he stimulated monkeys under light anaesthesia.

The map of the frontal eye field (Fig. 4), which we have made more precise in the

unanaesthetized monkey with permanent cortical electrodes, is not essentially different from that which Krieger et al.¹⁵ and Wagman et al.²⁷ described in monkeys who were unanaesthetized but immobilized by

a transverse section of the cervical cord. According to these authors, the cortical oculomotor representation is extended over a large area, but careful analysis of the results shows that the threshold of excitation

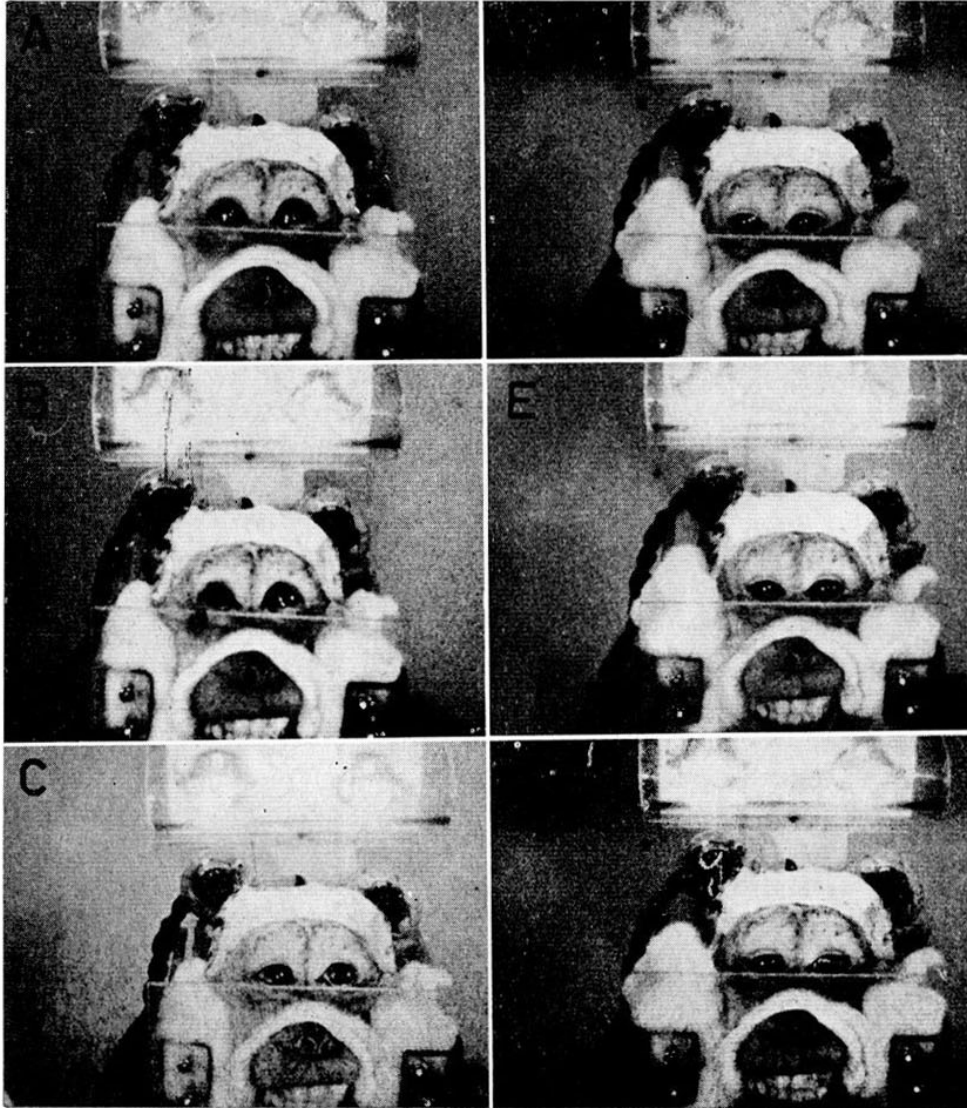


Fig. 2. — Stimulation of different regions of the eye field in the monkey with bilateral permanent electrodes: A. Left apex: oblique deviation upwards and to the right; B. Left apex + right apex: vertical and upward deviation; C. Right apex: oblique deviation upwards and to the left; D. Left VE: oblique deviation downwards and to the right; E. Left VE + right VE: vertical and downward deviation; F. Right VE: oblique deviation downwards and to the left (extracts from a cine-film: Monkey 41).

is lowest in the cortex bordering the concavity of the arcuate sulcus. It is here, therefore, that the functional differentiation of the cortex is most marked for ocular

movements. Furthermore, in these authors' schema, one finds a functional subdivision comparable with that which we have described notably for the sectors DE, DS, A

and V.S. As we have also noted in the course of our own chronic experiments, these authors have not found the movements of convergence or divergence described by Crosby et al.⁷ and by ourselves³ in acute experiments.

II. Destruction of the frontal eye field

We have studied the consequences of partial or complete destruction of the eye field in 24 monkeys, either by ablation, or by thermocoagulation, or by subpial suc-

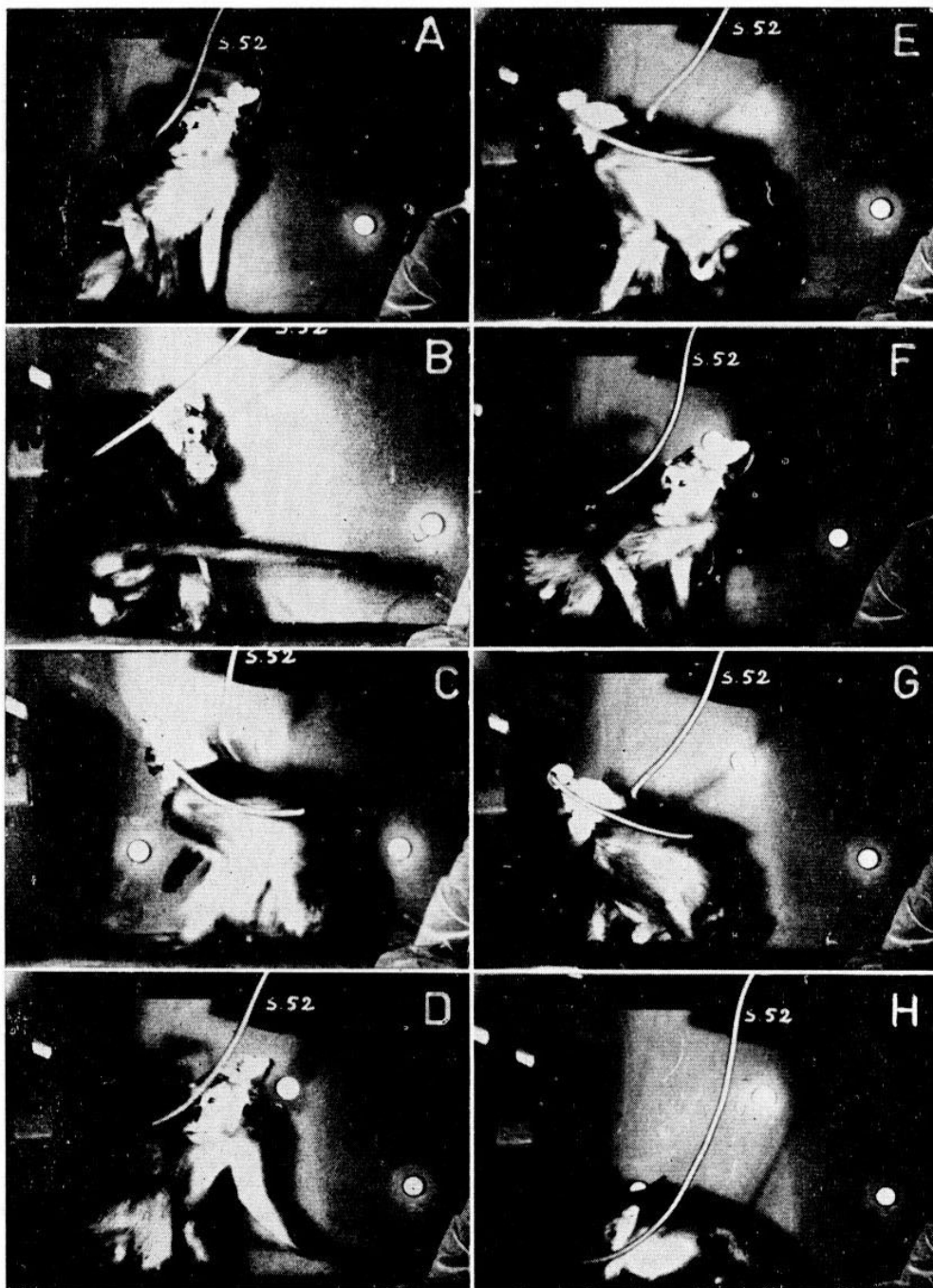


Fig. 3. — Continuous stimulation (7 volts, 0.5 millise., 70 C/S) of the left D.S. The monkey, freemoving in a glass case, made several circling movements to the right, then flattened itself against the floor (extracts from a cine-film: Monkey 52).

tion (Fig. 5). Post-operational disturbances may be divided into five categories:

1. *Oculomotor disturbances*: conjugate deviation of the eyes towards the lesioned side, paralysis of gaze towards the contralateral side, occasional nystagmus towards the lesioned side and some brief divergence or convergence movements of the

eyes. These disturbances are temporary and do not last for more than 1 to 4 days.

2. *Pupillary disturbances*: anisocoria, which varies as a function of the environmental light conditions. We have frequently noticed that the mydriasis which occurs in shadow and the myosis elicited by light are less pronounced on the contralateral side.

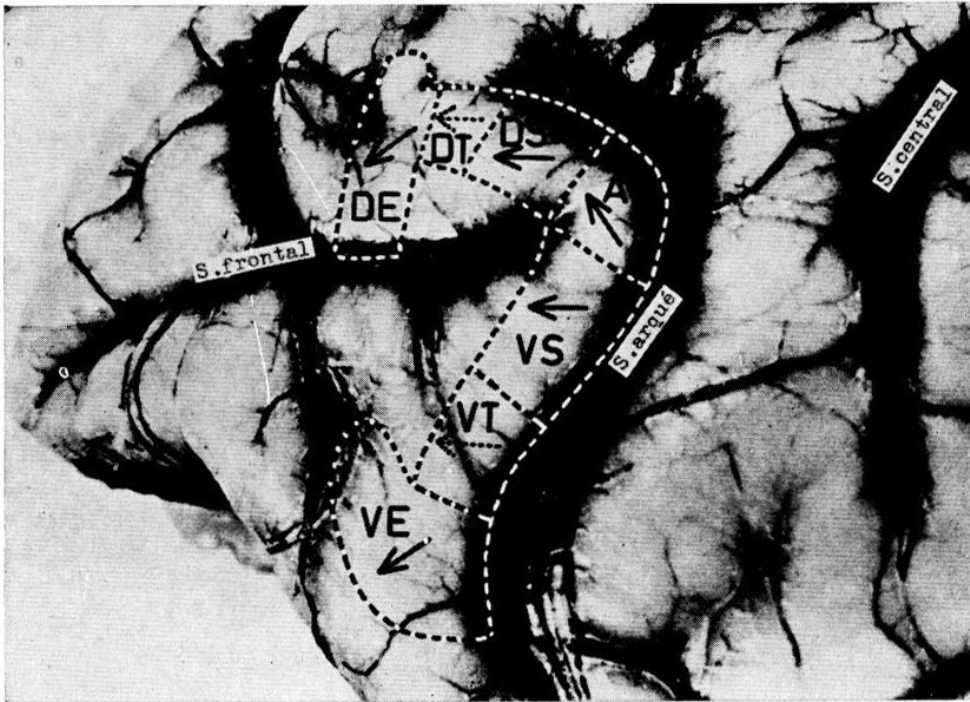


Fig. 4. — The schema in fig. 1, showing the functional subdivisions of the frontal eye field, is presented here for the left hemisphere of the monkey (*Macacus cynomolgus*). As the arrows show, each sector has its own oculomotor function, and the responses to stimulation of the dorsal branch are similar to those of the ventral branch, in mirror-image fashion. The sectors DT and VT do not provoke divergence or convergence of the eyes, but they do give rise to a horizontal ocular deviation which is characterized by its weakness, slowness and sometimes by its hesitant or sporadic nature.

It would thus seem that pupillary reflexes to light are reduced on the contralateral side or that these reflexes are exaggerated on the lesioned side. This anisocoria lasts for 2 to 10 days and sometimes even for more than 27 days.

3. *Disturbances in equilibrium*: these consist of a rotation of head and body, together with a forced circling movement towards the lesioned side (Fig. 6). This spectacular disturbance does not last for

more than 1 or 2 days, and reproduces, in the opposite direction, the results obtained by cortical stimulation. It emphasizes once again the relationships which exist between the oculogyral and vestibular systems.

4. *Visual deficit*: In the visual field on the contralateral side, the animal does not seem to see anything, to such an extent that the reflex of blinking at a threatening gesture disappears from this side

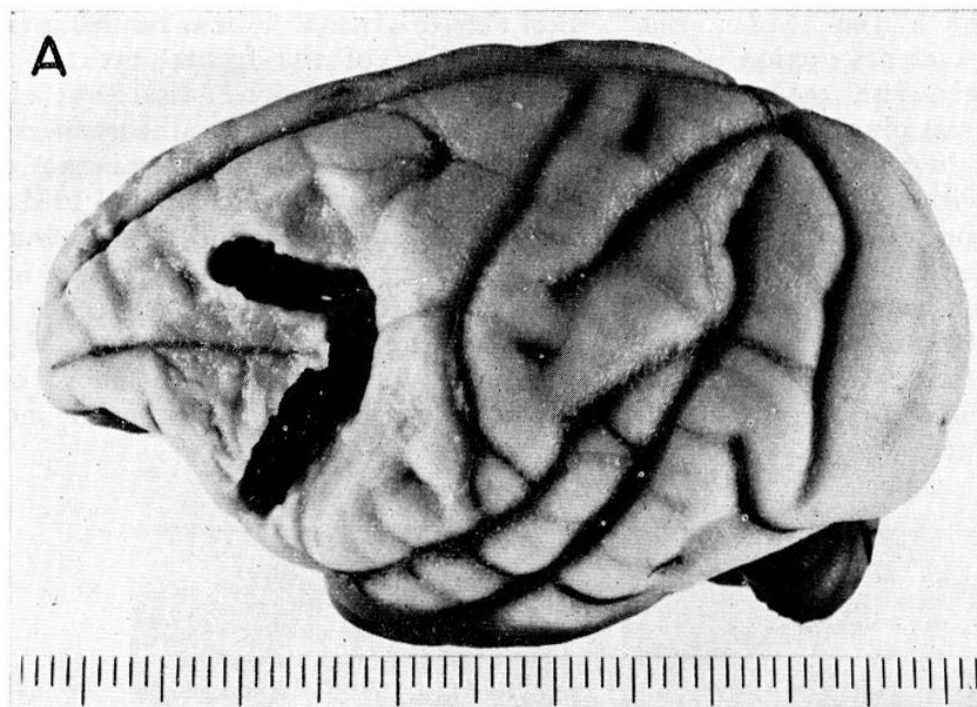


Fig. 5. — Lateral view of the left hemisphere, 26 days after ablation of the entire frontal eye field by subpial suction (Monkey 55).

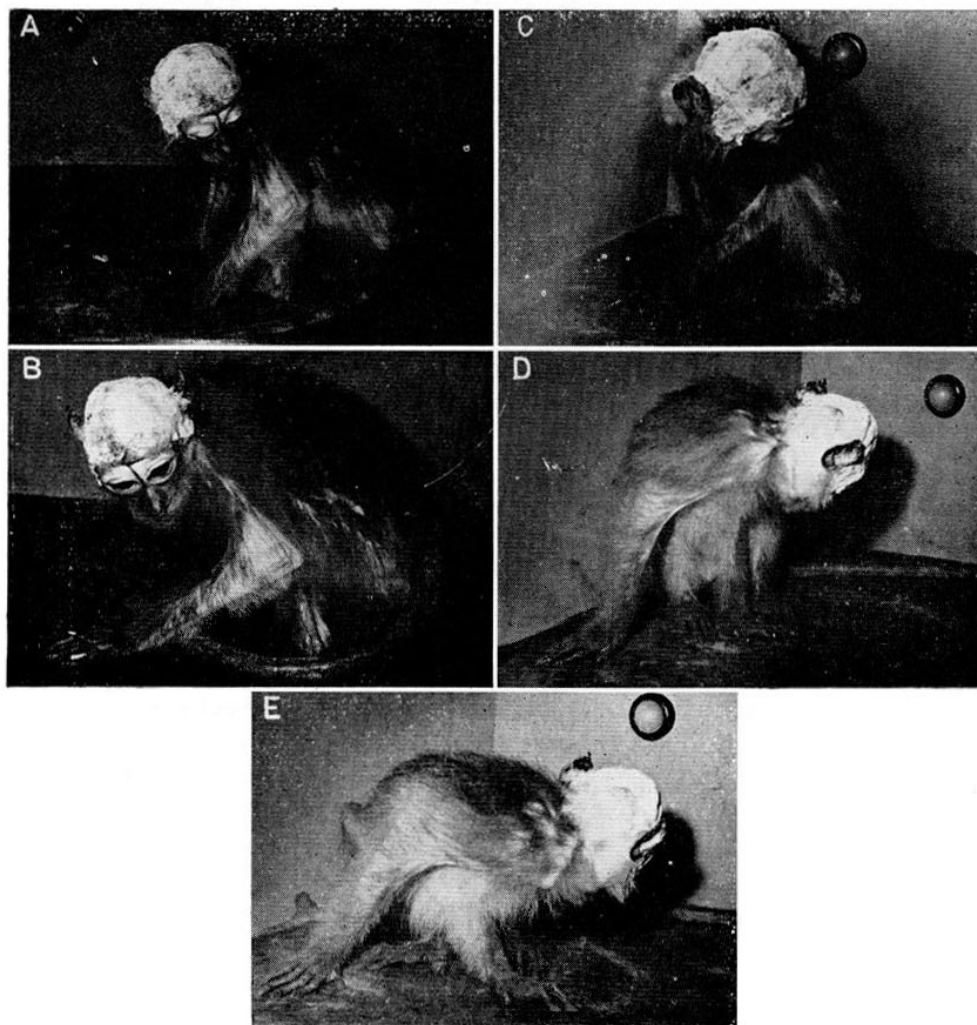


Fig. 6. — Nine hours after the destruction of the entire left eye field, the monkey exhibits a deviation of the head and body towards the lesioned side and a forced circling movement. Five successive phases of this are shown in views A to E (Monkey 58).

(Fig. 7). This is not a true hemianopsia, however, since bilateral destruction of the eye field does not give rise to such blindness. Moreover, several observations in the literature show that the visual fields remain normal in patients with an apparent hemianopsia on the side contralateral to a frontal lesion^{11, 17}. One has therefore to talk in terms of a pseudo-hemianopsia, or rather of a visual hemiagnosia. As will be seen below, this visual deficit lasts for about as long as the optokinetic nystagmus disturbances. In consequence, we are of the opi-

nion that this visual deficit, resulting from a destruction of the frontal eye field, is comparable with gnostic disorders which may accompany apraxic disturbances of frontal origin. This visual hemiagnosia of frontal origin could be compared to disorders of verbal understanding and verbal deafness which can accompany motor aphasia²⁴. It is for this reason that one can consider the frontal eye field to be a praxic centre, whose function is more complex than that of the pre-central motor cortex.

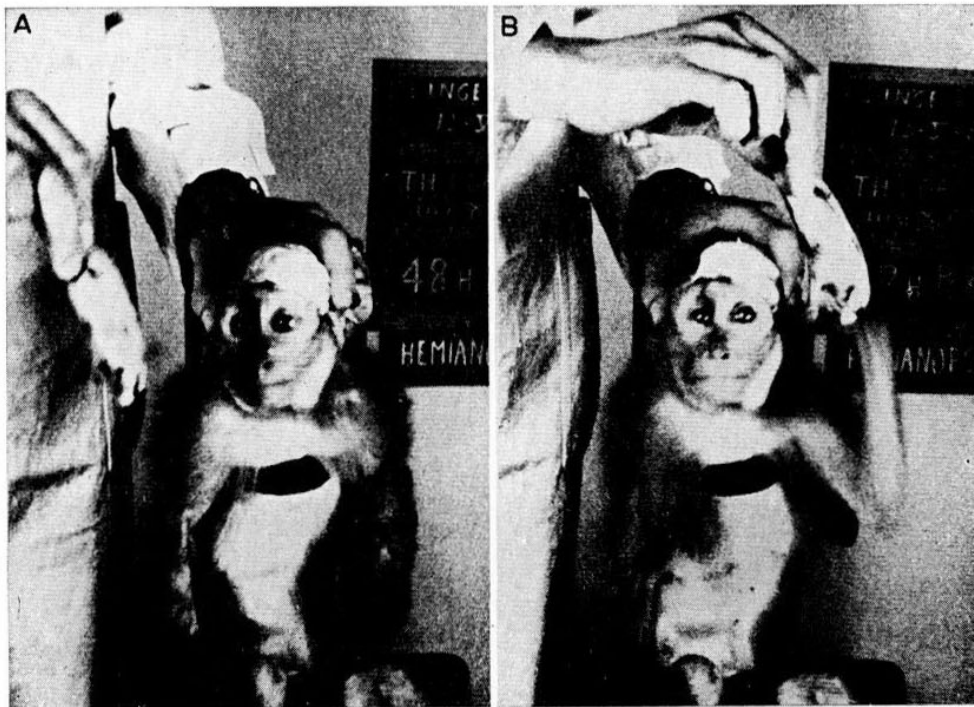


Fig. 7. — Having undergone thermocoagulation of the left eye field 48 hours earlier, this monkey ignores the banana presented to him in his right visual field (A), but he reaches for it as soon as it is moved towards the left side of the median line (extracts from a cine-film: Monkey 39).

This visual disorder of frontal origin should not be confused with the true hemianopsia which can be observed in certain cases of frontal tumor. Zülch^{31,32} has stressed the pathogenesis of softenings of the striated occipital area. This complication may be produced in cases of frontal tumor accompanied by considerable oedema of the cerebral hemisphere and temporal herniation with compression of the posterior cerebral artery.

Visual hemiagnosia of frontal origin may persist for 2 to 5 weeks. It is the only perceptual deficit which we have observed, and we have never been able to discover any other sensitive or sensory disturbance, contrary to the observations of Welch and Stuteville²⁹.

5. *Optokinetic nystagmus disturbances (O.K.N.)*: We have studied the various modifications of O.K.N. after 13 different interventions in the eye fields of 7 mon-

keys. The animal was placed inside a large rotating drum, according to the criteria defined by Krieger and Bender¹⁴, and ocular movements were registered by obtaining the corneo-retinal potentials.

O.K.N. in a normal monkey (Fig. 8) is characterized by regular movements of the eyes towards the right or towards the left,

in a synchronous or hypersynchronous manner, according to the speed of rotation of the drum. After the drum has stopped, a *direct* optokinetic afternystagmus (O.K.A.N.) often appears, lasting for about one minute. This is followed, in certain cases, by an *inverse and retarded* O.K.A.N. which may last for nearly 2 mi-

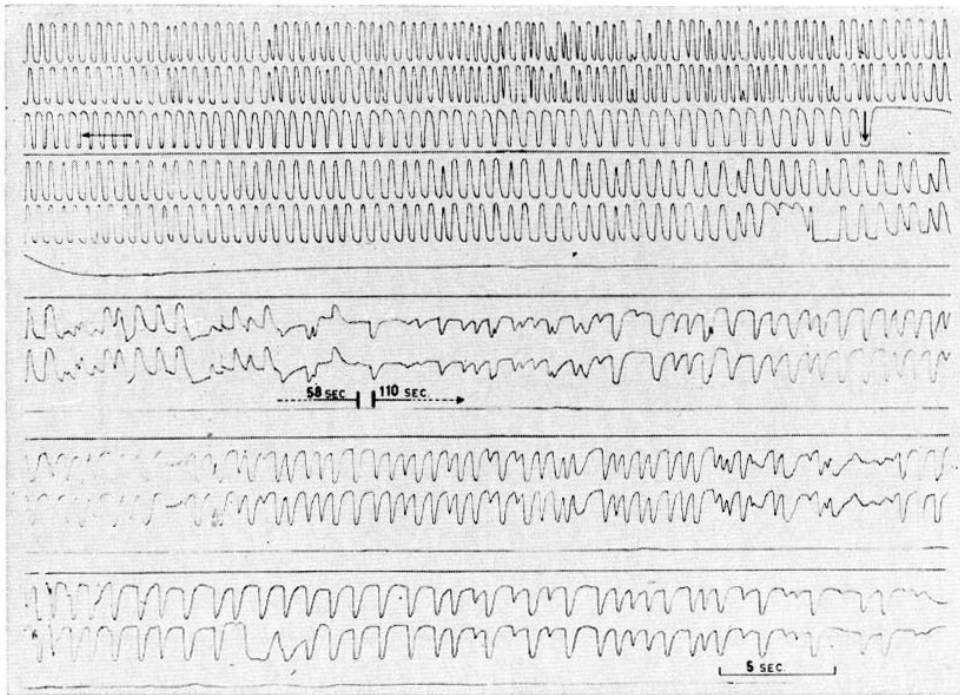


Fig. 8. — Continuous recording of O.K.N. in a normal monkey. The first two lines represent the movements of the right and left eyes respectively. The deflections of these lines upwards (or downwards) correspond to an ocular deviation to the right (or left). The rectilinear and curved deflections represent successively the rapid and slow phases of the nystagmus. The third line registers the photoelectric cell, which indicates the rotation of the drum around the animal. The horizontal arrow pointing left indicates that the drum is turning in an anticlockwise direction, i.e. that the black bands are moving towards the left in front of the animal's eyes. The vertical arrow indicates the stopping of the drum and the beginning of the dark period after an effective rotation of 6 minutes. It can be seen that O.K.N. is maintained for 58 seconds, as a direct O.K.A.N. Following this, an inverse and retarded O.K.A.N. progressively appears, and remains for 110 seconds.

minutes. This phenomenon of inversion of after-O.K.N. has not previously been described, and allows one to suggest an analogy with vestibular nystagmus.

O.K.N. disorders, provoked by the destruction of the frontal eye field, are complex, and only a brief résumé can be given here.

a) O.K.N. towards the contralateral side is very much more difficult to obtain, is less regular and slower than in the opposite direction. This phenomenon is due principally to a weakening of the rapid phase towards the undamaged side. These rapid jerks become more and more weak, and after a time it appears that the eyes

are fixed towards the lesioned side (permanent conjugate deviation). This fixation is eventually interrupted by a blinking of the eye-lids (fig. 9). Furthermore, the direct O.K.A.N. almost disappears and is replaced by an *inverse and immediate* O.K.A.N. which can last for 1 to 7 minutes.

b) *O.K.N. towards the lesioned side*, on the other hand, is better formed, more regular and more rapid. It is synchronous or hypersynchronous and is often accompanied by short, rapid, isolated or grouped jerks towards the side of the lesion. Direct O.K.A.N. is frequent and continues sometimes for almost 3 minutes (maximum 1

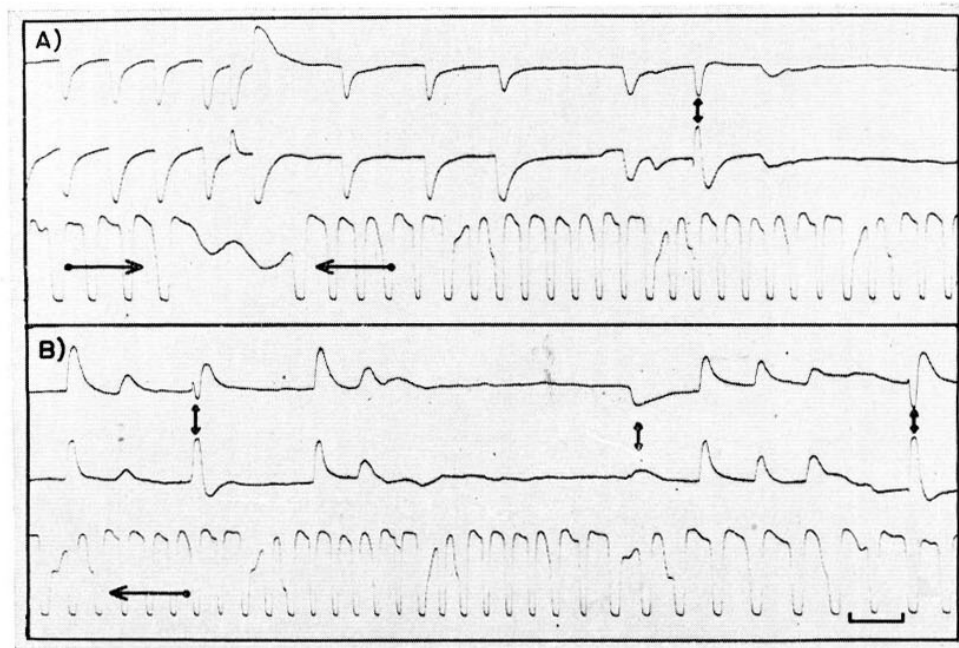


Fig. 9. — Disturbances of O.K.N., 5 days after destruction of the entire left eye field (Monkey 55). The O.K.N. to the left, induced by rotation of the drum to the right, is clearly formed (A). When the direction of rotation is reversed (to the left), O.K.N. towards the left is prolonged for several seconds more, until terminated by a blinking of the eye-lids (↑↓). After a period of ocular immobility, O.K.N. towards the right appears, irregularly and sporadically, regardless of the speed of the rotating drum (B). Note the 3 successive sequences of ocular response: 1) progressive weakening of the rapid phases towards the right (deflections of the two first lines upwards); 2) fixation (persistent deviation of the eyes to the left); 3) blinking of the eye-lids (↑↓). The horizontal line in the lower right-hand corner represents 1 second.

minute for normal monkeys). Inverse and retarded O.K.A.N. is extremely rare.

From a general point of view, these modifications of O.K.N. reflect, on the one hand, the weakening of the rapid phase towards the undamaged side, and on the other, the relative hypertonia of the oculogyral mechanism towards the lesioned side. They last for about 3 to 5 weeks and thus exceed the duration of the apparent

oculomotor disorders. This shows that nystagmographic research is a more exact method than that of simple, direct observation of ocular motility. It would therefore be profitable to use this method more frequently in human clinical work.

The frontal eye field thus intervenes in the production and in the regulation of the rapid phase of O.K.N. towards the contralateral side. Study of O.K.N. in the nor-

mal monkey or in the monkey whose oculomotor field has been destroyed, has also demonstrated that the rapid phase is not a simple "correction reflex" ⁶ of the optic axis. On the contrary, as Stenvers ²⁰ also thought, we are dealing with an active movement which we have called a "research movement" and which is the "primum mo-

vens" of O.K.N. In order to understand the complicated mechanism of O.K.N., we have put forward a schema of the neural pathways which could play a part in the production of the rapid and slow phases (Fig. 10).

The different phenomena observed after the destruction of the entire eye field are

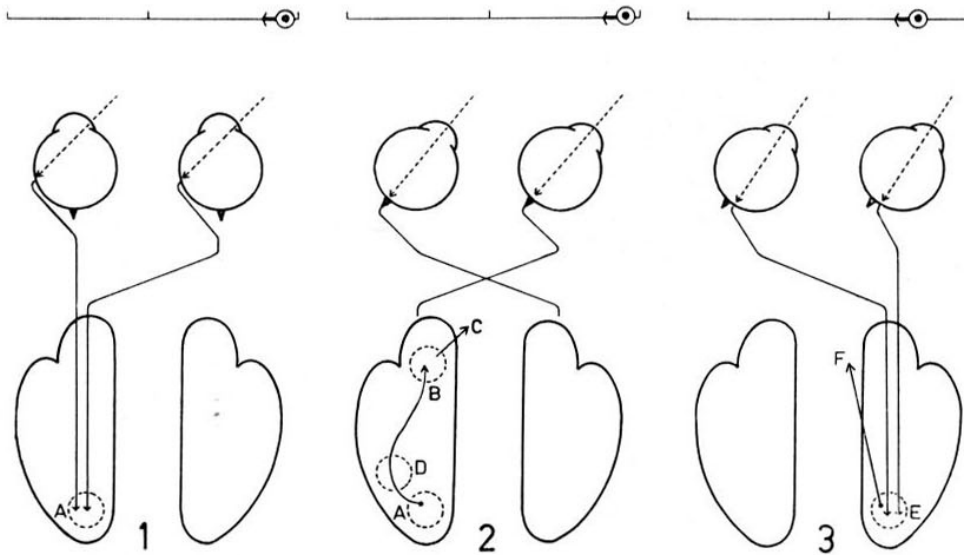


Fig. 10. — Schema of the neural pathways which may mediate in the production of the rapid and slow phases of O.K.N. — 1. When a moving object appears on the right side of the visual field, its image is perceived by the left occipital lobe (A). — 2. For macular vision, impulses are transmitted from the left occipital lobe homolateral frontal eye field (B), which then directs the "research movement" to the right (rapid phase of O.K.N.), by the mediation of the subcortical oculomotor centres (C). The occipito-frontal messages pass beneath the angular gyrus (D), where they perhaps are relayed (cf. observations on humans). — 3. The image of an object continuing to move to the left spreads to the right, overflows the macula and reaches in entirety the right occipital lobe (E). This constantly corrects the position of the eyes by a pursuit movement (slow phase of O.K.N.) in order to maintain the fixation reflex. This pursuit movement is directly controlled by the right occipital lobe, by means of the posterior oculomotor pathway (F).

also to be found with the same intensity and the same duration after the destruction of the ventral branch of the eye field. On the other hand, if the dorsal branch alone is destroyed, the external oculomotor disorders and the disturbances in equilibrium are almost entirely absent, while the pupillary disturbances, the visual deficit and

the disturbances of O.K.N. are almost as intense as when the destruction was total. This demonstrates that the dorsal branch has a secondary importance in comparison with the ventral branch, which must therefore be considered as the primary eye field. This conclusion is contrary to the hypothesis formulated several times by Crosby in the last few years.

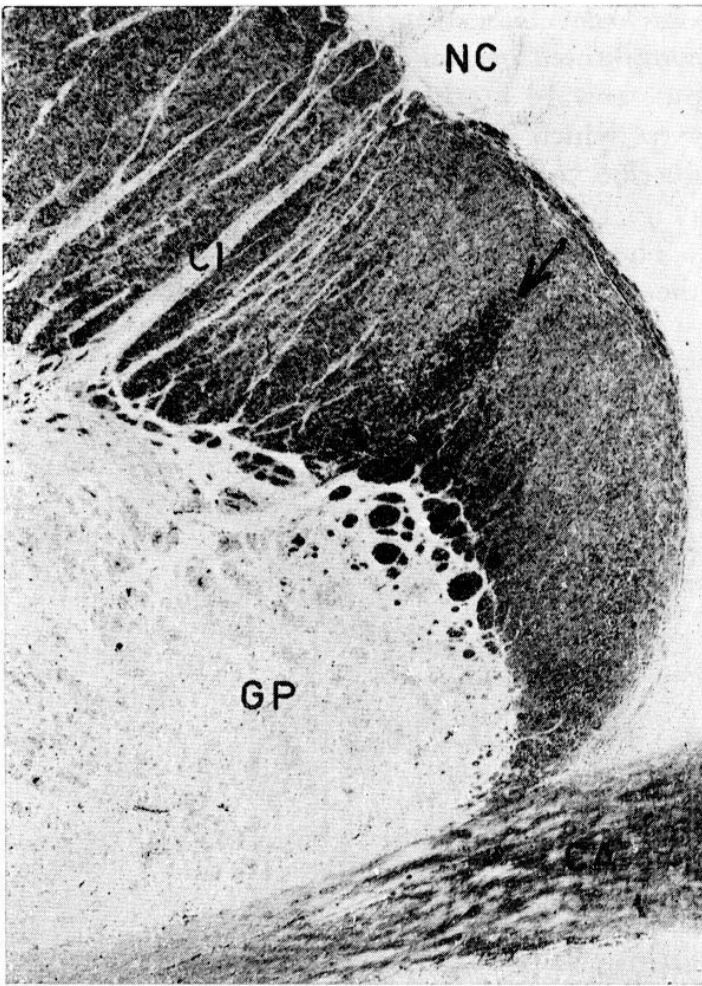


Fig. 11. — Frontal section passing through the anterior commissure (CA). In the anterior arm of the internal capsule (CI), the greater part of the degenerated fibres are grouped in a triangular mass, whose base rests against the globus pallidus (GP) and whose apex ($\downarrow$) is near the caudate nucleus (NC). Several bundles of degenerated fibres run into the juxta-capsular zone of the globus pallidus. (Monkey 40, with total left eye field destruction, 21 days before death. Marchi technique).

III. Efferent pathways from the frontal eye field

Using the Marchi technique, we have followed the corticofugal fibres leading from the eye field of 12 monkeys over a total of 4,600 serial sections. It is because of the larger number of monkeys used than in previous studies and also because sections were performed in various planes, from one monkey to the next —frontal,



Fig. 12. — Axial section, showing well the degenerated fibres which pass through the internal capsule (CI) and disappear into the zona incerta (ZI) and the lenticular fasciculus (H2). (Monkey 13, with destruction of the left ventral branch of the frontal eye fields, 15 days before death. No retouching of photograph. Marchi technique. Enlarged 105 X).

axial or horizontal— that we are able to give a detailed description of the path taken by the degenerate fibres.

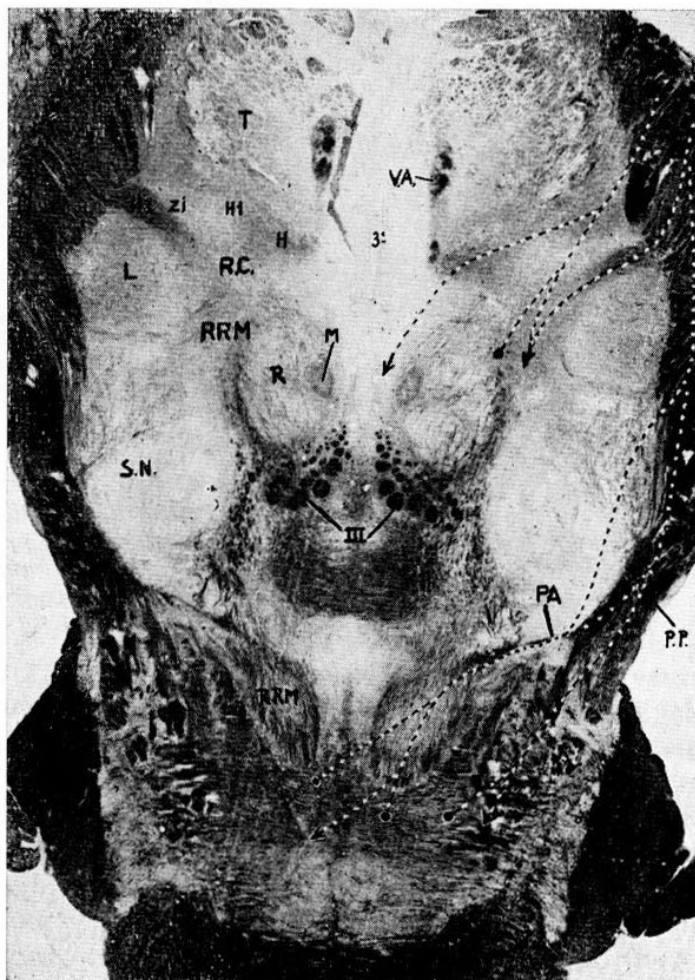
Besides the *associative* fibres going to the frontal, temporal and occipital cortex, and the *commisural* fibres going to the eye field and to the internal capsule of the opposite hemisphere, we have observed numerous *descending* fibres, grouped in the internal capsule in the form of a triangle whose base rests on the globus pallidus (Fig. 11). Part of these fibres also cross the juxta-capsular region of the pallidum. Af-

ter this, these fibres separate in two principal directions:

a) *The non-crossed cortico-diencephalo-mesencephalic pathway.* These fibres cross the ventro-lateral portion of the thalamus, the fields H 1 and H 2 of Forel and the zona incerta (Fig. 12). They terminate for the most part in the peri-aqueducal grey matter, in the oral region of the III nucleus, in the pretectum, in the superior colliculus and above all, in the homolateral mesencephalic reticular formation. The course of this pathway (Fig. 13) may be superimposed on the topography of the "adversive contraversive" system described by Hassler⁹. This author and several others have recently shown, in animals as well as in man, that stimulation or destruction of

these deeper regions, by stereotaxic methods, provokes symptoms closely comparable with those obtainable in the cortical eye field. It is for this reason that we consider that the anatomical substrate of the diencephalic apparatus for "contraversive" movements, such as was described by Hassler, could be constituted, at least in part, by these corticofugal fibres which cross these regions. Moreover, there is a remarkable similarity between the course of the non-crossed cortico-diencephalo-mesencephalic pathway, which we have described, and the oculo-motor pathways recently traced by Bender and Shanzer (1964) by numerous stimulation experiments and destruction of the brain stem of the monkey. Our observations also sup-

Fig. 13. — Frontal section passing through the thalamus (T) and the red nucleus (R). The dotted lines indicate schematically the course of the two large descending pathways emerging from the frontal eye field: 1) The non-crossed cortico-diencephalo-mesencephalic pathway: These fibres leave the internal capsule, cross the thalamus (T), the fields H 1 and H 2 of Forel, the zona incerta (ZI) and descend in two directions: a) into the central tegmental tract (RC) and into the medial lemniscus (RRM) towards the perirubric capsule and, above all, the mesencephalic reticular formation; b) into the field H of Forel and into the peri-aqueducal grey matter in the neighbourhood of the fascicle of Meynert (M), towards the III nuclear complex, the nuclei of Cajal and of Darkschewitsch, the pretectum and the superior colliculus. — 2) Déjerino's aberrant pyramidal system: These fibres descend into the median third of the pes pedunculi (PP) and partially into the locus niger (LN), under which they gather together to form a sheath of aberrant pyramidal fibres (PA). They then reach the medial lemniscus (RRM) and disperse into the pontine reticular formation, especially on the contralateral side. Certain fibres leave the median fascicles of the pontine pyramidal tract directly and also go



towards the bilateral reticular formation.

port the theory of Szentágothai^{21, 22}, according to which the supra-nuclear centre of the conjugate movements of the eyes towards the contralateral side would be situated in the mesencephalic reticular formation. This non-crossed cortico-diencephalo-mesencephalic pathway would thus conduct oculomotor impulses not only in the vertical plane but also in the horizontal.

b) Other fibres compose *classical Déjerine's aberrant pyramidal system* (Fig. 13). They descend in the median third of the pes pedunculi (Fig. 14), cross the locus niger and gather together in a bundle which passes to the medial lemniscus. These fibres end chiefly in the paramedian zone of the pontine reticular formation on both sides but mainly on the contralateral side (Fig. 15). We have never observed

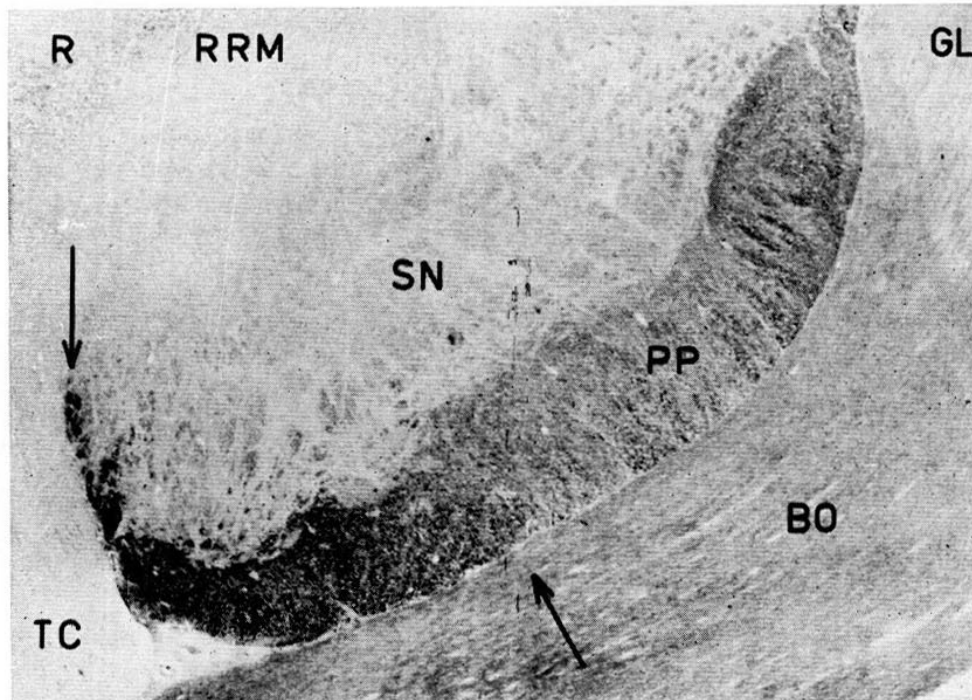


Fig. 14. — Horizontal section, passing through the red nucleus (R), the tuber cinereum (TC), the optic tract (BO) and the lateral geniculate body (GL). These degenerate fibres are concentrated in the median third of the pes pedunculi (PP). (Monkey 5, with left ventral branch destruction, 19 days before death. No retouching of microphotograph. Marchi technique. Enlarged 13 X).

these fibres to reach the VI nucleus and those which reach the vestibular nuclei on both sides are extremely rare. This cortico-pontine group could also conduct the oculomotor impulses by means of the pontine reticular formation, but we think that one must primarily attribute to it the function of control over the vestibular system or the system of wakefulness. These fibres would also be responsible for the awakening response which Smith¹⁹ and other authors have obtained by stimulation of the frontal

eye field. This awakening response was sometimes interpreted as an "eye centering" reaction or "midposition phenomenon"^{1, 2, 5, 27, 28}.

It is evident that our hodographic study does not allow one to determine the exact functions of the two anatomical pathways thus traced. The functions which we have proposed are hypotheses which neurophysiological experiments must verify.

Though our research clarifies the anatomo-

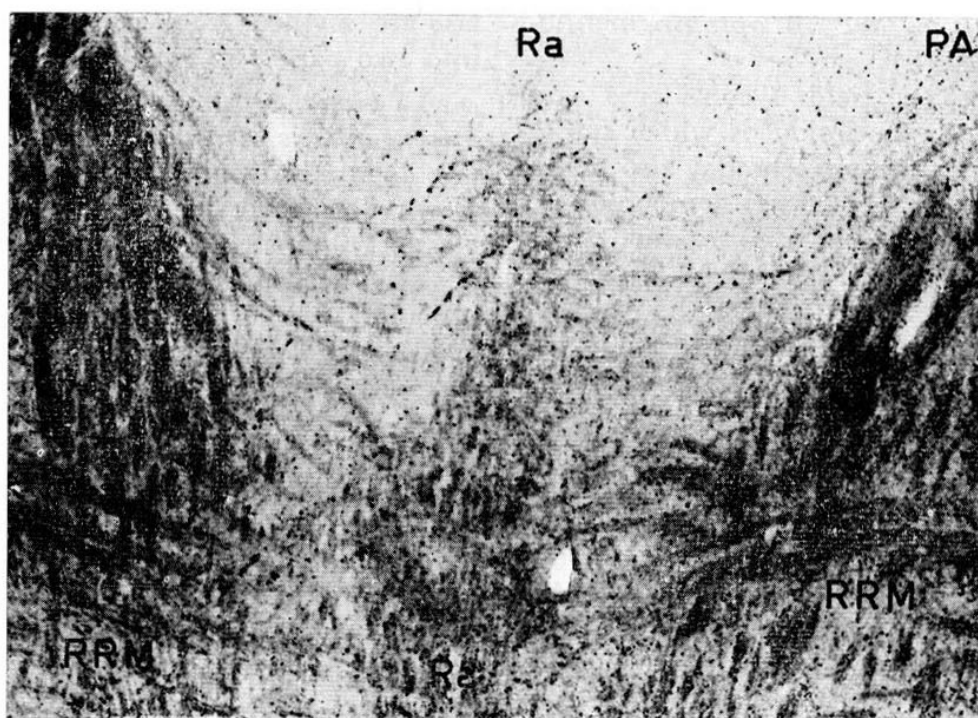


Fig. 15. — Axial section, passing through the median raphe (Ra) of the superior region of the pons and through the medial lemniscus (RRM) on either side. Several fibres originating in the left (on the right-hand-side, in the figure) cross the raphe and enter the contralateral pontine reticular formation. (Monkey 13, with left ventral branch destruction, 15 days before death. No retouching of microphotograph. Marchi technique. Enlarged 50 X).

mical course of the first neuronal link from the oculogyral pathway this is no true for the succeeding links, which are particularly complex²³. Indeed, as neuropathological observations and recent neurophysiolo-

gical experiments have shown, the subcortical oculomotor system appears to be very extensive, depending on "widely dispersed neuronal elements, which seem at least largely reticular".

S U M M A R Y

The experiments of this work were performed on 49 monkeys (*macaca mulatta*) and the results are divided into three parts.

1) *Electrical stimulation of the frontal eye field*, in acute experiments or, in the majority of the cases, with permanent electrodes on the cortex. The frontal eye field is localized in the concavity of the arcuate sulcus and is divided into areas, each of which representing *specific oculomotor functions*: horizontal deviation to the opposite side and obliquely upward or downward deviation to the contralateral side. As was shown by Crosby et al. (1952), the

responses to stimulation of the dorsal subfield are similar to those from the ventral subfield, in mirror-image fashion. Excitation of every point of the frontal eye field also elicits *accessory responses*: opening of the eyelids, dilatation of the pupils, turning of the head and trunk to the opposite side and circling movement toward contralateral side (by means of stronger stimuli).

2) *Partial or total destruction of the frontal eye field*. The signs and symptoms are grouped into five headings: disturbances in eye movements in pupils, in equili-

brium, in vision and in optokinetic nystagmus; (O.K.N.).

The frontal eye field is considered as a "praxic center", the lesion of which causes not only motor impairment but also manifestations of agnosia (visual hemiagnosia).

This visual defect lasts approximately as long as the disorders of O.K.N. The electro-nystagmographic study may be considered as a more refined method than usual clinical observation of the eye movements. The fast phase represents the "primum movens" of the O.K.N. and we call it "research movement" since it is an active movement dependent on the frontal eye field and it is not a correction reflex of the optic axis. Numerous normal and pathological electronystagmograms have shown that optokinetic after-nystagmus may be direct or inverted.

3) *Study of the efferent pathways from the frontal eye field.* The corticofugal fibres studied on 12 monkeys with the Marchi technique are grouped into associative, commissural and descending fibres. These

last are divided from the internal capsula into two parts:

a) *Non crossed cortico-diencephalo-mesencephalic pathway*, which constitutes the anatomical substratum of the diencephalic "contraversive" system described by Hassler (1956). These fibres distribute especially to the homolateral mesencephalic reticular formation which Szentágothai (1943, 1950) considered as the "supra-nuclear center" for the conjugate eye movements to the opposite side. This pathway is very similar to the oculomotor pathway recently defined by electric stimulation and lesions in the brainstem of monkey (Bender and Shanzer, 1964).

b) The other fibres constitute a portion of *Déjerine's aberrant pyramidal system*. They end chiefly in the paramedian zone of the pontine reticular formation, on both sides but mainly on the contralateral one. They are may be concerned with the control of the vestibular and awakening systems.

RESUMEN

Los experimentos de este trabajo fueron realizados en 49 monos (macaca mulatta) y los resultados son divididos en tres partes.

1) *Estimulación del campo visual frontal* en experimentos agudos o en la mayoría de los casos con electrodos permanentes en la corteza. El área visual frontal está situada en la concavidad del surco "arcuatus" y está formada por áreas que tienen asignadas cada una una *función oculomotora propia*: desviación horizontal, oblicua, hacia el lado opuesto o hacia arriba y hacia abajo. Como lo demostraron Crosby y otros (1952) las respuestas a la estimulación del subcampo dorsal son similares a las evocadas en el subcampo ventral a la manera de la imagen en espejo. La excitación de cualquier punto del campo visual frontal evoca además *respuestas secundarias*: apertura de los párpados, dilatación de las pupilas, rotación de la cabeza

y del tronco hacia el lado opuesto y movimiento giratorio hacia el lado opuesto (cuando se aplican estímulos más fuertes).

2) *Destrucción parcial o total del campo visual frontal.* Los signos y síntomas son agrupados bajo cinco títulos: alteraciones *oculomotoras*, alteraciones *pupilares*, perturbaciones del *equilibrio*, defectos *visuales* y modificaciones del *nistagmus optoquinético*. El campo visual frontal es considerado como un "centro práxico", cuya lesión causa no sólo alteraciones motoras sino también la aparición de agnosia (hemiagnosia visual). Este defecto se mantiene aproximadamente tanto tiempo como los disturbios del nistagmus optoquinético. El estudio electronistagmográfico agrega datos más precisos acerca de los mecanismos oculomotores a los que surgen de la simple observación clínica. La fase rápida representa el "primum movens" del nistagmus

optoquinético y lo hemos denominado "research movement" (movimiento de indagación) dado que es un movimiento activo que depende del campo visual frontal y no un reflejo de corrección del eje óptico.

El estudio de nistagmogramas patológicos y normales demostró que el postnistagmus optoquinético puede ser directo o inverso.

3) *Estudio de las vías eferentes del campo visual frontal.* La técnica de Marchi aplicada a 12 monos reveló, además de las fibras asociativas y comisurales la existencia de fibras descendentes que se dividen en dos vías:

a) *Vía córtico-diencefalo-mesencefálica no cruzada* que constituye el sustrato anatómico del aparato diencefálico para movimientos "contraversivos" (Hassler, 1956),

que se dirige principalmente hacia la formación reticular mesencefálica homolateral, considerada por Szentágothai (1943, 1950) como un "centro supra nuclear" para el movimiento conjugado de los ojos del lado opuesto. Esta vía es muy similar a la recientemente definida mediante estimulación eléctrica y lesiones al nivel del diencefalo y del tronco cerebral en el mono (Bender y Shanzer, 1964).

b) Las fibras que constituyen una porción de la *vía piramidal aberrante de Dejerine*, que terminan en la zona paramedial de la formación reticular protuberancial a ambos lados aunque en mayor grado del lado opuesto, cuya función podría estar en relación con el control de los sistemas vestibular y del despertar.

R É S U M É

Ce travail porte sur 49 singes macaques et se divise en trois parties.

1) *Stimulation électrique de l'aire oculogyre frontale*; de façon aiguë ou, dans plus de la moitié des cas, de façon chronique au moyen d'électrodes à demeure. L'aire oculogyre se trouve dans la concavité du sillon arqué et se divise en secteurs dont chacun a une fonction *oculomotrice propre*: déviation conjuguée des yeux soit horizontalement vers le côté opposé, soit obliquement vers le côté opposé et vers le haut ou vers le bas. En outre, comme l'ont montré Crosby et coll. (1952), la branche dorsale constitue l'image en miroir de la branche ventrale. Il faut ajouter que l'excitation de n'importe quel point de l'aire oculogyre provoque des *réponses accessoires*: ouverture des paupières, dilatation des deux pupilles, rotation de la tête et du corps vers le côté opposé et, si le stimulus est plus intense, mouvement de manège vers le côté opposé.

2) *Destruction partielle ou totale de l'aire oculogyre frontale.* Les phénomènes post-opératoires se répartissent en cinq groupes: troubles *oculomoteurs*, troubles

pupillaires, troubles de *l'équilibration*, déficit *visuel*, perturbations du *nystagmus optocinétique* (N.O.C.). L'aire oculogyre frontale constitue un centre praxique, dont la destruction engendre non seulement des désordres moteurs, mais aussi des troubles gnosiques (hémiagnosie visuelle). Ce déficit visuel dure à peu près aussi longtemps que les troubles du N.O.C., dont l'étude apporte des renseignements plus précis sur les mécanismes oculomoteurs que la simple observation directe de la motilité oculaire. La secousse rapide est le *primum movens* du N.O.C. et nous l'avons appelée "mouvement de recherche" pour montrer qu'il s'agit d'un mouvement actif dépendant de l'aire oculogyre et non d'un réflexe de correction de l'axe optique. L'étude de nombreux nistagmogrammes a montré que le post-N.O.C. peut être direct ou inversé, à l'état normal et pathologique.

3) *Etude hodographique des fibres efferentes, issues de l'aire oculogyre frontale.* La méthode de Marchi appliquée chez 12 singes a révélé, à côté de fibres associatives et commissurales, des fibres descendantes qui se divisent en deux voies à partir de

la capsule interne: a) *La voie cortico-diencephalo-mésencéphalique non croisée*, qui constitue le substratum anatomique de l'appareil diencephalique pour les mouvements "contraversifs" (Hassler, 1956) et qui aboutit notamment dans la formation réticulée mésencéphalique homolatérale, où Szentágothai (1943, 1950) place le centre supra-nucléaire des mouvements conjugués des yeux vers le côté opposé; cette voie coïncide avec la voie oculomotrice tracée

récemment par Bender et Shanzer (1964) au moyen de stimulations électriques et de lésions au niveau du diencephale et du tronc cérébral. b) Les fibres de la *voie pyramidale aberrante de Déjerine*, qui se perdent dans le secteur paramédian de la formation réticulée protubérantielle de chaque côté et surtout du côté opposé et dont la fonction pourrait être surtout le contrôle du système vestibulaire et du système d'éveil.

ZUSAMMENFASSUNG

Diese Untersuchung bezieht sich auf 49 Macacus-Affen. Sie enthält drei Teile.

1) *Elektrische Reizung der frontalen oculogyralen Hirnrinde* entweder während des akuten Experimentes oder, in über die Hälfte der Fälle, im chronischen Experiment mittels Dauer-Elektroden. Die oculogyrale Hirnrinde bewindet sich in der Konkavität des Sulcus arcuatus und lässt sich in verschiedenen Sektoren aufteilen, die je eine *spezifische oculomotorische Funktion* besitzen; konjugierte Drehbewegung der Augen entweder in horizontaler Richtung zur entgegengesetzter Seite und nach oben oder nach unten. Der dorsale Zweig bildet ausserdem wie durch Crosby et al. (1952) beschrieben wurde, das Spiegelbild des ventralen Teiles. Es ist hinzuzufügen dass die Reizung jedes Punktes der oculogyralen Hirnrinde *Nebenbewegungen* erzeugt: Öffnen der Augen, Erweiterung der Pupillen, Rotation des Hauptes und des Körpers zur entgegengesetzter Seite, und bei intensiveren Reizung, Manegebewegung zur entgegengesetzter Seite.

2) *Partielle oder totale Destruktion der frontalen oculogyralen Hirnrinde*. Die post-operativen Erscheinungen lassen sich in fünf Gruppen aufteilen: *oculomotorische Störungen*, *pupilläre Störungen*, *Gleichgewichts-Störungen*, *visueller Defekt*, *Störungen des optokinetischen Nystagmus* (O.K.N.). Die frontale oculogyrale Hirnrinde ist ein Zentrum der Praxis, dessen Destruktion nicht nur motorische Störungen

erzeugt, sondern auch Störungen der Gnosie. Der visuelle Defekt hält ungefähr genauso lang an wie die Störungen des O.K.N., dessen Untersuchung genauere Ergebnisse bezüglich der oculomotorischen Mechanismen liefert als die einfache Betrachtung der Augenmotilität. Die schnelle Zuckung ist das "primum movens" des O.K.N., die wir "Such-Bewegung" benennen, weil sie u.E. eine aktive Bewegung, abhängig der oculogyralen Hirnrinde und nicht ein Korrektionsreflex des optischen Achses ist. Die Untersuchung vieler Nystagmogrammen zeigte dass der O.K. post-Nystagmus direkt oder umgekehrt sein kann, im normalen wie im pathologischen Zustand.

3) *Hodographische Untersuchung der efferenten Fasern der frontalen oculogyralen Hirnrinde*. Die Färbung nach Marchi bei 12 Affen zeigte, ausser den assoziativen und kommissuralen Fasern, absteigende Fasern, die sich in der Capsula interna in zwei Bahnen aufteilen: a) *eine nicht-gekreuzte cortico-diencephalo-mesencephalische Bahn*, welche das anatomische Substrat des diencephalischen Mechanismus der contraversive Bewegungen darstellt (Hassler, 1956) und die in der homolateralen mesencephalischen Formatio reticularis endigt, wo Szentágothai (1943, 1950) das supra-nucléäre Zentrum der konjugierten Bewegungen der Augen zur entgegengesetzter Seite beschrieb. Diese Bahn ist identisch mit der oculomotorischen Bahn, welche

neulich durch Bender und Shanzer (1964) mittels elektrischen Reizungen und Läsionen im Diecephalon und Hirnstamm beschrieben wurde.

b) *Die Fasern der aberranten Pyramidenbahn von Déjerine*, die reichen in den

paramedianen Theil der Protuberantiellen Formatio reticularis beiderseits, vor allem aber in die entgegengesetzte Seite, und deren Funktion vielleicht die Kontrolle des vestibulären Systems und des Systems des Wachzustandes darstellen könnte.

DISCUSSION

(Dr. Stefan Shanzer - U.S.A.)

It is a privilege to discuss Dr. Brucher's paper and a pleasure to hear his important contribution, especially for those of us who are familiar with his monograph on the same subject. It is heartening to hear a consideration of eye movements in a waking organism since most of the recent authors seem to be aware of eye movements only during sleep. Dr. Brucher's investigation is divided into a study of the effects of stimulation, destruction, and of anatomic degeneration following frontal lesions. All these merit some comments.

Electrical stimulation resulted in contralateral conjugate deviation of the eye in the hands of most investigators during the past 95 years. But the detailed results have varied considerably both in the character of movement obtained and in the extent of the excitable area. Dr. Brucher's results confirm some of the results of Crosby and collaborators especially concerning the "mirror image" distribution of responses from the two banks of the arcuate sulcus. But a study from our department (Wagman et al., 1961) showed a less precisely geometrical pattern of distribution and indeed a much greater excitable area especially dorsolaterally to the arcuate sulcus on the surface of the hemisphere and also rostrally to the classical eyefield. And if stimulations were extended to the mesial surface of the hemisphere a similarly excitable area could be found resulting in a direct extension of the classical frontal eyefield. Stimulation of the frontal subcortex also yielded contralateral deviations, often horizontal but also oblique and occasionally up or down. No geometrical pattern could be discerned in the distribution of

oblique responses. This is quite unlike the occipital subcortex which faithfully follows the pattern obtained from surface stimulation namely downward or downward and contralateral (oblique) movements from the dorsal portions of the occipital lobe and upward or obliquely upward deviations from the ventral portions.

One should also remember that while the frontal and occipital regions are important in yielding eye deviations they are not unique. The temporal and posterior parietal cortex behaves similarly and thus almost the entire cortical surface with the exception of the regions immediately in front and in back of the rolandic sulcus is in a manner "oculomotor". This makes a concept of eye movement centers in the cerebrum untenable.

As Dr. Brucher emphasizes, it is important to remember that movement of the eyes is not an isolated response. In an alert freely moving monkey important postural adjustment of the head body and limbs will follow, and of course eyelid, facial and pupillary responses are found, often very pronounced and even giving rise to integrated seizure responses if considerably suprathreshold stimuli are used.

The results of destruction of frontal eyefields as reported by Dr. Brucher raise important problems. Most past investigators have also reported the alteration in posture, forced eye deviations to the side of the lesion and forced circling depending on the depth and extent of the "cortical" lesion. All these phenomena were usually fleeting and in most studies no significant behavioral deficit was apparent after the first few days. Dr. Brucher describes also a visual

deficit in his animals which he attributes to a "visual hemiagnosia". While I have no personal experience with this type of preparation, it is difficult to accept this hypothesis. Kennard and Ectors (1938) reported that monkey with left frontal "eyefield" lesion did not seem to reach for "peanut" in the right field of vision. These monkeys had more than cortical lesions, the damage extended deep into the caudate nucleus. If the frontal eyefield were indeed a "praxic center" bilateral lesions of the frontal eyefields should really result in a profound bilateral visual and perceptual dysfunction with severe consequences for the experimental animal. Such bilateral lesions do not affect the performance even on complex visual tasks as demonstrated among others by Pasik et al (1958) in our department. Similarly unilateral frontal ablations do not induce a deficit in optokinetic nystagmus in monkeys with previous ipsilateral occipital ablation. We are in full agreement with Dr. Brucher as to the importance of recording optokinetic nystagmus as an objective measure of function but in the experiments performed in our department no alteration in O.K.N. or O.K.A.N. was seen in these animals. It is possible that by using subtler techniques, for instance measurement of the velocity of the fast and slow components of nystagmus, some alteration could be found and indeed such studies are being performed at this time.

Finally concerning the results of the degeneration studies after frontal lesions. We have not performed such systematic studies. Dr. Brucher feels that his results fit in with our behavioral observation on the effects of stimulation and lesion of the depth structures. Both stimulations and lesions in our experiments were most effective in the paramedian brainstem area with ipsilateral effects being particularly strong in the pontine tegmentum and contralateral effects distributed more rostrally and dorsally in the midbrain and thalamus (Bender and Shanzer, 1964). It should be emphasized that the brainstem area in which a small lesion will result in demonstrable gaze deficit is much smaller than the area where oculomotor responses are present on electrical stimulation. Our experiments do not permit us to select one or two systems of fibers as sole mediators of the oculomotor reactions. More than one region of brainstem, containing complex nets of fibers and cell masses was involved. On occasion one may demonstrate a region in the brainstem which when destroyed will almost selectively abolish responses on electric stimulation of one frontal eyefield. And this may represent a correlation of Dr. Brucher's degeneration studies.

I would like to congratulate Dr. Brucher on this thorough, comprehensive and important contribution which explains many problems but also raises new important questions for those interested in oculomotor and visual functions.

REFERENCES

1. Bender, M. B.: The eye-centering system. A theoretical consideration. *Arch. Neurol. Psychiat. (Chic.)* 73, 685-699, 1955.
2. Bender, M. B.; Teng, P.; Weinstein, E. A.: Centering of eyes. A patterned eye movement. *Arch. Neurol. Psychiat. (Chic.)* 72, 282-295, 1954.
3. Brucher, J. M.: Etude anatomophysiologique de la voie oculomotrice volontaire. *Acta neurol. belg.* 55, 633-654, 1955.
4. Brucher, J. M.: L'aire oculogyre frontale du singe. Ses fonctions et ses voies efférentes. (Arscia, Bruxelles; Maloine, Paris, 1964).
5. Chusid, J. G.; Sugar, O.; French, J. D.: Corticocortical connections of the cerebral cortex lying within the arcuate and lunate sulci of the monkey (*Macaca Mulatta*). *J. Neuropath. exp. Neurol.* 7, 439-446, 1948.
6. Cogan, D. G.: *Neurology of the ocular muscles*. 2. edit. (Thomas, Springfield 1956).
7. Crosby, E. C.; Yoss, R. E.; Henderson, J. W.: The mammalian midbrain and isthmus regions. Part II. The fiber connections. D. The pattern for eye movements on the frontal eye field and the discharge of specific portions of this field to and through

- midbrain levels. *J. comp. Neurol.* 97, 357-381, 1952.
8. *Ferrier, D.*: The localization of function in the brain. *Proc. roy. Soc. B* 22, 229-232, 1874.
9. *Hassler, R.*: Die zentralen Apparate der Wendebewegungen. I. Ipsiversive Wendungen durch Reizung einer direkten vestibulo-thalamischen Bahn im Hirnstamm der Katze. II. Die neuronalen Apparate der vestibulären Korrekturwendungen und der Adversivbewegungen. *Arch. Psychiat. Nervenkr.* 194, 456-516, 1956.
10. *Hitzig, E.*: Untersuchungen über das Gehirn (A. Hirschwald, Berlin 1874).
11. *Huber, A.*: Augensymptome bei Hirntumoren (Hans Huber, Bern und Stuttgart 1956).
12. *Hyde, J. E.*; *Eliasson, S. G.*: Brain-stem induced eye movements in cats. *J. comp. Neurol.* 108, 139-172, 1957.
13. *Jampel, R. S.*: Convergence, divergence, pupillary reactions and accommodation of the eyes from faradic stimulation of the macaque brain. *J. comp. Neurol.* 115, 371-399, 1960.
14. *Krieger, H. P.*; *Bender, M. B.*: Optokinetic afternystagmus in the monkey. *Electroenceph. clin. Neurophysiol.* 8, 97-106, 1956.
15. *Krieger, H. P.*; *Wagman, I. H.*; *Papathodorou, C. A.*; *Bender, M. B.*: Oculomotor patterns elicited from the cerebrum of the alert cervically transected monkey. *Premier Congrès International de Sciences Neurologiques*, Bruxelles, 1957, vol. III, pp. 401-403 (Édité par L. van Bogaert et J. Radermecker. Pergamon Press, London 1959).
16. *Mott, F. W.*; *Schäfer, E. A.*: On associated eye movements produced on cortical faradization of the monkey's brain. *Brain* 13, 165-173, 1890.
17. *Silberpfennig, J.*: Contribution to the problem of eye movements. III. Disturbances of ocular movements with pseudohemianopsia in frontal lobe tumors. *Confin. neurol. (Basel)* 4, 1-13, 1941-42.
18. *Smith, W. K.*: Ocular responses elicited by electrical stimulation of the cerebral cortex. *Anat. Rec.* 64, (suppl.), 45, 1936.
19. *Smith, W. K.*: The frontal eye field, in *Bucy P. C.*: The precentral motor cortex; 2. edit. (University of Illinois Press, Urbana 1949).
20. *Stenvers, H. W.*: Les réactions optomotrices (Masson, Paris 1961).
21. *Szentágothai, J.*: Die zentrale Innervation der Augenbewegungen. *Arch. Psychiat. Nervenkr.* 116, 721-760, 1943.
22. *Szentágothai, J.*: Recherches expérimentales sur les voies oculogyres. *Sem. Hôp. Paris* 26, 2989-2995, 1950.
23. *Teuber, H.-L.*; *Bender, M. B.*: Neuro-ophthalmology: the oculomotor system. *Progr. Neurol. Psychiat.* 6, 148-178, 1951.
24. *Van Gehuchten, A.*: Les maladies nerveuses; 6e édition revue et mise à jour par P. Van Gehuchten (Uystpruyst, Louvain 1951).
25. *Vogt, C.*; *Vogt, O.*: Zur Kenntnis des elektrisch erregbaren Hirnrinden-Gebiete bei dem Säugtieren. *J. Psychol. Neurol. (Lpz.)* 8, 277-456, 1907.
26. *Vogt, C.*; *Vogt, O.*: Allgemeine Ergebnisse unserer Hirnforschung. IV. Mitteilung: Die physiologische Bedeutung der architektonischen Rindenfelderung auf Grund neuer Rindenreizungen. *J. Psychol. Neurol. (Lpz.)* 25, 279-462, 1919.
27. *Wagman, I. H.*; *Krieger, H. P.*; *Papathodorou, C. A.*; *Bender, M. B.*: Eye movements elicited by surface and depth stimulation of the frontal lobe of Macaque mulatta. *J. Comp. Neurol.* 117, 179-188, 1961.
28. *Wagman, I. H.*; *Werman, R.*; *Feldman, D. S.*; *Sugarman, L.*; *Krieger, H. P.*: The oculomotor effects of cortical and subcortical stimulation in the monkey. *J. Neuro-path. exp. Neurol.* 16, 269-277, 1957.
29. *Welch, K.*; *Stuteville, P.*: Experimental production of unilateral neglect in monkeys. *Brain* 81, 341-347, 1958.
30. *Werman, R.*; *Feldman, D. S.*; *Wagman, I. H.*: Cerebral pathways for conjugate eye deviation and centering. *Fed. Proc.* 14, 162, 1955.
31. *Zülch, K. J.*: Störungen des intrakraniellen Druckes. in *Handbuch der Neurochirurgie*; 1e Band, 1e Teil (Springer, Berlin 1959).
32. *Zülch, K. J.*: Die Pathogenese von Massenblutung und Erweichung unter besonderer Berücksichtigung klinischer Gesichtspunkte. *Acta neurochir. (Wien) suppl.* VII: 51-117, 1961.

The Frontal Lobes and their Function: Further Observations on Rodents, Carnivores, Subhuman Primates, and Man

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INTRODUCTION

It is now nearly a third of a century ago that John Fulton and Carlyle Jacobsen communicated their observations on behavioral changes after prefrontal lobectomy in primates to the Second International Congress of Neurology in London (Fulton & Jacobsen¹⁵). Their report launched frontal lobotomy in man, and thereby sharpened the paradox that clings to the study of frontal-lobe function at different phylogenetic levels. The paradox lies in an ap-

parent contrast: in the animal, behavioral consequences of frontal removals are clear-cut yet almost impossible to interpret, while observations on man, with frontal injury, ablation or disease, are suggestive of unitary interpretation, yet the facts themselves are under persistent controversy. A survey of the present state of the field, three decades later, suggests that the paradox is still with us.

For animals below man, recent work has confirmed and extended the findings of specific losses on delayed-response and delayed-alternation tasks, first detected by Jacobsen for the monkey over thirty years ago (Jacobsen³¹; Jacobsen & Nissen³²). Thus, rats, cats and Rhesus monkeys show specific and lasting impairment on such tasks** after bilateral removal of prefrontal

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** The delayed-response task, in its simplest form, involves presenting the animal with two food wells, or inverted cups. One of these is baited, in full view of the animal. An opaque screen is then interposed between animal and cups, for a specified delay period (often 5 seconds); the screen is raised and the animal permitted to look for the bait. If he uncovers the wrong (unbaited) cup, he is considered to have made an error on this particular trial. Most macaques with bilateral removals of the sulcus-principalis region in the frontal lobes perform at chance levels on this task un-

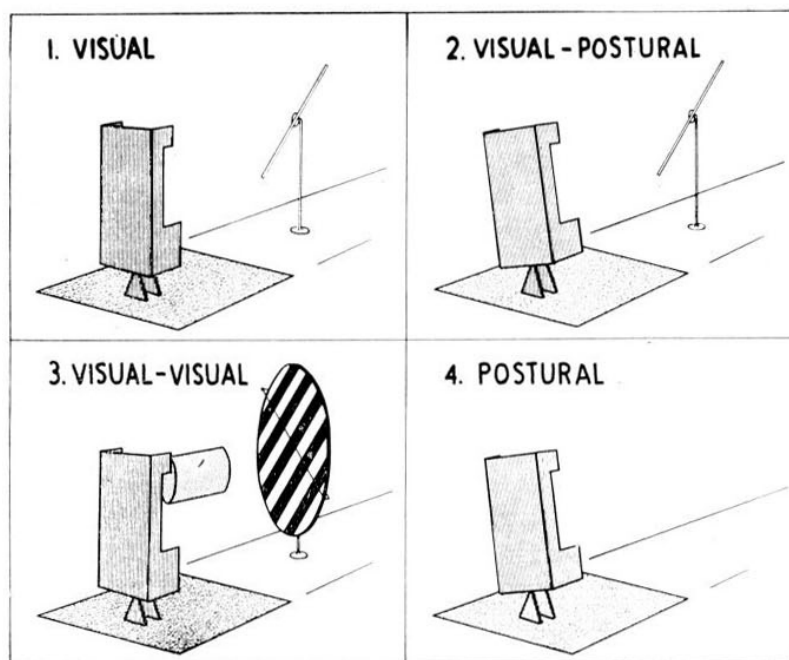


Fig. 1. — Diagrams showing experiments involving judgment of visual vertical (experiments 1, 2, 3), or of postural vertical (experiment 4), with body upright (experiments 1 & 3), and with body tilted (experiments 2 & 4). In experiment 1, the subject is upright and sets

a luminous line in a dark room to apparent vertical, under purely visual control. In experiment 2, the same visual judgment is made under conditions of abnormal posture (body tilted) hence "visual-postural conflict". In experiment 3, posture is normal but there is a conflicting (obliquely striped) visual background; against this background the subject has to set a black thread to the apparent vertical, under visual control. In experiment 4, the subject is blindfolded and has to bring the apparatus to the apparent vertical (purely "postural" task). Experiments 1 and 4 (the purely postural tasks), did not distinguish between men with anterior and posterior brain lesions, nor between either of these groups and controls without brain injury. Experiment 2 (visual-postural task) was done much more poorly by men with anterior penetration (see next figure), and experiment 3 (visual-visual conflict) more poorly by men with posterior than with anterior lesions, providing an instance of "double dissociation"

(After Teuber & Mishkin, 1954).

cortex, or head of caudate nucleus, or various related subcortical structures. In all of these species, electrical stimulation of

less special variations of procedure are introduced to assist them in their performance (Malmo,³⁹ Mishkin and Pribram,⁴³ Contrary to Jacobsen's initial impression³¹, the failure of the bifrontal macaque is not due to a loss of recent memory since the same animals can learn and retain visual discriminations quite well. Thus, the two-cup test becomes soluble for them as soon as one cup is made visually distinct from the other. The delayed-alternation task involves presentation of two cups, one of which is baited. After the animal has discovered the bait, he is given a series of trials with the bait being placed by the experimenter on each successive trial under that cup which had previously been unbaited. Again, various intratrial delays are introduced.

these same anatomical structures transiently interrupts accurate performance of these tasks, and stimulation in these regions during learning interferes with acquisition. Yet, in spite of this consistency in experimental results, the nature of the delayed-response deficit remains elusive.

By contrast, uncomplicated surgical removals of cortex, from anterior frontal regions in man, usually fail to produce lasting interference with delayed-response performance, and the literature on frontal-lobe lesions is conflicting with respect to positive after-effects, the reports ranging from those claiming extreme changes in emotional and intellectual function to those reporting minimal or no effects on behavior (compare Hebb²³, and Hécaen & Ajuria-guerra²⁴).

Under these circumstances, we have attempted to develop tasks that might be sensitive to fairly subtle but persistent changes in behavior after frontal-lobe lesions in man. The behavioral symptoms revealed by these tasks are superficially diverse, yet we believe they can be shown to reflect a single, underlying change in behavior. We believe further that this essential change in man, once formulated, might help us to understand the consistent but seemingly inexplicable symptoms of frontal-lobe removal in subhuman forms.

Characteristically, those tasks that seem to depend most specifically on the integrity of anterior forebrain structures in man are neither purely sensory, nor purely motor, but sensorimotor in the strict sense of that term; nor are they readily classified as involving "higher" functions in contradistinction to lower ones (Teuber^{58, 62}; Teuber & Mishkin⁶⁵; Teuber and Proc-

tor⁶⁶). Even decades after frontal trauma, patients may exhibit changes in performance on a number of these specialized tasks, including difficulty in judging the perceived vertical under conditions of body tilt, characteristic changes in reversal rates for figures with reversible perspective, trouble with voluntary visuomotor searching, and impairment on tasks involving rapid reversal of standpoint, while localizing designated spots on their own body. We shall attempt to show how these seemingly disparate forms of impairment might be subjected to a uniform interpretation, and how this interpretation in turn might illuminate the obscure nature of the delayed-response and alternation deficits after frontal lesions in species below man.

On either level, human or subhuman, these frontal-lobe syndromes cannot be analyzed successfully in traditional stimulus-response terms. As we have pointed out elsewhere (Teuber^{60, 61, 62}), their analysis requires a 180 degree turn: instead of proceeding as is customary from sensory input to motor output, the proper interpretation of frontal-lobe symptomatology seems to us to demand that we go from motor to sensory systems by invoking a mechanism which shunts, directly and centrally, the motor pathways of the forebrain into the sensory pathways (see also Sperry⁵⁵; v. Holst and Mittelstaedt²⁹; Teuber^{59, 60, 61}).

Specifically, we postulate a 'corollary-discharge mechanism' which depends, for its proper functioning, on the integrity of frontal lobes and basal ganglia. This hypothetical mechanism presets the sensory regions in the brain at the onset of voluntary motor acts, preparing the sensory system for those changes that result from normal execution of the intended movement. Disturbances in this central motor-to-sensory discharge, we propose, are at the root of frontal-lobe symptomatology and represent a major aspect of normal frontal-lobe function in animal and man.

In order to develop these interpretations in detail, we shall briefly review, first, the

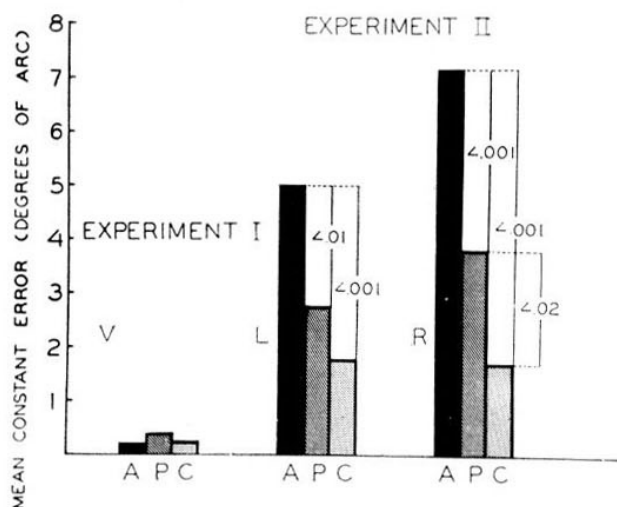


Fig. 2. — Results of experiments 1 and 2 (see preceding figure), in terms of average constant errors, in degrees of arc, for attempts at setting the visual vertical with body upright (experiment 1) and with body tilted (experiment 2): either 28° to the subjects' left (diagrams marked L) or right, respectively (diagrams marked R). A, P and C designate results for 20 men with anterior brain wounds, 20 with posterior brain wounds and 20 controls with peripheral nerve injuries but without cerebral involvement. Significant differences among results are shown next to the appropriate bar diagrams (From Teuber & Mishkin, 1954).

current findings on effects of frontal lesions in rodents and carnivores as well as in primates below man, and then turn to enumeration of our specific results obtained in man with frontal trauma. As will be seen, the behavioral effects of lesions in prefrontal cortex or anterior caudate nucleus are strikingly equivalent in all of the species considered here, in spite of the evolutionary changes in the organization of their prefrontal cortex.

OBSERVATIONS ON SUBHUMAN SPECIES

Rodents

Recent work in the M.I.T. Laboratories (Chorover and Gross⁸; Gross, Chorover and Cohen²¹) has shown that in the rat tests of alternation disclose marked impairment of acquisition and retention of these tasks after bilateral anterior cortical resections* while performance in a complex locomotor maze remains intact. Conversely, posterior cortical removals of comparable extent impair maze learning yet leave alternation unimpaired.

These experimental results thus draw a contrast between behavioral effects of two types of cortical removals, anterior and posterior. In this way, the results provide a particularly instructive instance of what we have called 'double dissociation of symptoms' (Teuber^{57, 58}): anterior lesions but not posterior produce alternation deficits and posterior lesions but not anterior produce impairment on the particular maze employed, (the so-called Hebb-Williams Maze, as described by Rabinovich and

Rosvold⁵¹). Such instances of clearcut dissociation are hard to come by, but they ensure topographic specificity of symptoms whenever such dissociations are found.

Beyond that, these recent findings on distinctly focal effects of anterior and posterior cortical lesions in the rat may well represent a belated vindication of Hunter's critique³⁰ of Lashley's mass-action hypothesis. It will be recalled that Lashley³⁵ claimed equal potency of neo-cortex for mediating performance in a particular kind of maze (Lashley's maze III). Large lesions interfered with accurate performance, whether measured by acquisition or retention, in proportion to the size of the lesion and irrespective of the site. Hunter argued, unsuccessfully, that such results were quite compatible with specific localization of functions: the larger the lesion, the greater the likelihood of invading several essential foci, and the more complex the task, the greater the probability that it would turn out to be vulnerable to lesions encroaching on more than one focus at a time.

As it happened, the crucial task used by Lashley to demonstrate lack of cortical specificity (his maze III) required adequate alternation behavior as well as effective visual orientation in a complex spatial array. The recent findings of Chorover and Gross in our laboratories suggest,

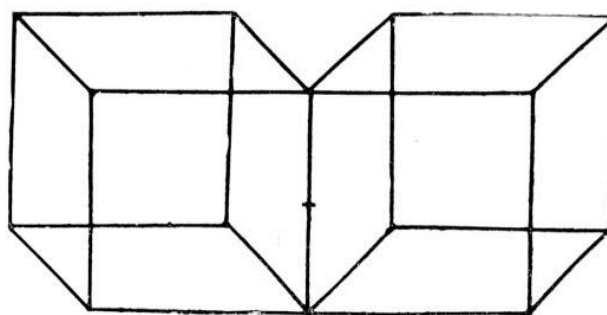


Fig. 3. — Double Necker cube, used in studies of spontaneous fluctuations of apparent perspective. The subject fixates the small crossbar on the center vertical, and signals perspective reversals by depressing a key on his left (for reversals of the left cube), on his right (for reversals of the right cube), and on both sides together (for simultaneous reversals of both cubes). (After Cohen, 1959; and Teuber, 1960).

* Even a species of such uncertain taxonomic status as *Tupaia glis* (the Indonesian tree shrew) which probably is neither an insectivore nor a primate shows loss of delayed response after anterior cortical lesions (unpublished observations in the M.I.T. laboratories). However, the interpretation of these results is rendered difficult by the absence of fully established homologies between the primate prefrontal cortex and the presumably corresponding portion of the tree shrew's frontal lobe, and by the comparative instability of a delayed-response performance in the intact tree shrew.

therefore, quite in keeping with Hunter's interpretation, that the alternation aspects of maze performance in rats are selectively vulnerable to anterior cortical lesions and that the spatial-orientation aspects are disturbed by posterior cortical lesions; hence, sufficiently large removals encroaching on anterior and posterior cortical fields will of necessity impair performance on maze III and similar tasks, and will do so the more readily the larger the combined lesion.*

The anterior cortical syndrome, in turn, has its analogues after appropriate subcortical destruction. Subcortical lesions placed in rats bilaterally in the head of the caudate, or in dorsal or ventral hippocampus, or in mediodorsal thalamus, have behavioral effects indistinguishable from those of anterior cortex in terms of the alternation task. The degree of impairment after caudate lesions in the rat increases with the size of the lesion as it does in the monkey.

It should be noted that the alternation tasks employed for the rat are similar to certain forms of delayed-alternation tests used with carnivores and primates. However, the cortical focus for these alterations of behavior in the rat may have to be further defined both anatomically and physiologically since the homologies between rodent and primate in this respect are still being worked out (comparative histologic studies progressing in Professor Nauta's laboratory at M.I.T.).

* It is important to note what these results do not mean: they do not preclude the possibility that some other task, less complex in nature, might yet be found on which rats with anterior or posterior neocortical lesions do equally badly. If there were no way of decomposing such a task into components vulnerable to different focal lesions, one would have established the existence of some general (non-localizable) function, as demanded by Lashley's hypothesis. We have argued, elsewhere, that such a task can be identified for man, strongly suggesting that a "general factor" might coexist with the numerous more specific ones (Teuber & Weinstein, ⁶⁸).

Carnivores

Most of the behavioral work on carnivores has been performed in laboratories other than ours, especially for cats by J. M. Warren at Pennsylvania State University (Warren ⁷⁵) and in dogs by S. Brutkowski ⁵; Lawicka & Konorski ^{36, 37}). In cats and dogs, bilateral prefrontal resections of cortex disturb alternation and delayed-response performance albeit somewhat less severely in the cat than in the monkey provided conditions are deemed comparable. Caudate lesions and caudate stimulation have effects equivalent to cortical removals from prefrontal areas. Evidence on effects of interference with hippocampal or mediodorsal thalamic structures is incomplete.

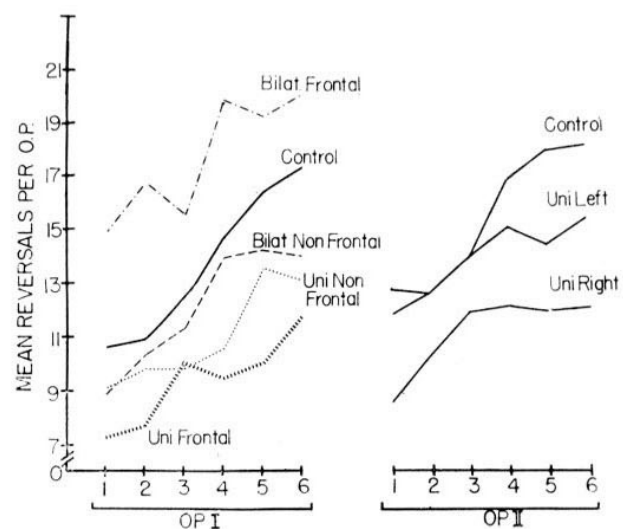


Fig. 4. — Results of experiments on spontaneous perspective fluctuations for a double Necker cube (shown in preceding figure). Mean reversals are shown for consecutive 15 second periods, over six observation periods (OP), i.e., for a total of 90 seconds. Note that the group of patients with bilateral frontal lesions shows abnormally high reversal rates, as compared with controls, while other lesion groups show a depression of reversal rates. Note also that unilateral frontal lesions show the greatest depression of reversals and that right unilateral lesions produce greater reduction than left (After Cohen, 1959; see also Teuber, 1960).

Macaque

In the Rhesus monkey ablation or stimulation of lateral prefrontal cortex (sulcus-principalis region, Blum³) specifically disrupts delayed response and delayed alternation (Mishkin and Pribram^{43, 44}; Pribram⁴⁸; Stamm⁵⁶; Weiskrantz, Mihailovic, & Gross⁷⁹), and destruction or stimulation of head of caudate, again produces similar effects (Rosvold & Delgado⁵²; Battig, Rosvold & Mishkin²; Dean and Davis¹²). Hippocampal lesions, if produced by suction, tend to disrupt performance of delayed-alternation tasks, but leave delayed response essentially unimpaired (Orbach, Milner, and Rasmussen⁴⁷; Pribram, Wilson, and Connors⁵⁰). The results of subtotal lesions in mediodorsal thalamus are less clear but a recent study by Schulman⁵³ suggests that total lesions in medialis dorsalis can abolish capacity for delayed response in the monkey. In addition, we should note that electrical

stimulation in the substantia nigra can likewise interfere with delayed-response performance in the macaque (Ciani⁹).

COMPARISON WITH EFFECTS IN MAN

So far the evidence for subhuman forms is beautifully consistent with regard to the specificity of the symptom and its localization, yet the physiologic meaning of the symptom has remained as elusive as ever. Some clarification may be obtained by turning to observations made on man with injury or disease of frontal lobe or basal ganglia. The situation with regard to man is complicated by the fact that recent work (Chorover and Cole⁷) has again confirmed that man does not show specific and reliable delayed-response or delayed-alternation deficits after uncomplicated frontal lesions, presumably because man solves these tasks by recourse to verbal mediation not available to infrahuman species.

Lasting deficit in man after frontal lesion on a visuo-pestural task

Yet we have suggested earlier (Teuber and Mishkin⁶⁵) that a perceptual task involving the setting of the visual vertical under various conditions of body tilt brings out a "frontal" deficit, and the same task is performed badly by patients with Parkinsonism both before and after pallidectomy or thalamectomy (Teuber and Proctor⁶⁶). Thus, in man, as in the lower primates, in carnivores, and in rodents, a task can be identified that is similarly vulnerable to prefrontal cortical lesions and to involvement of subjacent basal ganglia (Fig. 1, 2).

The search for other associated deficits in man after frontal lesions

These findings make it even more pressing to ask what these consistent signs of frontal lobe or basal ganglia disease might signify in terms of normal function. Some

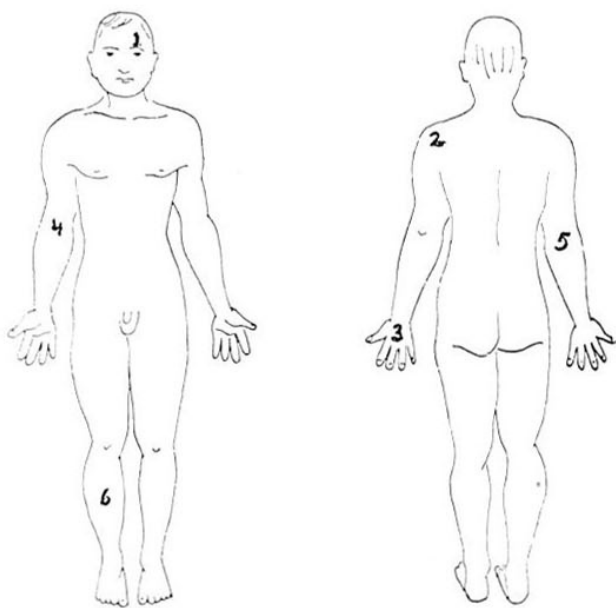


Fig. 5. — Sample figurines from a series of test charts for assessing "personal orientation". The subject, standing upright, faces the figurines, and indicates, by pointing, those parts of his own body which are marked by arabic numerals on the figurines. Note the requirement for repeated reversals of right-left orientation (from Semmes, Weinstein, Ghent & Teuber, 1963).

additional clues can be obtained by comparing the impressive number of achievements which are unimpaired after prefrontal lesions in man and by contrasting these negative findings with the few remaining positive signs which can be identified in addition to the defective performance on the visuo-postural task (Teuber⁶²).

These findings were obtained on 90 cases of frontal penetration by missiles in young adults (42 left, 22 right, 26 bilateral), as compared with 142 cases of similar penetrating brain wounds primarily implicating other cerebral lobes, and 118 controls with peripheral nerve injuries (also sustained in combat). Many of these cases

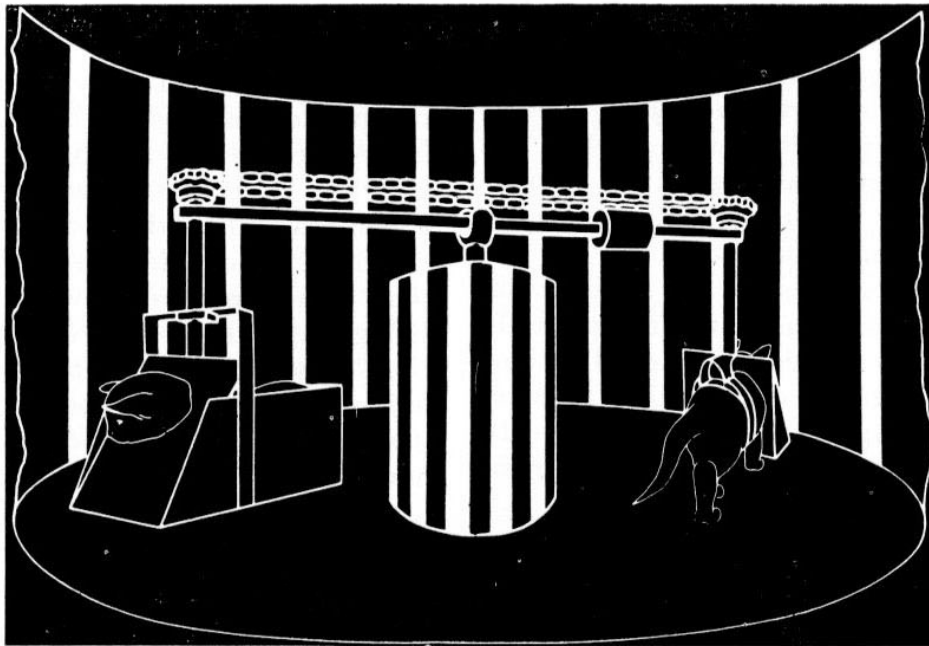


Fig. 6. — Schematic view of apparatus used by Richard Held and Alan Hein in their experiments on origins of sensorimotor control in kittens. All movements of the kitten on the right (the 'active' kitten) are transmitted by harness and pivot arrangements to the gondola which bears the kitten on the left (the 'passive' kitten). Visual experience of the active kitten is combined with self-produced motor output, while the otherwise identical visual experience of the passive kitten is not. For further details, see text (Based on Held & Hein, 1963).

have been followed by now for more than 15 years and have been subjected to numerous tests.

The negative findings for frontal-lobe cases include the following: flicker fusion (no reduction, Teuber, Battersby, & Bender⁶⁴); form boards, essentially normal performance or slight impairment, with posterior lesions being much more productive of impairment than frontal lesions (Teuber & Weinstein⁶⁷); various tests of recent memory (no impairment, Ghent, Mishkin, & Teuber¹⁶); intelligence test

performance, including data on a subgroup of the brain injured population tested before and after brain injury was sustained; here again, some patients with frontal lesions showed impairment but this impairment was significantly greater with left parieto-temporal penetrations, even after all cases clinically diagnosed as aphasics had been excluded (Weinstein & Teuber⁷⁸; Teuber & Weinstein⁶⁹). Similar findings (viz., only nonspecific reduction in efficiency) were encountered with various sorting tests and complex problem solving

tasks (Battersby, Teuber, & Bender¹; Teuber⁵⁸).

On the *positive side*, however, are findings of impairment on three tasks (in addition to the visuo-postural task); all of these are essentially perceptual-motor and all have certain other features in common:

1) A *visual search test* in which the patient searches with active head and eye movements for a number of patterns on a screen, in an array of other patterns. Here,

certain posterior lobe lesions can also produce deficits but recent work suggests that the mode of search differs for frontal and parieto-occipital lesions (Teuber, Battersby, & Bender⁶³).

2) A perceptual task involving reports of apparent *reversals of perspective* for an ambiguous line drawing (double Necker cube, Cohen¹⁰; Teuber⁵⁹). This task reveals maximal slowing of reversal rates with unilateral frontal lesions, and abnor-

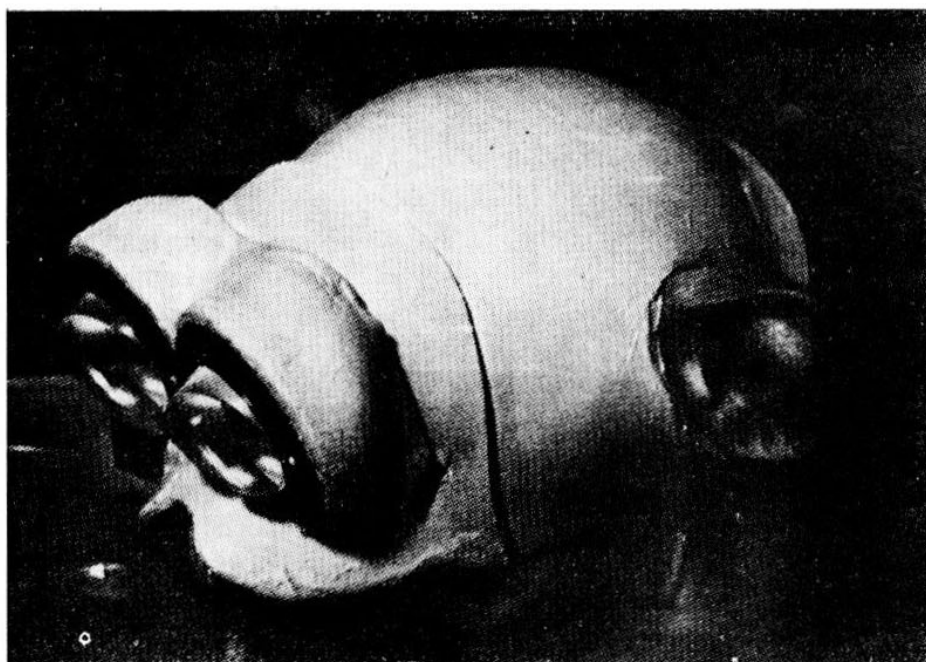


Fig. 7. — Monkey wearing helmet devised by Bossom for testing adaptation to displacing and distorting spectacles. Only the upper two thirds of the monkey's head are visible, but the prisms can be seen in the facial portion of the helmet. Normal monkeys wearing this device while seated in a primate chair adapt their reaching movements to the imposed visuo-spatial distortions in several hours. Monkeys with frontal lobectomies or with lesions of head of caudate nucleus fail to adapt. (From Bossom, 1965).

mally rapid fluctuations of perspective with bilateral frontal penetrations (Figs. 3, 4).

3) A *task of bodily orientation* (Semmes, Weinstein, Ghent, Teuber⁵⁴), involving rapid and repeated shifts in right-left reference: the patient has to indicate on his own body, successively, those parts that are numbered on pairs of schematic drawings of the human body, with one figure facing him, the other facing away (Fig. 5).

INTERPRETATION

The interpretation in functional terms to which we have come over the last few years invokes the concept of a motor-to-sensory action in which frontal lobes and, possibly, some of the anatomically related subcortical structures play a special role. According to these notions, these anterior brain mechanisms are involved in signall-

ing the impending consequences of bodily movement to the sensory systems, preparing the latter for the ensuing change and thus permitting the matching of the outcome of impending actions against the "intent". This hypothesis would provide a tentative interpretation of the delayed-response and delayed-alternation deficits (which are clearly not deficits of memory), as well as of the hyper-reactivity seen in most sub-human forms with prefrontal or anterior caudate lesions. The concept would likewise account in parsimonious fashion for all of the perceptual-motor changes we have observed in men with penetrating frontal lesions. It might fit the emergence of grasping and groping automatisms in severe frontal lobe disease (Denny-Brown¹³). Lastly, the proposed interpretations can predict at least some new behavioral observations before they are made.

Thus, we have suggested that the corollary discharge mechanism may provide the normal degrees of plasticity in sensorimotor coordination, the capacity to maintain perceptual constancies of size and direction during self-induced changes of posture, the subjective stability of the visual environment during voluntary shifts of gaze and the surprising capacity of the normal adult to adapt his sensorimotor performance to rearranged sensory input as shown by experiments involving the wearing of distorting and displacing spectacles (high-power prisms), or of pseudophones. What is important here, beyond the issues raised by frontal-lobe pathology, is the crucial but utterly neglected problem of voluntary motion. It is unclear how such achievements as voluntary reaching or voluntary control of gaze emerge from the matrix of grasping and groping automatisms in the normal infant (Twitchell⁷⁰). Yet it is clear that the neurologic problems of eye-hand coordination and of directed locomotion transcend the usual bounds of Sherringtonian reflex-physiology.

Voluntary eye movements may be a case in point. As we deliberately shift our gaze across a scene, the scene stands still; if, instead, we tap against our eye, moving

it mechanically in its orbit, the visual world shifts. Lastly, if we intend to move our eye while the extra-ocular muscles are paralyzed, the visual world jumps; it is as if we had suddenly become capable of visualizing our 'intent-to-move.' We interpret this series of conditions by saying that in the case of normal voluntary eye movements, a 'corollary discharge' is associated with the efferent signals, presetting the sensory system for the result of our movement. As long as the effect of the motion matches the intent, no movement is seen. However, if the motion of the eyes is abnormally (passively) produced, the scene shifts because the eye movement occurs without any corollary discharge to correct for its sensory consequences. Thirdly, the most interesting case: in acute extra-ocular palsy, the scene shifts subjectively in the absence of any physical displacement of contours across the retina, because the corollary discharge reaches the sensory systems unchecked by any reafferent feedback that would have resulted from the motion that was intended but not achieved. What we are proposing here amounts to the claim that our hypothetical mechanism, the corollary discharge, represents a physiologic marker for the voluntariness of self-produced motions. By contrast, passive movement is passive by virtue of lacking such a corollary discharge.

The importance of this distinction is illustrated in a series of perceptual experiments with normal adults, and with very young kittens and monkeys; this work is progressing at the M.I.T. laboratories in the hands of Professor Richard Held²⁶ and his associates, notably Alan Hein, Joseph Bauer, and others. They explore the necessary and sufficient conditions for sensorimotor adaptation to distorted inputs. For example, a normal adult wearing prismatic spectacles which systematically displace and distort all of the visual input is instructed to walk about actively for one hour. By the end of that hour of active exposure, the subjective distortions and displacements have decreased or altogether disappeared. If the spectacles are then re-

moved, the observer experiences a transient distortion of the scene in directions opposite to that experienced while wearing the prismatic spectacles. However, adaptation is completely lacking if the one-hour exposure to the distorted scene is obtained while the prism wearer is pushed about passively, in a wheelchair.

This crucial role of active movement in perceptual readaptations has now been confirmed in numerous supplemental experiments; beyond that, a more recent series of studies, primarily by Professors Held and Hein⁽²⁸⁾ also, Held & Bossom²⁶; Held & Freedman²⁷) has produced strong evidence for a similar role of active rather than passive exposure in the original acquisition during early development of normal sensorimotor control. In an already classical study, kittens are trained in the manner shown in figure 6. These animals are littermates raised in darkness except for a few hours a day during which one kitten walks actively about, while the other is carried passively by the first by means of a harness and pivot arrangement in a snugly fitting gondola. Under these conditions the active kitten in the pair shows normal form and depth perception when removed from the apparatus, while the passive kitten shows absence of shape and depth discrimination on the tests employed. It even fails to show visually guided placing when its limbs are moved against a serrated table edge.

Such experiments, and similar ones on the emergence of eye-hand coordination in young monkeys (work now in progress), strongly suggest a crucial role for self-produced (i.e., 'voluntary') movements in the origin of certain aspects of form and depth perception and in the achievement of sensorimotor coordination. We assume that the intervening link that has to be built up during early development and modified in the course of readaptation is the corollary discharge, tying the motor into the sensory system, and it is this link, we suggest, which is disturbed by certain frontal lesions and by equivalent lesions of basal ganglia and related structures.

It is therefore of the greatest interest to us that a former student and coworker of Professor Held, Dr. Joseph Bossom⁴ has now obtained direct evidence for selective impairment of prism adaptation in monkeys following frontal lobectomy or destructive lesions in the head of the caudate nucleus. By contrast, cortical removals of a similar extent from other lobes (occipital, parietal, or temporal, unilaterally or bilaterally) leave prism adaptation essentially unimpaired (Fig. 7).

RESIDUAL ISSUES

Our survey of frontal-lobe symptomatology in rodents, carnivores, and primates, including man, has led us to a unitary interpretation of frontal-lobe syndromes in these rather dissimilar species; yet many questions remain.

First of all, the presumptive anatomical homologues of prefrontal cortex at these different evolutionary levels need clearer delineation with modern histologic techniques (work now in progress in Professor Walle Nauta's laboratory at M.I.T.). In the Rhesus monkey the minimal effective lesion for producing delayed-response deficits straddles the sulcus principalis, but it is not obvious why this should be so since this critical region forms only part of the projection field of the mediodorsal thalamic nucleus (Walker^{72, 73, 74}; Pribram, Chow & Semmes⁴⁹), and may well be heterogeneous in terms of its other afferent and efferent connections (Nauta⁴⁶). Maximally effective lesions in carnivores and rodents respectively are not so well worked out. We should expect, however, that fairly analogous critical foci will be encountered once the standard homologues for various parts of prefrontal cortex have been elaborated across different species. Apparent discrepancies in the behavioral effects of, say, frontopolar removals in rodents and primates may simply mean that the removals thus far have not been equivalently placed.

However, the possibility remains that further pursuit of these anatomical studies might lead to a convincing subdivision of frontal-lobe syndromes, particularly in sub-human primates and man. Claims for such an empirical fractionation of the frontal-lobe syndrome have already been advanced; most of these claims focus on the distinction between behavioral effects of dorso-lateral and orbitofrontal removals. Supportive evidence for such a functional fractionation of prefrontal structures can be found primarily in recent summaries of work on carnivores and primates (Brutkowski⁶; Mishkin⁴⁵; Pribram⁴⁸), and, for man, in the detailed studies by Luria and his colleagues (Luria³⁸).

So far, however, many of these proposed fractional syndromes share common features; differing in degrees, they fall short of the specificity that would be implied by a double dissociation of symptoms. In this respect, it may be too early to claim that patterns of symptoms after selective prefrontal lesions could be as distinct and separable as the different aspects of the Klüver-Bucy syndrome which have been identified by appropriately fractional removals from the temporal lobes (Klüver and Bucy³⁴; Teuber⁵⁷).

A similar question arises with regard to certain specific findings for man in cases where prefrontal involvement is limited to one or the other cerebral hemisphere. Such laterality differences emerge quite clearly from the work of Milner and her associates, who find greater impairment on certain stylus mazes after right frontal removal (Milner^{41, 42}; Corkin¹¹), and, conversely, greater impairment of word fluency and of sorting-test performance after similar removals from a dominant left frontal lobe (Milner^{40, 42}). Similar trends can be identified in our own results, particularly with regard to Necker cube reversals, where maximal reduction in reversal rates appeared after right frontal lesions (as shown in Fig. 4). Even more closely similar results could be derived from a recent analysis of a modified visual-searching task: there, left frontal lesions, as one might expect, pro-

duced greater slowing in the search for letters and numerals, while right frontal lesions produced maximal slowing in the search for nonsense figures (see, also, Kimura³³). Observations such as these suggest that unilateral frontal symptoms can take the local color of the hemisphere involved, but these results do not detract from the existence of common features in the behavioral changes after right and left frontal lesions.

Right-left differences may have contributed their share to the perplexity which surrounds one of the oldest experimental procedures for demonstrating frontal-lobe impairment in man: the various tests of sorting and categorizing. These tasks have a long history (Goldstein^{17, 18}; Goldstein and Scheerer¹⁹; Grant and Berg²⁰; Halstead²²; Vygotski⁷¹; Weigl⁷⁷; Zeigarnik⁸⁰). Do these tasks, in fact, reveal specifically frontal deficits? Much of the uncertainty in earlier studies can be traced to the absence of appropriately matched groups of patients with cerebral lesions outside of the frontal lobes whose achievement on these tasks might be compared with that of frontal patients.

Yet, even when such controls are employed the findings remain contradictory: in our own hands, the so-called Wisconsin version of Weigl's test (Grant and Berg²⁰; see, Weigl⁷⁷) gave evidence for impaired performance in men with frontal lesions as a group, but there was equal or greater impairment in patients with posterior lobe lesions, especially if the dominant hemisphere was implicated. By contrast, recent studies in the Montreal laboratory (Milner⁴⁰) suggest a rather specific 'frontal' impairment on the Wisconsin version of Weigl's card-sorting test. However, there were differences in the presentation of the task: we did forewarn our patients that the principles of sorting would change throughout the test while the Montreal version required that the patient discover these changes of principles inductively, without any prior warning on the experimenter's part. Preliminary results comparing the two versions of the task for

the same population of patients suggest that a number of our frontal patients may indeed perform rather poorly once the warning is omitted.

Such results would be more in line with earlier claims for the sorting tests, yet the results would not necessarily contradict our interpretations of the essential frontal deficit. Difficulties in spontaneous yet appropriate shifting in principles of sorting on the patient's part could be still another manifestation of the same trouble which seemed to underly the impaired performance on various sensorimotor tasks. In fact our emphasis on these tasks was not meant to deny the possible existence of corresponding losses on other 'higher' levels, including those involving thought and deliberate actions. Rather, as we said initially, our hypothesis is meant to be neutral with regard to the customary distinctions of higher and lower levels of function.

It is therefore of considerable interest that sorting tests and stylus mazes have been observed to bring out a curious tendency in some of the frontal patients; they 'break rules', that is they violate the instructions given at the beginning of the test, no matter how often the experimenter reminds the patient of these rules (Milner^{40, 41}).

We have previously stressed (Teuber⁵⁸) that patients with severe bifrontal lesions might be remarkably competent in putting into words what a test such as the card-sorting task might require of them; they may cast one glance at the cards and announce correctly "this can be done according to color, form or number." What we had failed to notice was that this was just as true of some of the patients who did not manage to pass the test. In extreme instances, such patients continuously verbalized the rules of the game while disregarding them in their actions. It is this phenomenon which has fascinated Luria³⁸, who has described a number of striking cases.

With these considerations we have moved close to a description of severe frontal

changes in terms that might be reminiscent of the long-forgotten work of Feuchtwanger¹⁴. The complete neglect of his studies is undeserved; after all, he pioneered the use of contrasting groups by assessing the symptoms of frontal trauma (gunshot wounds incurred in the First World War) consistently against those of penetrating trauma in other cerebral lobes. But neglect of this work is understandable since Feuchtwanger's categories for describing the essential frontal impairment were so hopelessly unphysiologic. He characterized the crucial change as involving the patient's affect, his 'will', and his values. It is unfortunately true that present-day psychophysiology has no room for the will, and little room for values. These concepts were extruded during the last few decades when questions about neural bases of behavior were firmly cast in stimulus-response terms, and that means in terms of spinal-reflex physiology.

The persistent embarrassment caused by the frontal-lobe problem is that it refuses to stay in this mold. To understand frontal-lobe pathology and frontal-lobe function we have to turn the conventional reflex schema around. Instead of speaking of sensory inputs leading, sooner or later, to motor output, we must begin at the motor end, by considering the ways in which motor systems act, centrally, upon sensory systems. We have tried to indicate how this approach might provide a physiologic distinction between voluntary and involuntary action. Stated in these terms, much of Feuchtwanger's approach may yet be vindicated since there seems to be such a pervasive change in self-directed action after severe frontal damage.

Deliberate action involves anticipation of its own consequences. We propose that failure in this respect is a central feature of the frontal-lobe syndrome in animal and man. Deranged capacity for adjusting one's reactions to one's actions—owing to breakdown in normal mechanisms of corollary (motor-to-sensor) discharges—may be as much at the root of the animal's delayed response-deficit as it seems to lie at the

root of the varied and seemingly bizarre manifestations of frontal-lobe impairment in man. The paradox raised by Jacobsen's

discovery, thirty years ago, might yet disappear, leaving in its stead a new way of looking at sensorimotor functions.

S U M M A R Y

The consequences of removal of the frontal lobe in animals have been clearly stated, although their interpretation is almost impossible. Conversely, in man the interpretation of ablation or injury to the same region of the brain has been suggestively consistent even though the facts are still discussed.

Recent work on animals has confirmed specific losses on delayed-response and delayed-alternation tasks, but the nature of the delayed response deficiency is still uncertain.

On the other hand, no persistent interference with delayed-response performance was found in man after simple removals of anterior frontal cortex; disagreement still exists regarding positive after effects.

The author has tried to find slight but persistent changes in human behavior after frontal lesions in man and found a single underlying change in behavior.

Those tasks which appear to depend specifically from anterior frontal structure integrity in man are neither exclusively sensory nor exclusively motor but strictly sensorimotor.

The author tries to demonstrate how apparently dissimilar forms of alteration can be uniformly interpreted, and then lead to the understanding of the delayed-response and alternation deficiencies after frontal lesions in lower species.

He postulates a "corollary"-discharge

mechanism", which depends from frontal lobe and basal ganglia integrity for its correct functioning.

In recent years he had reached the interpretation of motor to sensory action, in which the frontal lobes and perhaps some anatomically related subcortical structures play an important role.

Accordingly, these frontal mechanisms are involved in the consequences of body movements on sensory systems warning the latter against the imminent change and allowing the balance of action against "intent".

In order to understand the pathology and the function of the frontal lobe, the conventional reflex pattern must be reversed, i.e. that the motor aspect must be considered firstly, establishing the way in which the motor systems act on the sensory ones.

A deliberate action implies anticipation of its own consequences. The author suggests that this failure is a central characteristic of the frontal lobe syndrome both in animals and in man.

The altered capacity to adjust reactions to actions in view of the disappearance of normal corollary-discharge mechanisms (motor-to-sensory) may be considered both as the cause of the delayed-response deficiency in animals as well as of the diverse and apparently strange signs of frontal lobe alteration in man.

R E S U M E N

En los animales las consecuencias de la extirpación del sector frontal sobre el comportamiento son bien definidas aunque casi imposibles de interpretar; sin embargo las observaciones en caso de daño

o ablación de la misma zona en el hombre son objeto de una interpretación suggestivamente uniforme, siendo muy controvertidos los hechos en sí.

Labores recientes han confirmado y am-

pliado en animales los hallazgos acerca de pérdidas específicas en lo que respecta a tareas con alternancia retardada y respuestas retardadas. Continúa siendo incierta la naturaleza de la deficiencia en la respuesta retardada.

Contrariamente a esto, las extirpaciones simples de la corteza frontal en el hombre no producen interferencias persistentes con la realización de la respuesta retardada; la literatura acerca de este punto es contradictoria en cuanto a la aparición de efectos secundarios positivos.

El autor ha intentado de encontrar tareas sensibles a modificaciones sutiles aunque persistentes en el comportamiento humano, posteriores a lesiones frontales. Pudo demostrarse que los síntomas reflejaban un cambio subyacente y único en el comportamiento.

Las tareas que parecen depender más específicamente de la integridad de las estructuras frontales anteriores en el hombre no son ni puramente sensitivas ni puramente motoras, sino estrictamente sensorio-motoras.

El autor intenta demostrar como formas de alteración aparentemente muy distintas pueden ser objeto de una interpretación uniforme, y como a su vez puede llevar a la comprensión de las deficiencias en la respuesta retardada y defectos en la alternancia posteriores a lesiones frontales en las especies inferiores.

Específicamente el autor postula un "mecanismo de descarga corolario" que para su buen funcionamiento depende de la in-

tegridad de los lóbulos frontales y los ganglios basales.

La interpretación en términos funcionales a la que llegó el autor en los últimos años implica el concepto de una acción motriz a sensorial en la que los lóbulos frontales y quizá algunas de las estructuras anatómicamente relacionadas desempeñan un papel importante.

De acuerdo a estas nociones, estos mecanismos frontales están involucrados en señalar las consecuencias de los movimientos del cuerpo sobre los sistemas sensitivos, preparando a estos últimos para el cambio a sobrevenir y permitiendo así la equiparación de la acción inminente contra el intento.

Para comprender la patología y la función del lóbulo frontal debemos invertir el esquema reflejo convencional, es decir que debemos considerar en que forma actúan los sistemas motores centralmente sobre los sensitivos.

La acción deliberada implica la anticipación de sus propias consecuencias.

El autor sugiere que la falla en este sentido es una característica central tanto en animales como en el hombre.

La alterada capacidad para ajustar las reacciones a las acciones debido a la desaparición de los mecanismos normales de descargas corolario (motriz a sensorial) puede considerarse como la raíz de la deficiencia de la respuesta retardada en el animal así como también de las diversas y aparentemente extrañas manifestaciones de la alteración del lóbulo frontal en el hombre.

R É S U M É

Dans les animaux les conséquences de l'extirpation du secteur frontal sur le comportement sont bien définies mais presque impossibles d'interpréter; cependant les observations faites chez l'homme en cas d'ablation ou atteinte de la même région admettent une interprétation suggestivement uniforme, les faits étant très controversés.

Des travaux récents ont confirmé des pertes spécifiques dans les animaux dans les tâches à alternance retardée et à réponse retardée, mais dans la réponse retardée la nature de la déficience continue à être incertaine.

Contrairement à ceci, les extirpations simples de l'écorce frontale antérieure chez

l'homme ne provoquent pas d'interférences persistentes dans la réalisation de la réponse retardée; on n'est pas d'accord sur l'apparition d'effets secondaires.

L'auteur a essayé de trouver des changements subtils bien que persistents dans le comportement humain après des lésions frontales chez l'homme et trouva un changement sous-jacent unique.

Les tâches qui dépendent spécifiquement de l'intégrité des structures frontales antérieures chez l'homme ne sont ni exclusivement sensorielles ni exclusivement motrices, mais strictement sensorimotrices.

L'auteur essaye de démontrer comment des formes d'altération apparemment très différentes peuvent admettre une interprétation uniforme, qui à son tour conduit à la compréhension de la nature des déficiences dans l'alternance et la réponse retardées après les lésions frontales dans les espèces inférieures.

Spécifiquement l'auteur postule un "mécanisme de décharge corollaire" qui pour son bon fonctionnement dépend de l'intégrité des lobes frontaux et des ganglions basaux.

Recentement l'auteur était arrivé à une interprétation impliquant le concept d'une action motrice-à-sensorielle dans laquelle les lobes frontaux et probablement quelques structures souscorticales anatomiquement liés à eux jouent un rôle spécial.

D'accord avec ces notions, ces mécanismes frontaux sont impliqués dans le signalement des conséquences des mouvements du corps sur les systèmes sensoriels; ils préparent ces derniers pour le changement à survenir en permettant ainsi l'équiparation de l'action imminente contre "l'intention".

Pour comprendre la pathologie et la fonction du lobe frontal nous devons inverser le schéma réflexe conventionnel. Au lieu de considérer des influx sensoriels conduisant à des effets moteurs, nous devons commencer par l'aspect moteur en établissant les formes dans lesquelles les systèmes moteurs agissent centralement sur les systèmes sensoriels.

L'action délibérée implique l'anticipation de ses propres conséquences.

L'auteur suggère que l'échec dans ce sens est une caractéristique centrale du syndrome du lobe frontal chez l'animal et chez l'homme.

La capacité altérée pour ajuster les réactions aux actions, due à la disparition des mécanismes normaux de décharge corollaire (motrice-à-sensorielle), peut être considérée comme la cause de la déficience de la réponse retardée chez l'animal ainsi que des différentes et apparemment étranges manifestations de l'altération du lobe frontal chez l'homme.

ZUSAMMENFASSUNG

Beim Tiere sind die Folgen im Verhalten nach frontalen Ablationen klar und dennoch fast unmöglich zu erklären, während die Beobachtungen beim Menschen mit frontalen Verletzungen oder Ablationen eine einheitliche Erklärung zulassen, obwohl die Tatsachen selbst einer dauernden Widersprüchlichkeit ausgesetzt sind.

Für Tiere haben unsere Arbeiten die Entdeckung spezifischer Verluste bei Aufgaben der verzögerten Antwort und der verzögerten Alternative bestätigt. Man

kennt noch nicht die Natur des Defizits der verzögerten Reaktion.

Im Gegensatz dazu, produzieren einfache chirurgische Abtragungen der Hirnrinde in der vorderen frontalen Region gewöhnlich beim Menschen keine dauernde Interferenz mit der verzögerten Reaktion, und die Literatur über Läsionen des frontalen Lappens sind widersprüchlich bezüglich der positiven Nacheffekte.

Der Autor hat versucht Aufgaben zu entwickeln, die empfindlich gegenüber ziemlich feinen aber beständigen Verän-

derungen im Verhalten nach Vorderlappenverletzungen beim Menschen sind. Die Verhaltenssymptome, die durch diese Aufgaben entdeckt wurden, sind oberflächlich verschieden, aber es kann demonstriert werden, dass sie eine einzelne unterliegende Veraenderung im Verhalten reflektieren.

Die Aufgaben, die am spezifischsten von der Integrität der vorderen Vorhirnstrukturen beim Menschen abzuhaengen scheinen, sind weder rein sensoriell noch rein motorisch, sondern sensitivo-motorisch im strikten Sinne des Ausdrucks.

Der Autor versucht zu zeigen, wie anscheinend vollkommen uneinheitliche Formen der Defekte einer einheitlichen Erklarung zugaenglich gemacht werden koennten und wie diese Erklarung die Natur der verzoeagerten Reaktion und des alternativen Defizits nach frontalen Laesionen bei unteren Spezies aufklaert.

Der Autor postuliert spezifisch den "parallelen Entladungsmechanismus", welcher, um richtig zu funktionieren von der Integrität der Frontallappen und der Basalganglia abhaengt.

Die Erklarung durch funktionellen Begriffe, zu der der Autor in den letzten Jahren gekommen ist, entspricht dem Begriff einer motorisch-zu-sensitiven Aktion, bei welcher die Frontallappen, und moeglicherweise einige subkortikale Strukturen, die mit ihnen in anatomischer Bezieh-

ung stehen, eine besondere Rolle spielen.

Gemaess diesen Kenntnissen, spielen diese Vorderhirnmechanismen eine Rolle beim Anzeigen der inhaerenten Folgen der Bewegungen des Koerpers an die sensoriellen Systeme, wobei letztere fuer die entstehende Veraenderung vorbereitet werden und dadurch einen Vergleich zwischen dem Resultat der inhaerenten Aktionen und der "Absicht" aufzustellen erlauben.

Um Stirnlappen-Pathologie und —Funktion zu verstehen, muss man das conventionelle Reflexschema vollkommen auf den Kopf stellen, und am motorischen Ende anfangen, indem wir die Art, in der die motorischen Systeme zentral auf die sensoriellen Systeme wirken, in Betracht ziehen.

Bewusstes Handeln schliesst in sich die Voraussage ihrer eigenen Folgen ein. Der Autor ist der Meinung, dass ein Fehlschlagen in diesem Falle ein zentraler Zug des Stirnlappensyndroms bei Tieren und Menschen ist.

Die zerfahrene Faehigkeit, die Reaktionen an seine Handlungen anzupassen, indem die normalen Mechanismen der beigeordneten (motorisch-nach-sensoriell) Entladungen zusammengebrochen sind, mag am Ursprung des Defizits der verzoeagerten Reaktion sein sowie auch am Ursprung der verschiedenartigen und bizarren Manifestationen Stirnhirnlappenfunktionsverschlechterung beim Menschen.

REFERENCES

1. Battersby, W. S.; Teuber, H.-L. & Bender, M. B.: Problem-solving behavior in men with frontal or occipital brain injuries. *J. Psychol.*, 35, 229-351, 1953.
2. Battig, K.; Rosvold, H. E. & Mishkin, M.: Comparison of the effects of frontal and caudate lesions on delayed response and alternation in monkeys. *J. comp. physiol. Psychol.*, 53, 400-401, 1960.
3. Blum, R. A.: Effects of subtotal lesions of frontal granular cortex on delayed reaction in monkeys. *Arch. Neurol. Psychiat.* (Chicago), 67, 375-386, 1952.
4. Bossom, J.: The effect of brain lesions on prism adaptation in monkeys. *Psychon. Sci.*, 2, 45-46, 1965.
5. Brutkowski, S.: The solution of a difficult inhibitory task (alternation) by normal and prefrontal dogs. *Acta Biol. exp.* (Warsaw), 19, 301-312, 1959.
6. Brutkowski, S.: Fronto-limbic mechanisms in differentiation. *Proc. 18th Int. Congr. Psychol.* (Moscow), 10, 25-35, 1966.
7. Chorover, S. L. & Cole, M.: Delayed alternation performance in patients with cerebral lesions. *Neuropsychologia*, 4, 1-7, 1966.
8. Chorover, S. L. & Gross, C. G.: Caudate nucleus lesions: behavioral effects in the rat. *Science*, 141, 826-827, 1963.
9. Cianci, S. N.: Effects of cortical and

subcortical stimulation on delayed response in monkeys. *Exp. Neurol.*, 1965, 11, 104-114.

10. Cohen, L.: Perception of reversible figures after brain injury. *Arch. Neurol. Psychiat.* (Chicago), 81, 765-775, 1959.

11. Corkin, Suzanne: Tactually-guided maze learning in man: Effects of unilateral cortical excisions and bilateral hippocampal lesions. *Neuropsychologia*, 3, 339-351, 1965.

12. Dean, W. H. & Davis, G. D.: Behavior following caudate lesions in Rhesus monkey. *J. Neurophysiol.*, 22, 524-537, 1959.

13. Denny-Brown, D.: The frontal lobes and their functions. In: *Modern trends in neurology*, A. Feiling (editor). New York: Hoeber, 13-89, 1951.

14. Feuchtwanger, E.: Die Funktionen des Stirnhirns, ihre Pathologie und Psychologie. *Monogr. a.d. Ges. geb. d. Neurol. Psychiat.* O. Foerster, K. Williams (editors). Heft 38, Berlin: Springer Verlag, 4-194, 1923.

15. Fulton, J. F. & Jacobsen, C. F.: The functions of the frontal lobes, a comparative study in monkeys, chimpanzees, and man. *Abstr. 2nd Int. neurol. Congr.*, London, 70-71, 1935.

16. Ghent, Lila, Mishkin, M. & Teuber, H.-L.: Short-term memory after frontal-lobe injury in man. *J. comp. physiol. Psychol.*, 55, 705-709, 1962.

17. Goldstein, K.: Die Lokalisation in der Grosshirnrinde. In: *Handbuch der normalen und pathologischen Physiologie* (A. Bethe et al., editors), 10, 600-842, 1927.

18. Goldstein, K.: The significance of the frontal lobes for mental performances. *J. Neurol. Psychopathol.*, 17, 27-40, 1936.

19. Goldstein, K. & Scheerer, M.: Abstract & concrete behavior: an experimental study with special tests. *Psychol. Monogr.*, 53, no. 2 (Whole no. 239). Evanston, Ill.: Amer. Psychol. Assoc., 1941.

20. Grant, D. A. & Berg, Esta A.: A behavioral analysis of degrees of reinforcement and ease of shifting to new responses in a Weigl-type card-sorting problem. *J. exp. Psychol.*, 38, 404-411, 1948.

21. Gross, C. G.; Chorover, S. L. & Cohen, S. M.: Caudate, cortical, hippocampal and dorsal thalamic lesions in rats: Alternation and Hebb-Williams maze performance. *Neuropsychologia*, 5, 53-68, 1965.

22. Halstead, W. C.: Brain and intelligence. Chicago: Univ. Chicago Press, 1947.

23. Hebb, D. O.: Man's frontal lobes: a critical review. *Arch. Neurol. Psychiat.*, (Chicago), 54, 421-438, 1945.

24. Hécaen, H. & de Ajuriaguerra, J.:

Troubles mentaux au cours des tumeurs intracrâniennes. Paris: Masson et Cie., 1956.

25. Held, R.: Exposure-history as a factor in maintaining stability of perception and coordination. *J. nerv. ment. Dis.*, 32, 26-32, 1961.

26. Held, R. & Bossom, J.: Neonatal deprivation and adult rearrangement: Complementary techniques for analyzing plastic sensory-motor coordinations. *J. comp. physiol. Psychol.*, 54, 33-37, 1961.

27. Held, R. & Freedman, S. J.: Plasticity in human sensorimotor control. *Science*, 142, 445-462, 1963.

28. Held, R. & Hein, A.: Movement-produced stimulation in the development of visually guided behavior. *J. comp. physiol. Psychol.*, 56, 872-876, 1963.

29. Holst, E. v. & Mittelstaedt, H.: Das Reafferenzprinzip (Wechselwirkungen zwischen Zentralnervensystem und Peripherie). *Naturwiss.*, 37, 464-476, 1950.

30. Hunter, W. S.: A consideration of Lashley's theory of the equipotentiality of cerebral action. *J. gen. Psychol.*, 3, 455-468, 1930.

31. Jacobsen, C. F.: Functions of the frontal association areas in primates. *Arch. Neurol. Psychiat.*, (Chicago), 33, 558-569, 1935.

32. Jacobsen, C. F. & Nissen, H. W.: Studies of cerebral functions in primates. IV: The effects of frontal lobe lesions on the delayed alternation habit in monkeys. *J. comp. Psychol.*, 23, 101-111, 1937.

33. Kimura, Doreen: Dual functional asymmetry of the brain in visual perception. *Neuropsychologia*, 4, 275-295, 1966.

34. Klüver, H. & Bucy, P. C.: Preliminary analysis of functions of the temporal lobes in monkeys. *Arch. Neurol. Psychiat.*, (Chicago), 42, 979-1000, 1939.

35. Lashley, K. S.: *Brain mechanisms and intelligence*. Chicago: Univ. Chicago Press, 1929.

36. Lawicka, Waclawa & Konorski, J.: The physiological mechanism of delayed reactions. III. The effects of prefrontal ablations on delayed reactions in dogs. *Acta Biol. exp.* (Warsaw), 19, 221-231, 1959.

37. Lawicka, Waclawa & Konorski, J.: The effects of prefrontal lobectomies on the delayed responses in cats. *Acta Biol. exp.* (Warsaw), 21, 141-156.

38. Luria, A. R.: *Higher cortical functions in man*. New York: Basic Books, 1966.

39. Malmö, R. B.: Interference factors in delayed response in monkeys after removal

- of frontal lobes. *J. Neurophysiol.*, 5, 295-308, 1942.
40. Milner, Brenda: Some effects of frontal lobectomy in man. Chapter 15, pp. 313-334, in Warren, J. M. Akert, K. (editor), *The frontal granular cortex and behavior*. New York: McGraw-Hill, 1964.
41. Milner, Brenda: Visually-guided maze learning in man: Effects of bilateral hippocampal, bilateral frontal, and unilateral cerebral lesions. *Neuropsychologia*, 3, 317-338, 1965.
42. Milner, Brenda: Effects of frontal lobectomy in man. *Pro. 18th Internat. Congr. Psychol.*, Moscow, Symposium Vol. 10, 219, 1966.
43. Mishkin, M. & Pribram, K. H.: Analysis of the effects of frontal lesions in monkeys: I. Variations of delayed alternation. *J. comp. physiol. psychol.*, 48, 492-495, 1955.
44. Minshkin, M. & Pribram, K. H.: Analysis of effects of frontal lesions in the monkey: II. Variations of delayed response. *J. comp. physiol. Psychol.*, 42, 36-40, 1956.
45. Mishkin, M.; Vest, Beverly; Wexler, M. and Rosvold, H. E.: A re-examination of the effects of frontal lesions on object alternations. *Proc. 18th Internat. Congr. Psychol.*, Moscow, Symposium Vol. 10, pp. 43-49, 1966.
46. Nauta, W. J. H.: Some efferent connections of the prefrontal cortex in the monkey. Chapter 19 (pp. 397-409) in: Warren, J. M. & Akert, K. (editors): *The frontal granular cortex and behavior*. New York: McGraw-Hill, 1964.
47. Orbach, J.; Milner, Brenda & Rasmussen, T.: Learning and retention in monkeys after amygdalo-hippocampal resection. *AMA Arch. Neurol.*, 3, 230-251, 1960.
48. Pribram, K. H.: A further experimental analysis of the behavioral deficit that follows injury to the primate frontal cortex. *Exp. Neurol.*, 3, 432-466, 1961.
49. Pribram, K. H.; Chow, K. L. & Semmes, Josephine: Limit and organization of the cortical projection from the medial thalamic nucleus in monkey. *J. comp. Neurol.*, 98, 433-448, 1953.
50. Pribram, K. H.; Wilson, W. A. & Connors, J.: Effects of lesions of the medial forebrain on alternation behavior of rhesus monkeys. *Exp. Neurol.*, 6, 36-47, 1962.
51. Rabinovich, N. S. & Rosvold, H. E.: A closed field intelligence test for rats. *Sanad. J. Psychol.*, 5, 122-128, 1951.
52. Rosvold, H. E. & Delgado, J. M. R.: The effect on delayed-alternation test performance of stimulating or destroying electrically structures within the frontal lobes of the monkey's brain. *J. comp. physiol. psychol.*, 49, 365-372, 1956.
53. Schulman, S.: Impaired delayed response from thalamic lesions. *Studies in monkeys. AMA Arch. Neurol.*, 11, 477-499, 1964.
54. Semmes, Josephine; Weinstein, S.; Ghent, Lila & Teuber, H. L.: Correlates of impaired orientation in personal and extra-personal space. *Brain*, 86, 747-772, 1963.
55. Sperry, R. W.: Neural basis of the spontaneous optokinetic response produced by visual inversion. *J. comp. physiol. Psychol.*, 43, 482-489, 1950.
56. Stamm, J. S.: Electrical stimulation of frontal cortex in monkeys during learning of an alternation task. *J. Neurophysiol.*, 24, 414-426, 1961.
57. Teuber, H.-L.: Physiological psychology. *Ann. Rev. Psychol.*, 6, 267-296, 1955.
58. Teuber, H.-L.: Some alterations in behavior after cerebral lesions in man. In: A. D. Bass (editor): *Evolution of nervous control from primitive organisms to man*. Washington, D. C. Amer. Assoc. Adv. Science., 157-194, 1959.
59. Teuber, H.-L.: Perception: Chapter LXV in J. Field, H. W. Magoun, & V. E. Hall (editors), *Handbook of Physiology, Sect. I., Neurophysiology*, Vol. 3, Washington, D. C.: Amer. Physiol. Soc., 1960.
60. Teuber, H.-L.: Sensory deprivation, sensory suppression and agnosia: notes for a neurologic theory. *J. nerv. ment. Dis.*, 132, 32-40, 1961, a.
61. Teuber, H.-L.: Brain and behavior (summation). *Int. Conf. on Brain and Behavior*. Mary A. B. Brazier (editor). Washington D. C.: Amer. Inst. biol. Sci., pp. 393-420, 1961, b.
62. Teuber, H.-L.: The riddle of frontal-lobe function in man. Chapter 20 (pp. 410-444) in Warren, J. M. & Akert, G., (editors): *The frontal granular cortex and behavior*. New York: McGraw-Hill, 1964.
63. Teuber, H.-L.; Battersby, W. S. & Bender, M. B.: Changes in visual searching performance following cerebral lesions. *Amer. J. Physiol.*, 159, 592, 1949.
64. Teuber, H.-L.; Battersby, W. S. & Bender, M. B.: *Visual field defects after penetrating missile wounds of the brain*. Commonwealth Fund. Cambridge, Mass.: Harvard Univ. Press, 1960.
65. Teuber, H.-L. & Mishkin, M.: Judgment of visual and postural vertical after brain injury. *J. Psychol.*, 38, 161-175, 1954.
66. Teuber, H.-L. & Proctor, Florry: Some effects of basal ganglia lesions in sub-

human primates and man. *Neuropsychologia*, 2, 85-93, 1964.

67. Teuber, H.-L. & Weinstein, S.: Performance on a formboard task after penetrating brain injury. *J. Psychol.*, 38, 177-190, 1954.

68. Teuber, H.-L. & Weinstein, S.: Ability to discover hidden figures after cerebral lesions. *Arch. Neurol. Psychiat.* (Chicago), 76, 369-379, 1956.

69. Teuber, H.-L. & Weinstein, S.: Equipotentiality versus cortical localization. *Science*, 127, 241-242, 1958.

70. Twitchell, T. E.: The automatic grasping responses of infants. *Neuropsychologia*, 3, 242-259, 1965.

71. Vygotski, L. S.: *Thought and language*. Cambridge, Mass.: MIT Press, 1961 (English transl.).

72. Walker, A. E.: *The primate thalamus*. Chicago: Univ. Chicago Press, 1938.

73. Walker, A. E.: A cytoarchitectural study of the prefrontal areas of the macaque monkey. *J. comp. Neurol.*, 73, 59-86, 1940 a.

74. Walker, A. E.: The medial thalamic nucleus. A comparative anatomical, phy-

siological and clinical study. *J. comp. Neurol.*, 73, 87-115, 1940 b.

75. Warren, J. M.: The behavior of carnivores and primates with lesions in the prefrontal cortex. Chapter 9 (pp. 168-191) in: Warren, J. M. & Akert, K. (editors): *The frontal granular cortex and behavior*. New York: McGraw-Hill, 1964.

76. Warren, J. M. & Akert, K. (editors): *The frontal granular cortex and behavior*. New York: McGraw-Hill, 1964.

77. Weigl, E.: On the psychology of so-called processes of abstraction. *J. abnorm. soc. Psychol.*, 36, 3-33, 1941 (transl. by Margaret J. Rioch from the original: "Zur Psychologie sogenannter Abstraktionsprozesse". *Z. Psychol.*, 103, 2-45, 1927).

78. Weinstein, S. & Teuber, H.-L.: Effects of penetrating brain injury on intelligence test scores. *Science*, 125, 1036-1037, 1957.

79. Weiskrantz, L.; Mihailovic, L. & Gross, C. G.: Effects of stimulation of frontal cortex and hippocampus on behavior in the monkey. *Brain*, 85, 487-504, 1962.

80. Zeigarnik, B. V.: *Pathology of thinking*. Moscow: Moscow Univ. Press, 1961. (In Russian).

Extrapyramidal Motor Areas of Cat's Frontal Lobe: their Functional and Architectonic Differentiation

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During the mapping of the mammalian cerebral cortex by stimulation-technique the term extrapyramidal motor areas was created by C. and O. Vogt in 1907²⁸ for the first time. This was 4 years after the creation of cerebral architectonics and 4 years before the discovery of the extrapyramidal or striatal motor disturbances in 1911²⁹ by G. Vogt and Wilson. The functional meaning of the extrapyramidal motor areas however remained obscure although not a few investigation tried to elucidate it. But even their relation to the extrapyramidal motor disturbances could not be clarified. Only the description of adverse movements as stimulation effects and of an inhibitory area for facial and masticatory movements in the basal part of area 8³⁰ was an indication, what they have to do normally.

The second step was the interpretation of the turning, raising, sinking and rotation movements as extrapyramidal by W. R. Hess in 1940. It became clear that these direction specific movements which are equivalent to the conjugated eye movements in higher forms do not depend from an intact pyramidal tract.

The stimulated substrata seemed to be restricted to mesencephalic and diencephalic structures. But some of the best rotating and turning movements were elicited from

special thalamic nuclei which are known to be cortex-dependent. Even after the subcortical neuronal systems had been defined which are responsible for each of the direction specific movements, the problem remained whether these subcortical apparatus have cortical connexions and relays.

The supposition of cortical relays of each of these subcortical neuronal systems induced me to investigate the cortical projection fields of the thalamic nuclei with the same stimulation technique, which was created by Hess and used in subcortical ganglia. Only the stimulation frequencies regularly used were extended to 30/sec. In a first communication (1960) the precentral extrapyramidal areas proved to react on stimulation by direction specific movements.

For the cytoarchitectonic areas of the cat's cerebral cortex, which were not described by Brodmann in his classical book, one was left to Gurewitsch and Chatschaturian⁹. But their map differed too much from the maps for the monkey and man. Thus we preferred to reinvestigate the cortical architectonic fields in the frontal third of cat's brain.

This map, as far as it belongs to the treated problems, was constructed for 15 individual hemispheres in collaboration with K. Muhs - Clement.

Material and methods

The frontal cortex of the cat was reinvestigated by combined cyto— and myeloarchitectonic methods in serial sections of all directions. Sharp borderlines between the areas and subareas were tried to draw.

The frontal quarter of the cat's cerebral cortex was stimulated, through very small bore holes in the unopened skull, by three 0,25 mm. thick electrodes (tip exposure for 1 mm.) in a distance of 1,5 mm. Used were the frequencies of 4, 8, 30 at low vol-

tages and low current strength not exceeding 0,5 mA. The cats were unrestrained unanesthetized and without premedication. The stimulation effects were recorded in film strips, which could be reproduced many times for study.

Results

In the frontal cerebral cortex of the cat most of the cortical areas defined by Brodmann and Vogt in man and cercopithecus

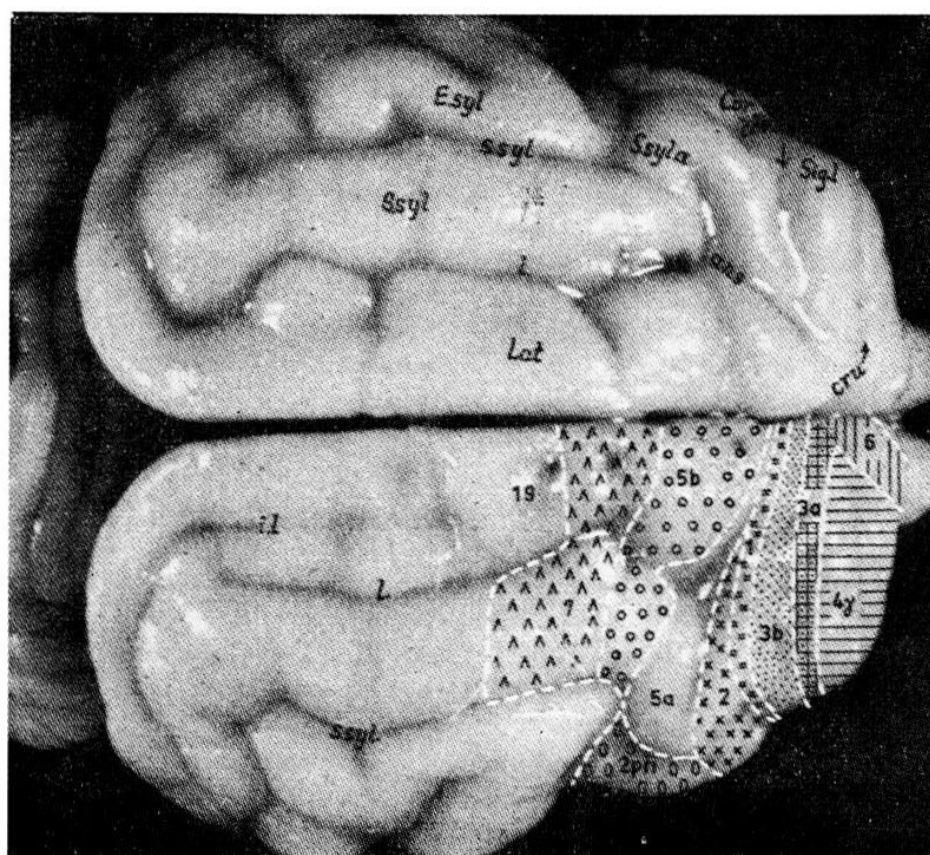


Fig. 1. — Cytarchitectonic map of the frontal pole of cat's brain. According the BRODMANN-VOGT nomenclature. In the left hemisphere the sulci are labelled. Notice the long and deep postcruciate dimple. (Arrow). The anterior border of postcruciate dimple coincides with the border between motor (4 γ) and somatosensory cortex (3 a).

can be found, if all the characteristics of combined cyto— and myeloarchitecture are considered. (Fig. 1).

The cruciate sulcus of the cat which is 10-12 mm. deep contains an agranular cortex of great extent in its upper and lower

lip. The lower lip is occupied by three kinds of high cortical fields, which are equivalent with the area 6 a of the human and primate cortex. The fundus and the upper lip of the cruciate sulcus are occupied by four subfields of area 4 (fig. 2).

Because of their relevance for the extrapyramidal motor systems the subfields of area 4 and 6 α are delineated and described here more in detail on two sagittal sections. Fig. 2 shows the myeloarchitectonic areas on a sagittal section of the cruciate sulcus, which is 11 mm. deep. In the dorsal lip the height of cortex is 1,3 mm. at most in the ventral lip its range is 1,8 to 2,3 mm. although both lips are cut orthograde. The high areas belong to area 6 α , the shallow ones on the dorsal lip to area 4. Both are devoid from a real inner granular layer

(IV). In the area 4 region the darkness decreases in direction to the fundus of the sulcus. Even in area 4 γ two strips of Baillarger can be distinguished, an outer and an inner, in contrast to astriate area 4 γ of the human. The rather sudden decrease in darkness and the disappearance of the strips of Baillarger marks the border line to the area 4 δ . The shallowest subfield the area 4 supra fundum (4 s. fu), is a little higher but less rich in fibres, especially in the layers V and VI. The fundus of the cruciate sulcus is also occupied by a sub-

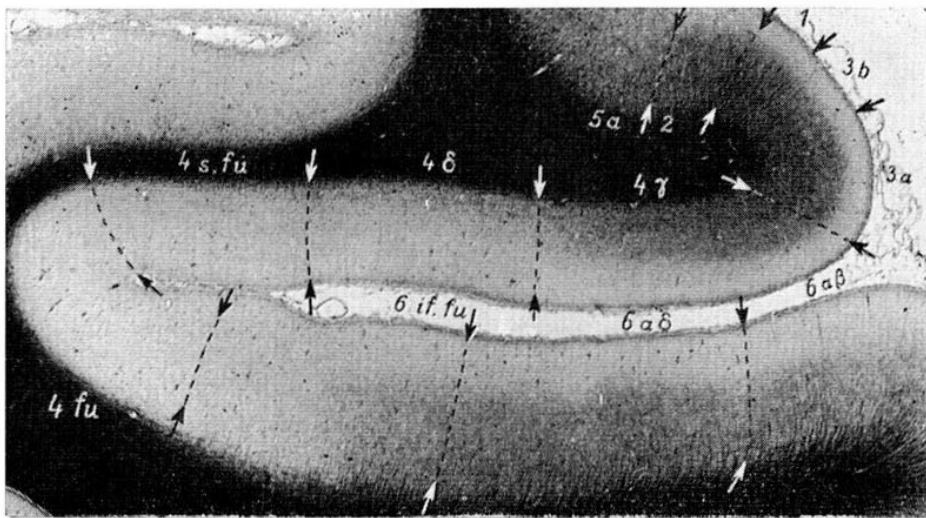


Fig. 2. — The myeloarchitectonic picture of the sensori motor cortex on a sagittal section in fibre staining. The subfields of area 6 are higher than the corresponding subfields of area 4 in the upper wall. In the left upper corner the splenial sulcus appears.

field of area 4, the area 4 in fundo (4 fu). It has the palest myeloarchitectonic structure among all four fields.

Where the area 4 fu increases in height suddenly, the area 6 α begins with the subfield area 6 if.fu (=infra fundum) (below the bottom of the furrow). This most occipital subfield becomes darker in the direction of the surface, so that near the frontal border the outer strip of Baillarger is distinct. In front of the border line the darkest myeloarchitectonic subfield of area 6 α is installed. Mainly within and below the outer strip of Baillarger the single fibres are very dense and the outer strip broad and conspicuous. This outer strip fades in the

superficial subfield 6 α β , although the number of radii is much increased. Compared with the postcentral fields area 3 α , 3 β , 1 and 2 the fiber structure of area 6 α δ is very pale.

The immediately next section in this sagittal series is stained for nerve cells: Fig. 3. The difference in height between area 6 α and area 4 is conspicuous. The subfields of area 6 α surpass the subfields of area 4 mainly in the height of the layers III, VI and the deeper part of V. From the surface to the bottom of the cruciate sulcus the size and the density of the large pyramids (layer V) decrease considerably, just as the cell density in the layer III and

II in three steps. In the area 4 s. fu and 6 if. fu the cortical layers are not well articulated but merge into one another (illaminatae). The V layer is subdivided and clearly separated from the III, which is provided merely with small pyramids in the area 6 a δ . This designation is to prefer to 6 a α proposed by Muhs and myself two years ago because the homology to the area 6 a α in the human is not proven at all but rather improbable. The distinction from area 6 a β is possible on account of the larger and much more densely packed pyramids in the V. layer and the more co-

lumnar arrangement of nerve cells to the surface.

In Area 4 the most distinct layer formation is found in area 4 γ and next in area 4 fu, although this is a very shallow structure in the fundus. The cytoarchitectonic differences between the 3 deep subfields of area 4 in the cruciate sulcus are less clear and less important than in area 6 a.

Most parts of area 4 are hidden in the cruciate sulcus. On the surface of the posterior sigmoid gyrus only a narrow zone is real motor cortex. It borders sometimes the postcruciate dimple which is the borderline

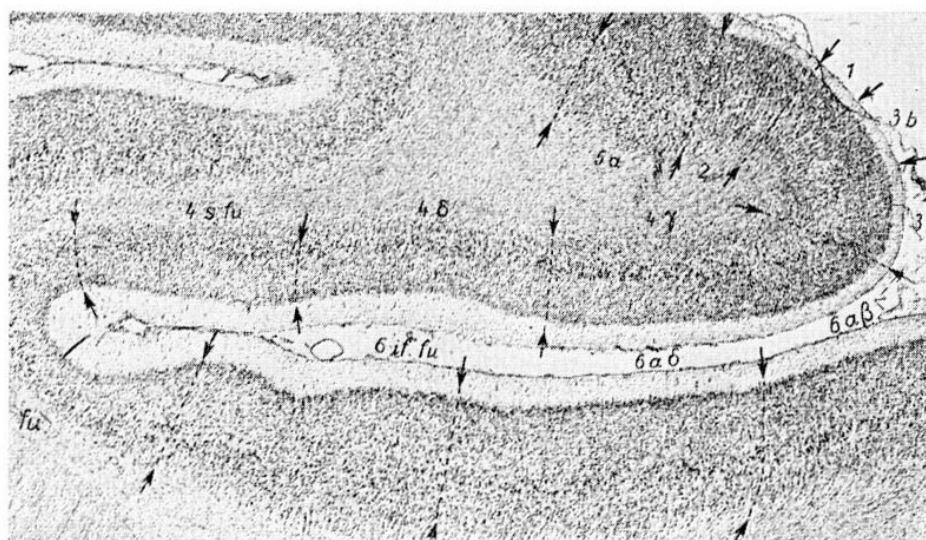


Fig. 3. — The cytoarchitectonic agranular subfields of the cruciate sulcus on a sagittal section through the cat's brain. Above the cruciate sulcus lie the cytoarchitectonic fields of posterior sigmoid gyrus (3a, 3b, 1 + 2).

between the agranular motor and the granular somatosensory cortex although the most rostral granular area 3 a has only a narrow and light granular layer. The postcruciate or central dimple (Fig. 1) seems to be the homologon of the central sulcus of the primates as first stated by Campbell in 1905. From all the subfields of area 6 merely the area 6 a β lies on the surface. The cortical fields in the praesylvian sulcus and on the gyrus proreus are not subdivided by the same cytoarchitectonic methods so far.

This congruous pattern of the sensorimotor cortical fields in carnivores and primates is very important. There is no consid-

erable difference although the carnivores are not direct ancestors of the primates. The constant pattern does not prove the derivation of primates but can be taken for a homology basing on the same structural arrangement and the same relative position in all mammals investigated so far.

Thereby it may be assumed that the sensorimotor cortex has the same organization probably in all mammals even in the original insectivores. The homology is however problematic in respect to the subfields of area 4 and area 6 a. Because the structural differences of these subfields seen in the cat are so indistinct and perhaps species-specific, that physiological characteristics

will be needed for their homologization in other genera and families.

For most of the motor or premotor cortical fields it can be taken as established that they receive subcortical projection fibers. Thus they are no more association — but projection — fields in the anatomical sense. Furthermore they are not extrapyra-

midal fields in the strict sense, because many of them give origin to direct cortico-spinal fibres. The term extrapyramidal motor fields should however be taken as a physiological rather than an anatomical concept because a great part also of the sensory and associative or integrative cortical fields have a certain number of direct cor-

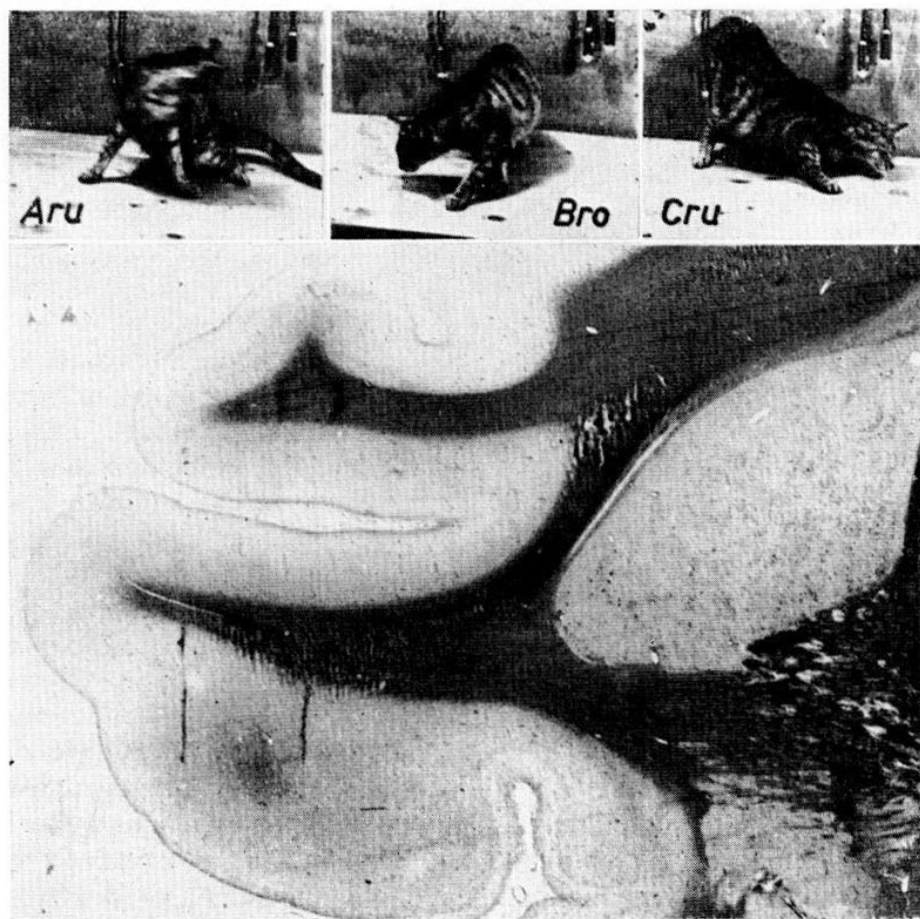


Fig. 4. — Stimulation effects from the frontal pole of the cat's cortex. During the stimulation of Aru (the left vertical electrode trace in the presylvian gyrus) a fast contraversive turning of head and trunk guided by the eye occurs. The stimulation of Bro (electrode point in the white matter of gyrus sigmoideus anterior 2 mm above Aru) elicited an ipsiversive slow turning guided by the right ear. The stimulation of Cru 3 mm caudal from Aru in presylvian gyrus produced a lowering of head and forebody and a discrete contraversive turning.

tico-spinal efferents. In spite of it their functional activity remains intact for the most part after chronic interruption of the pyramidal tract. Therefore the term extrapyramidal should not be rejected for these precentral motor fields too.

Differentiation of frontal cortical fields by stimulation technique

Different methods of stimulation were used for investigations of subcortical structures since more than 100 years. 60 years

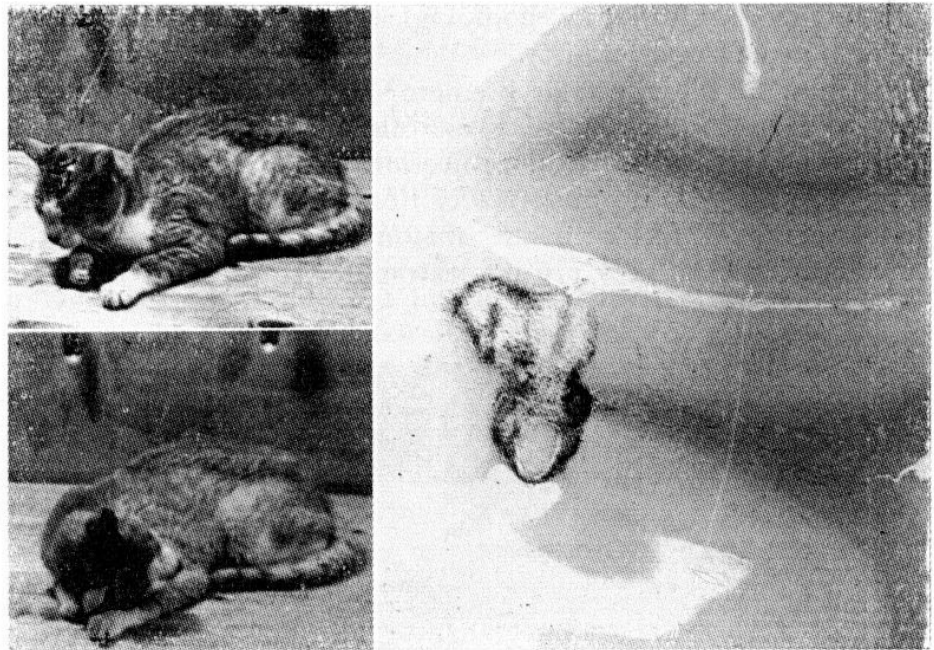


Fig. 5 a. — The stimulation of deeper part of presylvian sulcus (Cru) elicits a rotation of the head of 90°.

ago the technique of preparing fine electrodes with small active surfaces and the kind of stimulatory currents has been improved. But the stimulation method has become more perfect as W. R. Hess created

the method of stimulations in unanesthetized and freely moving unrestrained cat by low frequency impulses. This method first published 40 years ago has begun to be propagated in the Western hemisphere not earlier than 10 years ago called a new trend.

W. R. Hess¹⁷ differentiated the direction specific movements 25 years ago. Basing on his collection of kinematographic records and brain serial sections, the neuronal substrata of each single direction specific movement could be defined. The rotatory movements around the longitudinal axis of the body are represented in the interstitial nucleus of Cajal and its fiber connections, ascending to some thalamic nuclei and descending in the posterior longitudinal fascicle¹⁵. This was partly foreseen by Muskens²⁵. Raising movements are elicited by stimulation of the prestitial nucleus on the caudal border of the hypothalamus and its fiber connections in the hypothalamus and midbrain.

Lowering movements appear during stimulations not only of the posterior commissure but also of the precommissural nucleus (nucleus of the posterior commissure) and its descending connections in the posterior longitudinal fascicle. If the movements of the head and trunk were suppressed by fixation, conjugated eye move-

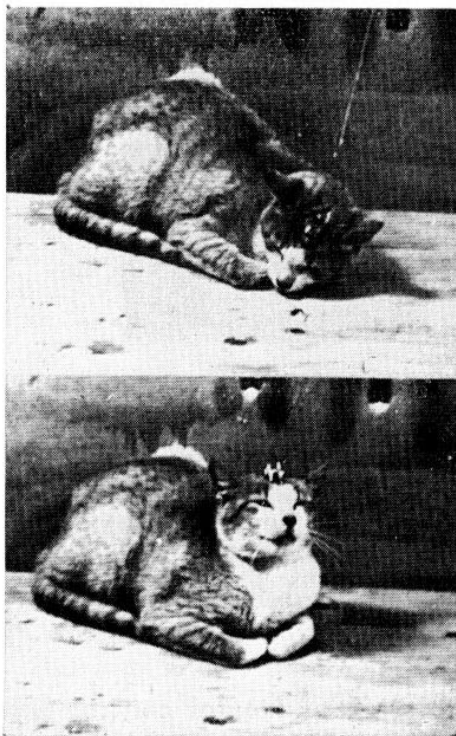


Fig. 5 b. — Stimulation effect of point *Alu* in the dorsal wall of suprasylvian sulcus produces a raising of the head with opening of the eyes and dilatation of the pupil.

ments in the same direction occur. These gaze movements were seen in monkey experiments by Hyde and Eliasson²⁰, after separation of the brain from the spinal cord in the *encéphale isolé* preparation. The single gaze directions were obtained from similar midbrain regions but they could not

be referred to neuronal systems for the lack of Marchi technique. In the last years some unpublished stimulation experiments in *Callithrix*-monkeys with a little modified Hess technique showed the same localization of the rotating, raising, lowering and turning movements.

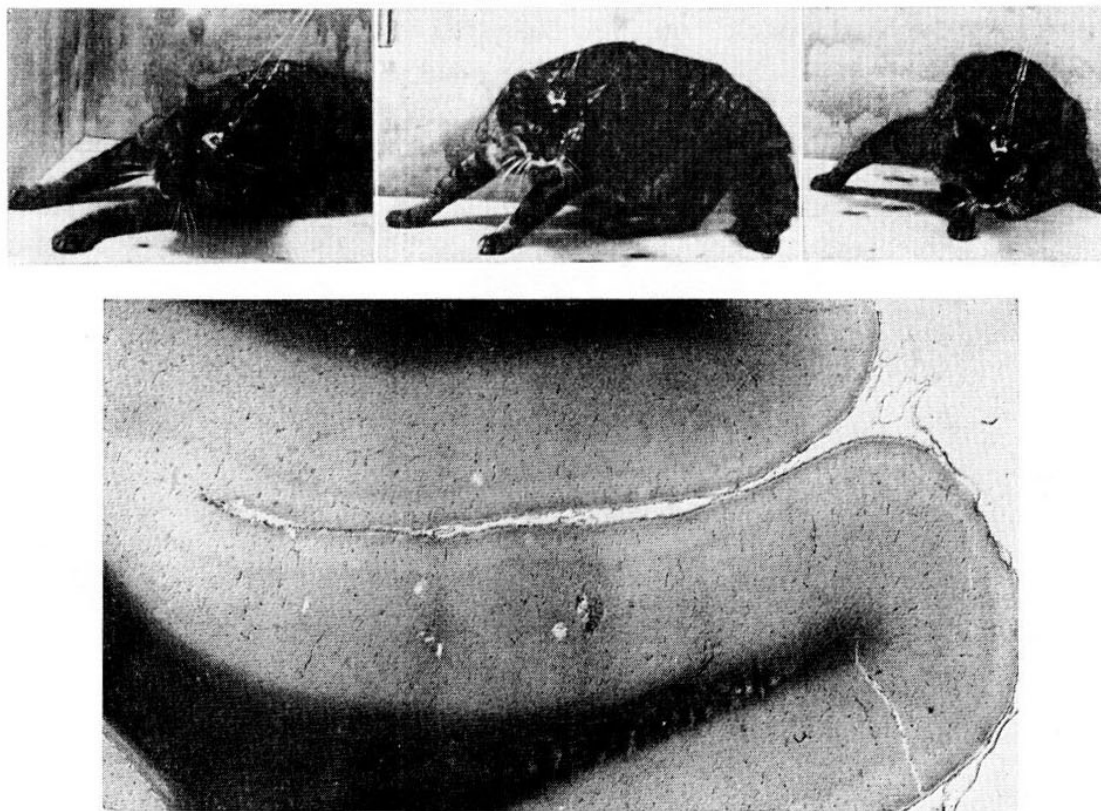


Fig. 6. — Stimulation effects from the area 6 a δ and borderline of 6 a δ and 6 if. fu (Clo). The stimulation of electrode Alo and Blo which are situated in area 6 a δ produces an ipsiversive turning of head and body in two different levels, Alo combined with lowering. The stimulation of area 6 if. fu (Clo) elicits a rotation of the head and trunk to the left side, combined with slight ipsiversive turning.

The turning movements (in the horizontal plane) or the horizontal eye deviations have a different neuronal localization, whether they go to the same or to the opposite side of stimulation. The ipsiversive turning is the typical stimulation effect of an ipsilateral vestibulo-reticulo-thalamic tract with the site of fibre recruiting in a restricted sector of midbrain's reticular formation. The thalamic termination lies in the internal part of an intermediate ventral nucleus.

The adversive movements are the contraversive turnings. The responsible neuronal systems are spread out through the fore-brain and diencephalon, so that the localization was possible only after new stimulation experiments. The substratum which was earlier supposed to be in the zona incerta, proved now to be in the pallidum and entopeduncular nucleus and their efferent pathways, also crossing among other structures the zona incerta (Montanelli and Hassler)²⁴.

The adversive movements have extensive cortical representations already known since Beevor and Horsley¹ and C. and O. Vogt²⁸ and best studied in the human by Foerster⁶. Each of the primary sensory fields is flanked by an area for adversive movements (Kleist)²³.

For most of these neuronal apparatus of direction specific or eye movements some extensions into the ventral nuclei of the thalamus have been demonstrated. These ventral nuclei project to the cerebral cortex. Therefore it was to expect that from the specific cortical projection fields the same stimulation effects could be obtained.

With the same technique of implanted electrodes in the freely moving cat all direction specific movements can be elicited, especially if 30 stimuli per second are also applied.

Fig. 4 shows one cat's experiment, in which each of three stimulation points separated only 1,5 mm. from one another provided another direction specific movement: The rostral electrode Aru led to an adversive movement of the whole body. Stimulated is the upper surface of the presylvian sulcus; 1,5 mm. more caudal and 2 mm. more dorsal (Bro) the stimulation produces a turning to the same side (ipsi-

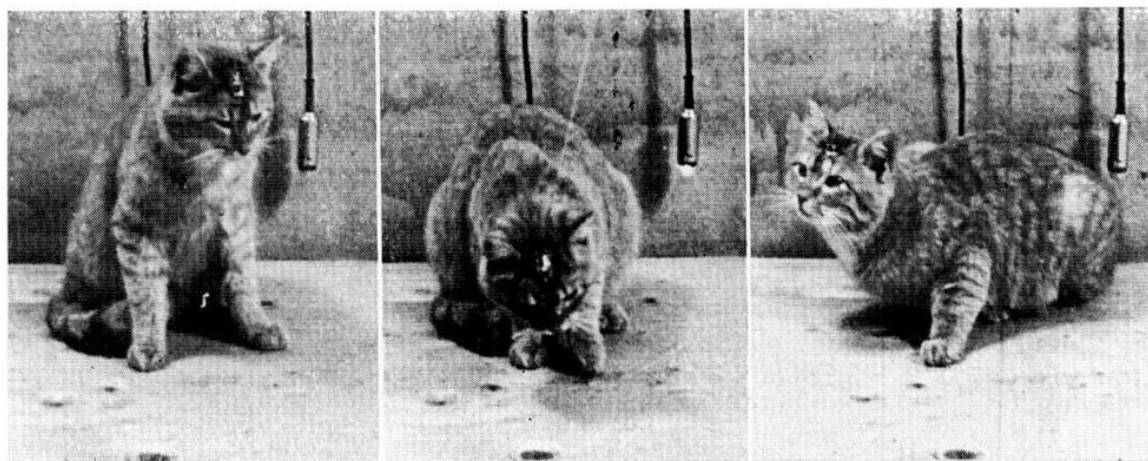


Fig. 7. — Lowering of the head and forebody during stimulation of the medial wall of presylvian gyrus.

versive). The stimulated area is the white matter below the cruciate sulcus more exactly below the area 6 a δ . 1,2 mm. more caudal again another stimulation effect is a marked lowering of the head and the neck with slight contralateral turning. Produced is this effect from the upper surface of the presylvian sulcus but 2,7 mm. more caudal than the contraversive turning.

If in another experiment a cortical region about 1 mm. more medial is stimulated 30 times the second, a clear rotating of the head appears. (Fig. 5 a).

2 mm. above in the area 6 a δ the stimulation effect was an ipsiversive turning again. In the other hemisphere a raising of the head occurred as stimulation effect

(Fig. 5 b) of the rostral most cortex of the anterior sigmoid gyrus, where it merges with the gyrus proreus.

Three stimulations, each 1,3 mm. behind the other in a sagittal plane (Fig. 6) in the area 6 a δ of the lower lip of cruciate sulcus elicited always a turning to the stimulated side. In the middle stimulation point turning was uncomplicated, in the rostral point combined with a slight lowering of the head and in the caudal point combined with a marked rotation. The latter point lies on the border line between area 6 a δ and 6 if. fu, the rostralmost point on the rostral border of area 6 a δ and in the white matter below it, which contains also the projection fibres of the anterior sigmoid gyrus. The com-

mon structure stimulated on all the three points is the area 6 a δ .

In a last example (fig. 7) the stimulation of the medial wall of the presylvian gyrus elicited a clear sinking movement. As after-image the cat raises the head and eyes. In the other hemisphere the stimula-

tion of a more lateral portion of the presylvian gyrus (Fig. 8) produced a contraversive turning of the head. If this was prevented by fixation of the head merely the eyes made a conjugate deviation to the contralateral side with pupil dilatation (Fig. 8). This demonstrates that the direc-

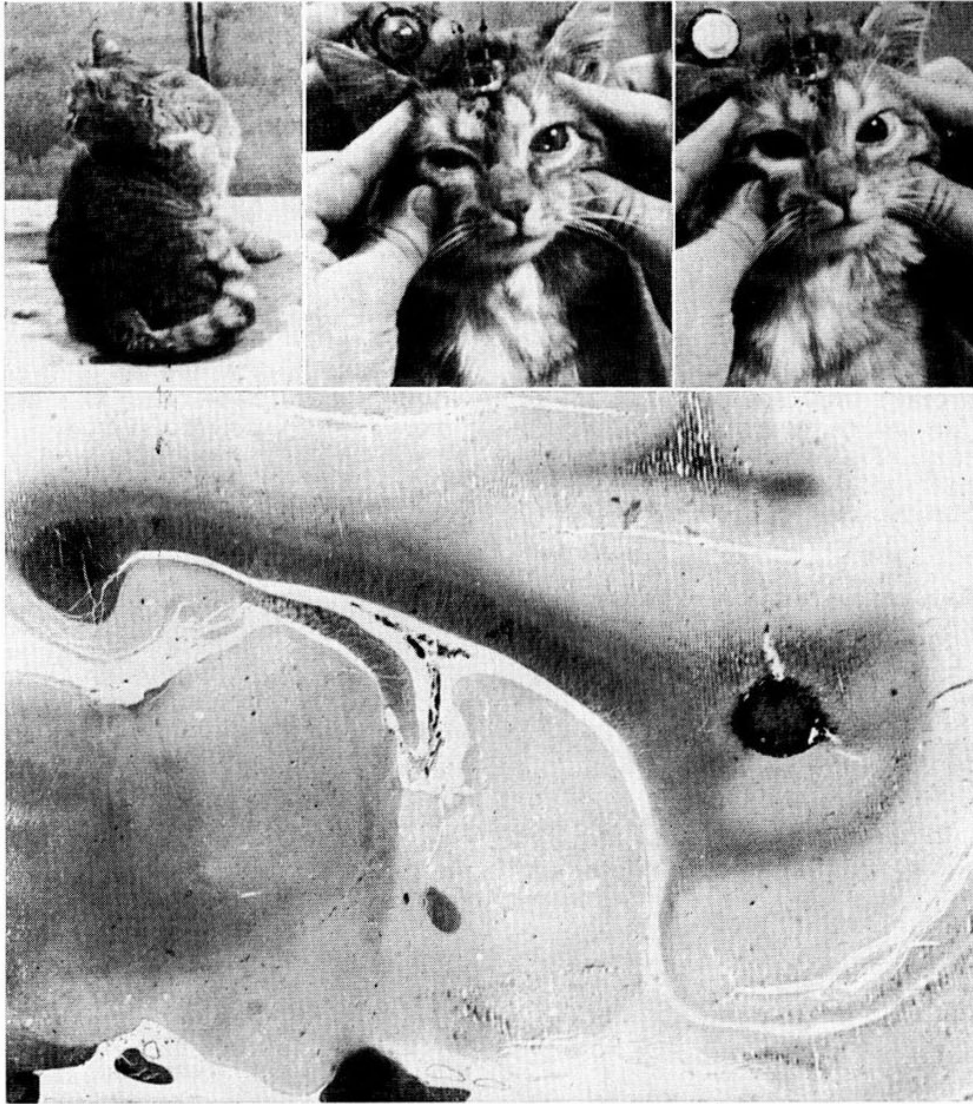


Fig. 8. — Stimulation effect of superior wall of presylvian sulcus, marked by a small coagulation sagittal section elicited a typical adversive movement of the head (a). — If the head is fixed before stimulation (w) the stimulation elicits merely a conjugated deviation of the eyes to contralateral side with considerable dilatation of the pupils.

tion specific movements of the head and trunk are produced by the same neuronal system as the gaze movements. Whether the eyes or the head deviate, depends only from the unrestrained or fixed situation of the head.

Survey of stimulation foci for direction specific movements

There is a clear difference between the stimulation effects elicited from the cortex within the cruciate sulcus and the cortex

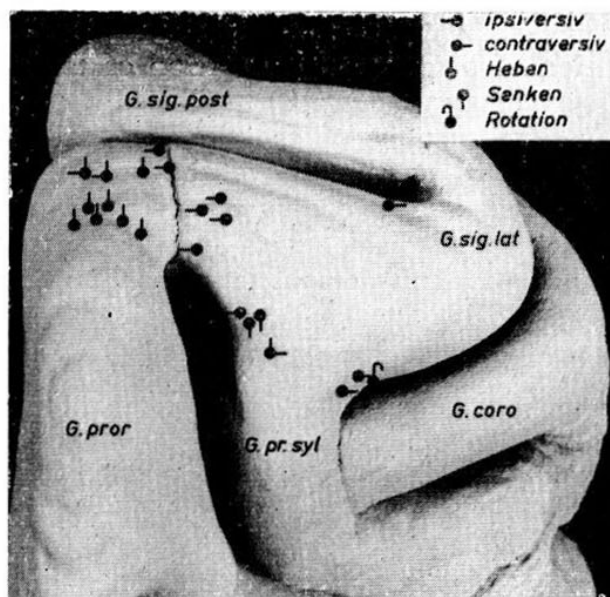


Fig. 9. — Reconstruction of the cat's frontal pole with stimulation effects of gyrus sigmoideus anterior, gyrus proreus and gyrus praesylvius. The more lateral the stimulation was applied, so more contraversive turning occurs. The raising effects are accumulated on the conjunction of gyrus proreus and gyrus sigmoideus anterior.

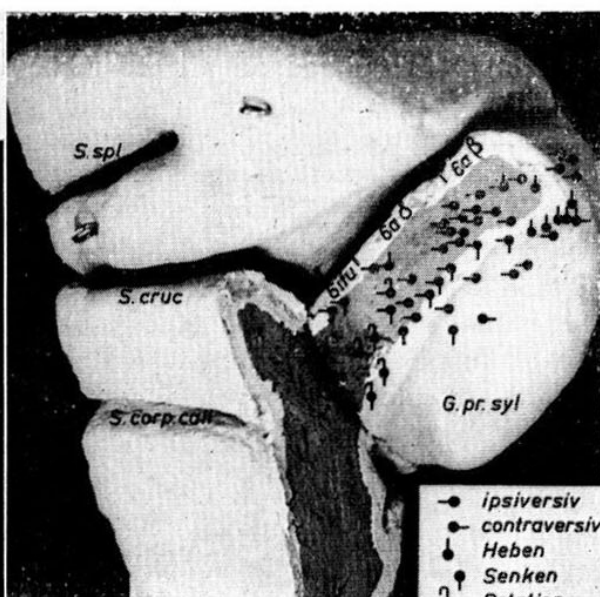


Fig. 10. — Stimulation effects of the medial wall of gyrus praesylvius demonstrated after removal of gyrus proreus. In the region of area 6 a δ nearly all stimulations produced ipsiversive turning. More caudal rotation appears.

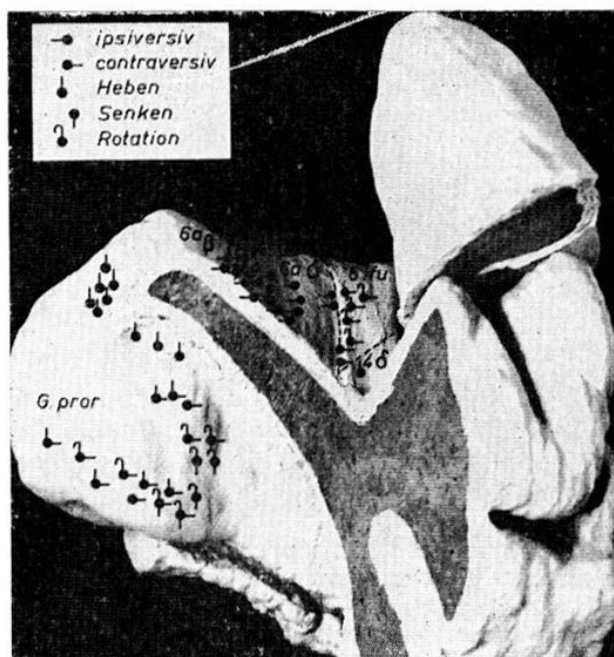


Fig. 11. — On the lateral wall of gyrus proreus the stimulation effects are marked. In the height raising effects and on the lower part rotation combined with contraversive turning. The gyrus praesylvius is removed.



Fig. 12. — Reconstruction of the frontal pole of the cat's cortex with removal of the dorsal wall of cruciate sulcus. Accumulation of ipsiversive turning in area 6 a δ and its borders. In area 6 a β and in front of anterior sigmoid gyrus accumulation of raising movements. In area 6 i fu rotation of the head frequently combined with contraversive turning occurs.

of the frontal pole (Fig. 9) especially from the border of the presylvian gyrus and sulcus. The medial wall of the presylvian sulcus is formed by the gyrus proreus, the lateral wall by the presylvian gyrus, which becomes superficial on its course to the base of the piriform lobe. The more lateral and the more caudal a stimulation point lies, the more its stimulation is followed by contraversive movements (Fig. 11). There is a clear cut localization. This region may correspond, after having been localized

exactly, to the lateral portion of area 8 in primates. (Fig. 10).

Surprisingly also in the depth of the cruciate sulcus, more exactly in area 6 if.fu, a contraversive turning (Fig. 12) occurs in 7 of 10 stimulations. Another accumulation of stimulation foci lies on lateral and rostral wall of gyrus proreus and its fusion with the anterior sigmoid gyrus. These are the raising movements which never appear from lateral foci. Whether this cortex is agranular or dys-

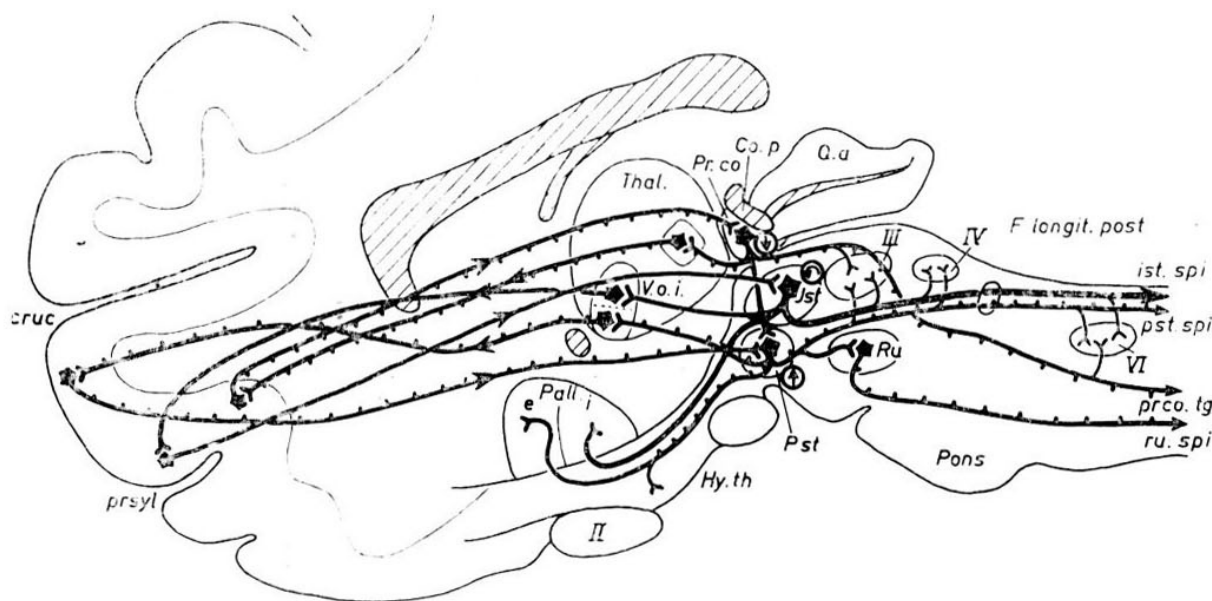


Fig. 13. — Schematic drawing of neuronal systems for direction specific movements on the sagittal plane. The connections of nucleus interstitialis (i st) nucleus prepositus (P. st) and of Nucleus praecommissuralis (P.r.co) with their thalamo cortical continuations are demonstrated. The cortical areas bring about their effects by returnline to the three midbrain nuclei which regulate the direction specific movements. The same systems regulate the conjugated eye movements in higher mammals.

granular or belonging to the granular prefrontal cortex is still to be decided. The representation was surprisingly high up and borders the anterior part of sigmoid gyrus.

The localization of the lowering movement of the head seems to be clear: the lowering movements appear more frequent, when the stimulation electrode proceeds to the depth of the presylvian sulcus, mainly its upper end. But very seldom these movements are pure lowering, mostly

they are combined with rotatory or ipsiversive turning.

But the most interesting finding is the unequivocal concentration of stimulation foci for ipsiversive movements. These are concentrated in the area 6 a δ . All the twentyfour stimulation foci lie in this area or in the medullary core below 6 a δ (Fig. 10). No stimulation in this area 6 a δ happened without an ipsiversive turning of the head or even all the body.

A little more caudal in the cruciate sul-

cus on the border to the area 6 if.fu (or 6 a illaminata) the number of ipsiversive turning effects decreases and more and more rotating of the head (to the same side) appears (Fig. 12). But the correlation of the rotating to the area 6 if.fu is not so strong as this of ipsiversive turning to area 6 a δ . Rotating of the head was also registered during stimulations of the deepest part of gyrus proreus (Fig. 11).

Evaluating these 90 foci of circumscribed stimulation in the frontal pole of the cat a correlative conclusion can be drawn for the ipsiversive movement and area 6 a δ — to avoid errors of homologization this term is preferred to the misleading area 6 a α .

The other conclusion is the congruence between raising movements and the borderland between area 6 a β and the most dorsal part of gyrus proreus. There another subfield of area 6 a is installed not clearly differentiated so far.

Even for the other direction specific effects however localisatory differentiation is suggested, although we can not define the exact subfield within the agranular or dysgranular frontal cortex. But the trend of segregation of the specific stimulation foci is evident.

DISCUSSION

If the precentral extrapyramidal cortical fields are investigated by a special stimulation technique they reveal to be cortical representations of direction specific head and trunk movements and vicariously of gaze or conjugated eye movements.

The latter statement is not surprising; then it is known since 1884 by Ferrier, afterwards by Schäfer and Russell (1894) that the precentral motor cortex is bordered rostrally by an excitable cortex regulating eye movement. The same was to assume for the cat's cortex. But the clear separation for single direction of gaze movements in the cat's precentral extrapyramidal cortex was not suspected.

The reason why these observations had not been done before for the cat's motor

cortex is the simple fact of an improvement in stimulation methods, that the advice of W. R. Hess was followed: to work with the freely moving unanesthetized animal through implanted very fine electrodes and near threshold stimuli of low frequency. This methodologic refinement must be combined with a precise localization of the stimulated area defined by architectonic investigation.

In respect to the conjugated eye movements it is interesting that the gaze movements to the stimulated side has a separate localization in the cruciate sulcus. This sulcus does not correspond to the central sulcus in primates and man but is a significant enlargement of the motor cortex surface, because it is bordered only by subfields of area 4 (upper lip) and area 6 a (lower lip). Within the lower lip the stimulation must be restricted to the area 6 a δ or its fiber layer to elicit ipsiversive movements. In the cat too the ipsilateral side of the body is represented in a subfield of area 6 a as demonstrated by Bucy for the monkey thirty two years ago, even not pointed out for the gaze. My forecast of ipsiversive representation in area 3 a basing on the cortical projection of ventral thalamic nuclei is not confirmed.

Misleading was the scattered termination of the ipsilateral vestibulo-reticulo-thalamic pathway which simulated a termination in the external instead of the internal part of intermediate ventral nucleus (V. im. e instead of V. im. i). For the area 3 a Oscarsson and Rosen²⁶ detected in the meantime that it is the cortical projection of fast muscle afferents (I A) and its thalamic nucleus is the external part of intermediate ventral nucleus (V. im e).

If the head movements are not restrained but free the cat also performed head and body movements in response to stimulations of the extrapyramidal motor fields. This is perhaps a little more unexpected. So far only for the contraversive or adversive movements of the head and trunk a cortical localization was discussed and only by Foerster and after him by Roettgen also for ipsiversive turning. But all direction

specific head and trunk movements, even the rotation, raising and lowering have their cortical representations. They are called by W. R. Hess extrapyramidal and for differentiation from the clinical term extrapyramidal supravestibular. Each of the supravestibular systems has its circumscribed cortical representation. The greater part of extrapyramidal motor fields are fields of direction specific head and trunk movements. Thus the biological meaning of these extrapyramidal areas is now a little more understood.

From a functional point of view a great part of so called extrapyramidal motor areas are the thalamo-cortical continuations of the subcortical supravestibular systems (Fig. 13).

Functional differences between the thalamo-cortical and the supravestibular neuronal systems responsible for one direction of movement exist in so far as the subcortical systems are tonically active in the awake state which does not take place in the thalamo-cortical systems. The consequence of this tonic activity is the mirror like elimination effect after unilateral destruction of one direction specific system. From the cortical systems no enduring elimination effect occurs. The true regulation of all movements in one direction is performed in the subcortical share. Perhaps the cortical share has to adapt the automatic movement corrections to the voluntary or intended movements in one or the other direction. If one direction specific movement—for instance rotating to the left side—is part of a voluntary action, then no corrective movement appears, which is pre-

sent always, if the same movement sets in passively by outer forces.

The movements in the horizontal plane, the turning either to the same or to the opposite side, have cortical representations, which are a little more spread out or included in the motor-cortex.

A lateral part of area 8 and perhaps the most caudal subfield of area 6 a are the responsible cortical structures for contraversive or adversive movements at least in the frontal pole of the hemisphere. The area 6 a δ is the cortical representation of ipsiversive movements. It is clear that these cortical apparatus for movements in the same plane are always interdependent.

Here a bridge from the concept of supravestibular extrapyramidal system to the extrapyramidal systems in the clinicopathologic sense is thrown. The contraversive movements have their most important substrates in the pallidum and entopeduncular nucleus (Hassler and Montanelli and Hassler), which are integrating parts of the subcortical extrapyramidal system. The cortical continuations of these systems—by mediation of special thalamic nuclei (V.o.a)—are true extrapyramidal motor fields.

All the extrapyramidal motor fields including these for movements in the vertical plane and around the long axis of the body have efferent descending projections. Some of these pass as cortico-spinal systems to the region of the motoneurons, others mediate only the cortical impulses to the supravestibular centres for the movements of the same direction. They are not operating but by means of the subcortical portions.

S U M M A R Y

The organization of the cat's frontal motor cortex is structurally in accordance with that of the primate's frontal lobe. Nearly all architectonic fields and subfields of primate can be identified in the cat. This fact suggests that all mammals have

the same pattern of motor fields with an identical relative position.

The differentiation of the cat's frontal cortex by a little modified Hess stimulation technique shows an impressive multiplicity of stimulation effects specific for

each subfield. Most of them are direction specific movements or vicariously conjugated eye movements. Whether the first or the second appears, depends on the unrestrained or restrained posture of the head.

The ipsiversive movements are obtained in the cortical level by stimulations of area 6 a δ in the lower lip of the cruciate sulcus. The caudally joint subarea 6 *infra fundum* or *illaminata* yields rotating and not constantly contraversive movements.

On the lower bank of the anterior sig-

moid gyrus and the cortical regions surrounding the rostral most part of presylvian sulcus locally separated representations for each of the direction specific movements exist.

The functional meaning of extrapyramidal motor fields is that they are thalamocortical connexions of the supravestibular and of the pallidar systems for direction specific head and trunk or gaze movements.

R E S U M E N

La organización de la corteza motora en el gato concuerda desde el punto de vista de la estructura con la del lóbulo frontal de los primates. Casi todas las áreas y subáreas arquitectónicas de los primates pueden ser identificadas en el gato. Este hecho sugiere la existencia de una disposición de las áreas motoras común a todos los mamíferos, caracterizada por idéntica posición relativa de las mismas.

La diferenciación de la corteza frontal del gato por la técnica de Hess algo modificada demuestra una notable multiplicación de efectos estimulantes específicos para cada subárea. La mayor parte de éstos son ya sea movimientos específicos en su dirección o movimientos oculares conjugados adaptados. Según que la postura de la cabeza esté fijada o cambie, aparecen el primero o el segundo de los movimientos enunciados.

Se obtiene movimientos hacia el mismo lado a nivel cortical mediante la estimulación del área 6 a δ en el labio inferior del surco "cruciatus". El subárea 6 "infra fundum" adyacente en el sentido caudal da lugar a movimientos de rotación y no constantemente contraversivos. En la vertiente inferior de la circunvolución sigmoides y de las regiones corticales que rodean la parte más anterior de la cisura presilviana existen representaciones locales independientes para cada uno de los movimientos específicos de dirección.

La significación funcional de las áreas motoras extrapiramidales consiste en que constituyen conexiones talamocorticales de los sistemas supravestibular y palidial para los movimientos de dirección específicos de la cabeza, el tronco y la mirada.

R É S U M É

L'organisation de l'écorce motrice dans le chat est, du point de vue de sa structure, en concordance avec celle du lobe frontal des primates. Presque toutes les aires et sub-aires architectoniques des primates peuvent être identifiées dans le chat. Ce fait suggère l'existence d'une certaine disposition des aires motrices, commune à tous

les mammifères, caractérisée par une position relative identique des mêmes.

La différenciation de l'écorce motrice du chat obtenue par moyen d'une technique de Hess un peu modifiée démontre une remarquable multiplication des effets stimulants spécifiques pour chaque sub-aire, dont la plupart sont ou bien des mouvements spé-

cifiques dans leur direction ou bien des mouvements oculaires conjugués adaptés. Selon que la position de la tête soit fixe ou changeante apparaissent le premier ou le deuxième des mouvements énoncés.

On obtient des mouvements vers le même côté au niveau cortical par moyen de la stimulation de l'aire 6 a δ au bord inférieur du sulcus "cruciatu". La sub-aire 6 "infra fundum" adjacente dans le sens caudal provoque des mouvements de rotation non constamment contraversifs. Sur le versant inférieur de la circunvolution sig-

moides et des régions corticales qui sont autour de la partie la plus antérieure du sulcus presylvien il y a des représentations locales indépendantes pour chacun des mouvements spécifiques de direction.

La signification fonctionnelle des aires motrices extrapyramidales consiste à ce qu'elles constituent des connexions thalamo-corticales des systèmes supravestibulaire et palidal pour les mouvements de direction spécifiques de la tête, le tronc et le regard.

ZUSAMMENFASSUNG

Die Organisation der motorischen frontalen Hirnrinde bei der Katze stimmt in ihrer Struktur mit der des frontalen Lappens bei den Primaten überein. Fast alle architektonischen Felder und Unterfelder bei den Primaten können bei der Katze wieder-gefunden werden. Diese Tatsache legt nahe, dass bei allen Säugetieren die Struktur der motorischen Felder dieselbe ist mit identischer relativer Position.

Die Differenzierung der Frontalrinde der Katze durch eine etwas modifizierte Hess'sche Reiztechnik weist eine eindrucksvolle Vielheit von Reizungseffekten auf, die spezifisch für jedes Unterfeld ist. Die meisten davon sind Richtungsspezifische Bewegungen oder vikariierende konjugierte Augenbewegungen. Ob das Erste oder das Zweite auftritt, hängt von der gezwungenen oder ungezwungenen Haltung des Kopfes ab.

Die ipsiversive Bewegungen erhält man in der kortikalen Sphäre durch die Reizung der Felder 6 a δ und der unteren Lippe des Sulcus cruciatu, das sich kaudal anschließende Feld 6 infrafundum oder ilaminierte erzeugt rotierende und nicht immer kontraversive Bewegungen.

An der unteren Kante des Gyrus sigmoides anterior und in den kortikalen Gegenden, die den größten rostralen Teil des Sulcus praesylvianus umgeben, bestehen lokal separierte Repräsentationen für jede der richtungsspezifischen Bewegungen.

Die funktionelle Bedeutung der extrapyramidalen motorischen Felder besteht darin, dass sie thalamo-kortikale Verbindungen darstellen.

Die funktionelle Bedeutung der extrapyramidalen motorischen Felder besteht darin, dass sie thalamo-kortikale Verbindungen darstellen.

REFERENCES

1. Beevor, C. E. and Horsley, V.: A further minute analysis by electrical stimulation of the so called motor region of the cortex cerebri in the monkey (*Macacus sinicus*). Phil. Trans. 179B, 205-256 (1888).
2. Brodmann, K.: Vergleichende Lokalisationslehre der Großhirnrinde in ihren Prinzipien dargestellt auf Grund des Zellenbaues. J. A. Barth, Leipzig (1909).
3. Bucy, P. C.: Electrical excitability and cyto-architecture of the premotor cortex in monkeys. Arch. Neurol. 30, 1205-1225 (1933).
4. Bucy, P. C. and Fulton, J. F.: Ipsilateral representation in the motor and premotor cortex of monkeys Brain 56, 318-342 (1933).
5. Ferrier, D.: The functions of the brain. Smith Eldor London 1876, 323 pp.
6. Foerster, O.: Motorische Felder und Bahnen. Hdb. Neurol. VI. 1-357 (1936).
7. Fulton, J. F.: Functional localisation in the frontal lobes and the cerebellum. Oxford 1949.

8. *Fulton, F. J. & Jacobson, C. F. & Kennard, M. A.*: Relation of the frontal lobes to posture and forced grasping in monkeys. *Brain* 55, 524-536 (1932).
9. *Gurewitsch, M. and Chatchaturian, A.*: Zur Cytoarchitektonik der Großhirnrinde der Feliden. *Z. Anat. Entwicklg.* 87, 100-138 (1928).
10. *Hassler, R.*: Forels Haubenfaszikel als vestibuläre empfindungsbahn mit Bemerkungen über einige andere sekundäre Bahnen des Vestibularis und Trigemini. *Arch. Psychiatr.* 180, 23-53 (1948).
11. *Hassler, R.*: Die zentralen Apparate der Wendebewegungen. *Arch. f. Psychiatr.* 194, 456-480 (1956).
12. *Hassler, R.*: Die extrapyramidalen Rindensysteme und die zentrale Regelung der Motorik. *Dtsch. Z. Nervenheilk.* 175, 223-258 (1956).
13. *Hassler, R.*: Über die Bedeutung des pallidären Systems für Parkinsonsyndrom und Psychomotorik nach Erfahrungen bei gezielten Hirnoperationen. *Rapp. I. Congr. Internat. Neurochir. Brüssel 1957*, pp. 176-178.
14. *Hassler, R.*: Spezifische und unspezifische Systeme des menschlichen Zwischenhirns. In: *Lectures on the Diencephalon*. Edit.: W. Bargmann and J. P. Schade. Amsterdam 1964; 1-32.
15. *Hassler, R. und Hess, W. R.*: Experimentelle und anatomische Befunde über die Drehbewegungen und ihre nervösen Apparate. *Arch. Psychiatr.* 192, 488-526 (1954).
16. *Hassler, R. und Muhs-Clement, K.*: Architektonischer Aufbau des sensomotorischen und Parietalen Cortex der Katze. *J. Hirnforsch.* 6, 377-420 (1964).
17. *Hess, W. R.*: Charakter der im Zwischenhirn ausgelösten Bewegungseffekte. Ein Beitrag zur extrapyramidal gesteuerten Motorik. *Pflügers Arch.* 244, 767-786 (1941).
18. *Hess, W. R.*: Physiologische Aspekte der extrapyramidalen Motorik. *Nervenarzt* 15, 457-466 (1942).
19. *Hess, W. R.*: Das Zwischenhirn. Syndrome, Lokalisationen und Funktionen. Benno Schwabe, Basel, 2. Aufl. 1954.
20. *Hyde, J. E. und Eliasson, S. G.*: Brainstem induced eye movements in cats. *J. Comp. Neur.* 108, 139-172 (1957).
21. *Hyde, J. E. und Toczek, St.*: Functional relation of interstitial nucleus to rotatory movements evoked from zona incerta stimulation. *J. Neurophysiol.* 25, 455-466 (1962).
22. *Jung, R. und Hassler, R.*: The extrapyramidal motor system. *Handbook Physiol. Neurophysiol. II.* 863-927 (1959).
23. *Kleist, K.*: *Gehirnpathologie*. Leipzig 1934.
24. *Montanelli, R. P. und Hassler, R.*: Motor effects elicited by stimulation of the pallido-thalamic system in the cat. In: *Lectures on the Diencephalon*. Edit.: W. Bargmann and J. P. Schade. Amsterdam 1964; 56-66.
25. *Muskens, L. J. J.*: An anatomico-physiological study of the posterior longitudinal bundle in its relation to forced movements. *Brain* 36, 352-426 (1914).
26. *Oscarsson, O. und Rosén, I.*: Projection to Cerebral Cortex of Large Muscle-Spindle Afferents in Forelimb Nerves of the cat. *J. Physiol.* 169, 924-945 (1963).
27. *Russell, J. S. R.*: An experimental investigation of eye movements. *J. Physiol.* 17, 1-26 (1894/95).
28. *Vogt, C. und O.*: Zur Kenntnis der elektrisch erregbaren Hirnrindengebiete bei Säugetieren. *J. Psychol. u. Neur.* 8, 277-456 (1907).
29. *Vogt, C.*: Quelques considerations générales à "propos du syndrome du corps strié". *J. Psychol. u. Neur.* 18, 479-488 (1911).
30. *Vogt, C. und O.*: Allgemeinere Ergebnisse unserer Hirnforschung. *J. Psychol. u. Neur.* 25, 273-462 (1919).
31. *Vogt, C. und O.*: Zur Lehre der Erkrankungen des striären Systems. *J. Psychol. u. Neur.* 25, Erg. B., 631-846 (1920).
32. *Vogt, M.*: Über omnilaminäre strukturdifferenzen und lineare Grenzen der architektonischen Felder der hinteren Zentralwindung des Menschen. *J. Psychol. u. Neurol.* 35, 177-193 (1928).
33. *Wilson, S. A. K.*: Progressive Lenticular Degeneration: A Familial Nervous Disease Associated with Cirrhosis of the liver. *Brain* 34, 295-509 (1912).

Thalamic Afferents to the Frontal Lobe: of the Macaque*

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Afferents of the frontal lobe can be only from three sources: thalamus, other lobes of the cerebrum, and striatal complex. The very existence of the last category is controversial, and since we have not been in a position to see striato-cortical connections they will not be discussed here.

Corticocortical connections may be studied anatomically by one of the fiber degeneration methods, broadly classified as Marchi or Nauta, and physiologically by cortical potentials evoked either electrically or by strychnine, but not by retrograde degeneration. Our two volumes on connections of the cerebral cortex^{9, 10} have dealt with cortico-cortical connections *in extenso*; it will not be reiterated here.

Thalamocortical connections can be studied either by retrograde cell degeneration after localized cortical injury or by fiber degeneration methods after direct thalamic lesions. Nearly all the existing studies have utilized the first of these approaches.

The retrogressive changes in specific thalamic nuclei were discovered by Monakow in 1882 but little use was made of this for working out thalamocortical relations in a systematic way until 1923 when Minkowski¹³ made lesions on individual gyri of macaques and localized the resulting cell degeneration in the thalamic nuclei. He came to the conclusion that an anterior-posterior correlation exists, in a specific pattern that conforms to the general correlations accepted today, so far as it went, except

that he believed that anterior nucleus projects to prefrontal cortex and central nucleus of Luys projects to frontal operculum. He also showed a dorsoventral correlation between VPL and postcentral gyrus.

LeGros Clark, between 1932³ and 1953⁴, exploited the method of retrograde degeneration after experimental cortical lesions at first in the rat, then in the macaque, clarifying and precisizing the topographical plan considerably.

Approximately coeval with the work of LeGros Clark, Walker studied the primate thalamus^{17, 18}, principally by the degeneration method but extending his studies to fiber degenerations of the thalamic afferent pathways, and into the chimpanzee, as a form closer to man.

More recently Mettler¹² and Chow^{1, 2} have restudied thalamocortical relations in the macaque and others have studied various mammalian forms, including man, always with the same approach: localized lesion of cerebral cortex followed by a mapping of the region of thalamic cell degeneration after a suitable period. From these studies has grown up a rather settled body of doctrine on thalamocortical relationships, except for certain undecided details, and it might be added, a vague uneasiness.

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So far as the frontal lobe is concerned, the consensus is about as follows. *Ventralis anterior* and *ventralis lateralis** supply premotor cortex, *medialis* supplies the prefrontal region, while *lateralis anterior* sends to motor or premotor areas, or both. While this accounts for the principal nuclei of the forward part of the thalamus, it is not the whole story. Retrograde degeneration in the somesthetic nuclei after area 4 lesions was seen by Clark⁴ and Chow and Pribram², though this finding has not disturbed the concept of one nucleus for one cortical region, and the implied doctrine of point-for-point specificity.

Several studies, including our own, have demonstrated cellular degeneration in the *paracentralis* that varies in location with the cortical site lesioned, and we have observed localized distribution of corticothalamic within that nucleus. Chow¹ demonstrated local representation of the cortex within the reticular thalamic nucleus. So here are three systems—principal, intralaminar and reticular—each with somewhat parallel localized representation on the cerebral cortex. An upset of the doctrine of local specificity has been avoided by regarding these others as waking or alerting systems, though some physiological evidence is against the operation of such a mechanism.

When we canvass the thalamic supply of area 4 we find that it receives from *ventralis lateralis*, *paracentralis*, *reticularis*, *ventralis posterior lateralis*, *ventralis posterior medialis*, *lateralis anterior*, *medialis pars externa*, and as we shall show, *ventralis posterior inferior*. Layer IV of cerebral cortex is generally considered to be specialized to receive thalamic projections, but the area that receives most widely from the thalamus has no fourth layer at all.

Any notion that the cerebral cortex mirrors the spatial organization of the thalamus,

as might be inferred from the summarizing diagrams of some workers, is further dispelled by the fact that the intensity of thalamic distribution over the cerebral cortex varies enormously from area to area, and was already shown in an intensity distribution surface map of the monkey cerebral cortex by Walker in 1938. Such a depiction fails to show the even more emphatic contrasts between distribution on gyri and their adjacent sulci. Surface areal differences more concern the temporal and occipital lobes, but the absence of thalamic terminations in the arcuate and principal sulci of the monkey is striking, with the result that areas 8 and 46, which are primarily sulcal, are poorly provided with thalamic afferents, admitting certain local exceptions. Even areas whose configuration is nearly flat, as area 11, may show gross differences in the concentration of thalamic afferents they receive in their several subareas.

It is well recognized that thalamic nuclei may or may not degenerate after decortication, as determining the existence of a cortical connection, but there is also partial cell loss after topectomy and shrinkage or paling of the surviving cells to be considered. LeGros Clark, in studying the somesthetic nucleus, states that destruction of area 2 produces no cell loss, but a 25 % reduction in cell size; removal of areas 1 and 2 gives a partial cell loss in the back of the nucleus; while topectomy of area 3 alone produces a partial cell loss throughout the nucleus.

In addition to all these observations are the theoretical considerations (1) that there may be cortical stations which receive from cells so diffusely scattered over the thalamus that cell change cannot be demonstrated, and (2) that there may be thalamic nuclei which distribute so widely over the cortex that degeneration is not seen after topectomy. Possibly, also, there are nuclei resistant to cell change: most other divisions of the brain show no retrograde degeneration when their terminals are destroyed. Must all parts of the thalamus show retrograde degeneration,

* According to our observations nucleus *ventralis lateralis* of Walker is separable into a nucleus *dorsomedialis* and a *ventralis ventralis*. The former shows degeneration of corticothalamic connections after extensive lesions of area 6, the latter after lesions of area 4.

itself an exception in the brain? Might it not even be possible that the observed degeneration is a transneuronal one from deprivation of the corticothalamic supply, or at least be dependent on the combination of loss of their field of discharge and decrease of their field of stimulation?

Virtually all the cortical topectomies illustrated in the literature are quite large, however considered. It ought to be possible to discover small areas of cell degeneration after small cortical lesions, if the distribution is at all punctate. Possibly such were attempted and nothing found.

With all these structures in mind, one might imagine that an attempt would be made to settle problems of thalamic projection by direct small stereotaxic lesions in the thalamus, followed by a study of the course and distribution of the degenerating fibers. Stereotaxic machines are used daily by investigators of the brain, but it is difficult to divine why they have not been applied more to the problems of thalamocortical relationships. A complication is that the penetration of the corona or capsule by the electrode throws a shower of degenerating fibers in both directions. Actually, however, the projections of the thalamic nuclei are so concentrated and made up of such coarse fibers that they can be easily traced in Marchis. Moreover, the course of the corticopetal fibers is so distinct from that of the corticofugal ones that anyone experienced with tracing fibers after cortical lesions can distinguish in an isolated section with which category he is dealing.

Except for the early work of Sachs¹⁶, one of the first applications of the stereotaxic machine, and the random jabs of Poliak¹⁴, beautifully worked up however, our only predecessor in this work was Crouch^{5, 6} who made a series of discrete stereotaxic lesions in the macaque. His primary interest was in internuclear thalamic connections but he reported also on thalamocortical radiations and first discovered many of the connections which we will be reporting in this paper from a study of our own lesions.

Ours too were stereotaxic thalamic lesions of the macaque, but our approach to the thalamic nuclei from the opposite side of the brain, in order to avoid damage to the capsule or corona of the lesion side, administered by a stereotaxic machine on a new principle, devised by the present writer. Our interest was, primarily in thalamocortical radiations and our preoccupation was in establishing exact positions, courses and distribution patterns of the fibers.

The lesions were performed by our graduate student Edward Maibenco and were reconstructed fully in his doctoral thesis in 1957¹¹. Dr. Maibenco has since gone into another kind of work and the results of his thesis remain unpublished. On restudy by the writer some significant changes were found necessary and they have been reconstructed anew from study of the sections.

The machine referred to is illustrated in figure 1. It is built on the principle of a duplicator. The lesioning arm and indicator arm are yoked so that the position of the tips and the three-dimensional angle of each correspond, within a limited universe. A mounted frozen serial section of a comparable brain is set up in the proper position on one side, and the desired point, when touched with the indicator tip, is duplicated in the living brain positioned alongside. Any arbitrary approach may be made, without calculation, and extreme angles of entry may be chosen. The machine is particularly applicable to species or stages of development for which no stereotaxic atlases exist. All that is necessary is to mount stained frozen sections of a corresponding animal or a littermate on the control side.

The reconstructions of Maibenco were made as standard slice reconstructions on the outlines used by the present author for reporting all work in our laboratory, but to save space reconstructions used here are medial aspects of the course of the degenerated fibers laid into a half-shell of the internal configuration of the cerebral cortex.

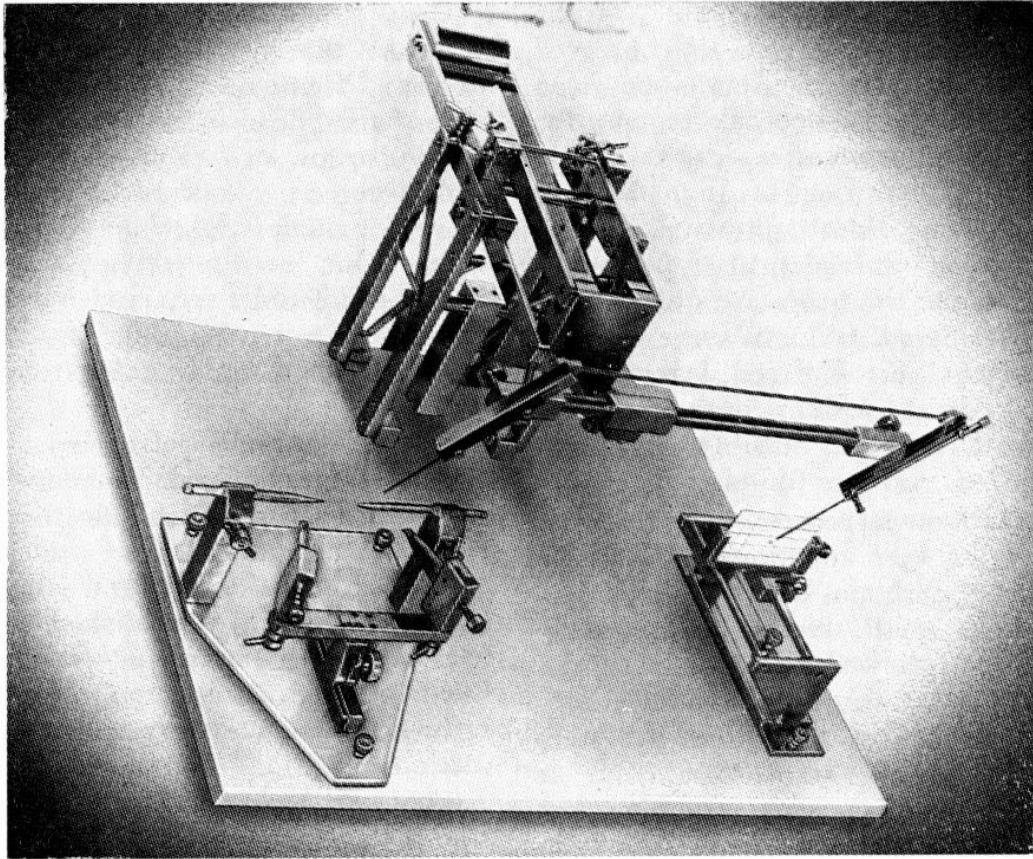


Fig. 1

Stereotaxic machine on duplicator principle. Used for making thalamic lesions from opposite side in this study. (Photo courtesy C. H. Stoelting Company, Chicago 24, the builders).

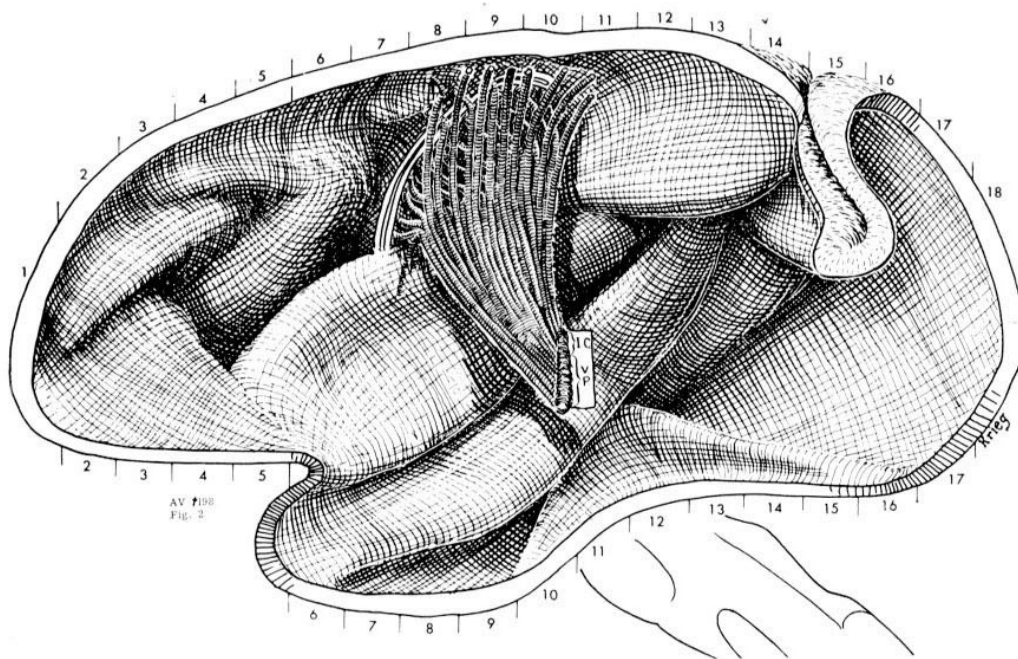


Fig. 2

Lesion 198. Large lesion in VPL plus somesthetic radiation.

Ventralis posterior lateralis

We shall begin with an exception for this lesion († 198, fig. 2) is of the VPL of the side on which the electrode entered, and in its lateral approach penetrated the somesthetic radiation. The effect is that of a virtually complete destruction of the lower part of VPL, sparing VPM and all other nuclei, except reticular.

Because of the coarseness and closeness of the fibers of the somesthetic radiation there is no difficulty in following it to its end. The internal capsule behind the pyramidal tract is virtually taken over by the somesthetic radiation. On nearing the central sulcus the stalks continue without change of direction into the precentral gyrus and terminate in the motor cortex of area 4.

A powerful contingent of fibers passes into the postcentral gyrus, but they branch off in a peculiar manner, leaving the main bundle at an abrupt right angle, only a few bending and flowing into the gyrus in the natural manner. They end throughout areas 3, 1 and 2.

Lesion 199 (fig. 3) makes a sloping entry into the medial region of VPL, barely avoiding VPM. The radiation is in two

slightly separated but distinct units. The first part of the course of the fibers is nearly horizontally through the internal capsule, in small fascicles. Then they climb dorsally in the outer half of the capsule, coursing quite outside of the corona deep to the central sulcus. Because the fibers are fewer the details of the separation can be seen better than in the previous example. The region of separation is composed of fiber segments each of which runs either dorsally into the precentral alba, or laterally to enter the postcentral gyrus. Once inside the gyral alba the fibers curve gradually to conform to the bent profile of this gyrus. It is rare to be in a position to witness an actual turning, because of the essentially segmented nature of Marchi material. In the few examples seen, mostly outlying, they seem to make a sharp bend, not a T, as would be expected if the postcentral element is a true collateral. This dilemma will continue to dog us throughout this report. The split in the projection was a fortunate occurrence because it showed that there is no scatter or mixture of the units: they are quite parallel in their entire alba course. We are forced to the concept that local representation of stations

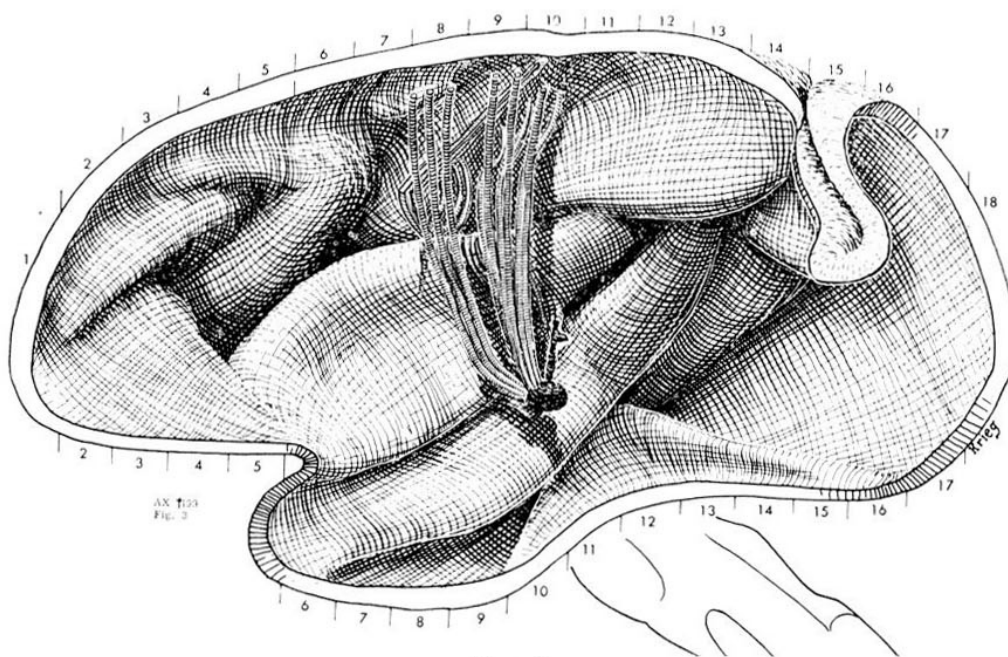


Fig. 3
Lesion 199. Two small lesions to VPL.

in the thalamus, and hence bodily stations, instead of being to cortical points, is to lines of cortex which runs across pre-and postcentral gyri and that dermatomal segments are represented as a succession of strips across gyri. There is no reason to believe that the succession and proportion between the bodily segments is otherwise than has been shown by the various workers. Topographically corresponding stations are lower in the postcentral sulcus, corresponding to the observed obliquity of the central sulcus on the cerebral surface.

Ventralis posterior inferior

Lesion 195 (fig. 4) pierces VPI in its course. Though it also pierces the medial nucleus and the internal capsule there is no confusion in the origin and course of the degenerated fibers from VPI. Unlike the radiation of the somesthetic nucleus the fibers run directly dorsally medial to the internal capsule, enter it halfway up the thalamus and are distributed to the gyral cortex of area 4, apparently confined to its dorsal part. The fibers are sparse and scattered, but quite coarse. This and some

other observations have led to the surmise that the dorsal edge of the motor area has some general character or is distributive in nature. Maibenco's observation that VPI sends to globus pallidus was not sustained.

Lateralis anterior

Lesion 197 (fig. 5) is a discrete involvement of less than two millimeters in diameter of what we regard as the ventral part of lateralis anterior. It is just in front of VPL in an illdefined region which for Walker would be in his massive VL. The radiation is pure, and easily followed. The fibers migrate obliquely laterally and forward, entering the capsule near the dorso-lateral edge of the thalamus. Still running forward and laterally, they traverse it, and finding themselves close under the posterior spur of the arcuate sulcus, separate into dorsomedial and ventrolateral groups, continuing their course close under the cortex.

The former group fan out in the superior arcuate fissure, and on reaching the dorsal peak turn forward, terminating in gyral cortex all along the way: area 6,

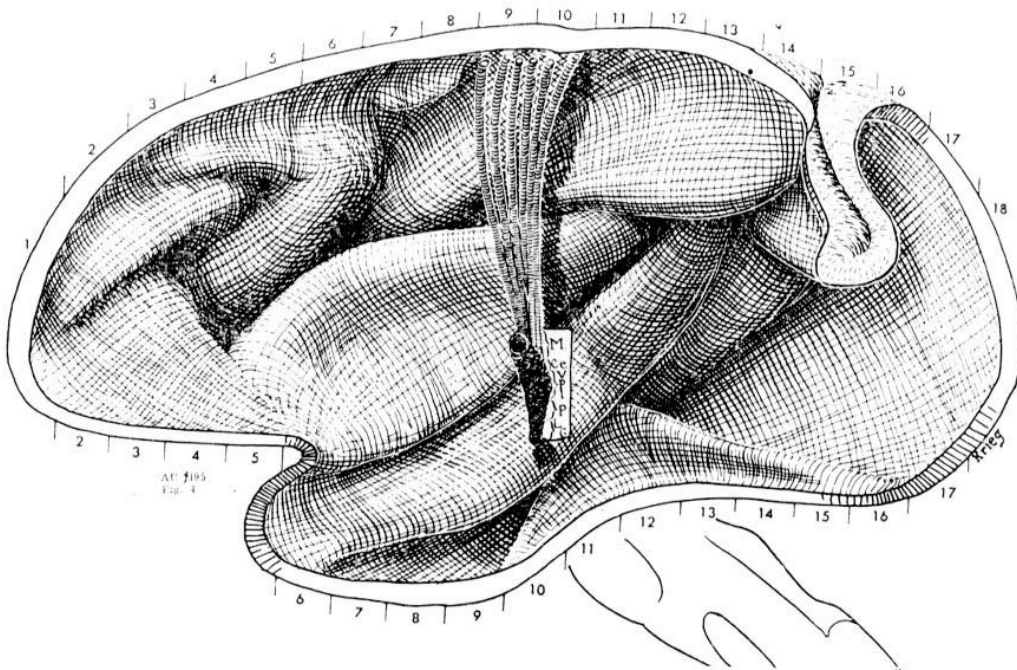


Fig. 4

Lesion 195. Destruction of most of VPI. Penetration of medialis (M), Centralis (Ce), Cerebral peduncle (P), and lateral geniculate (LG).

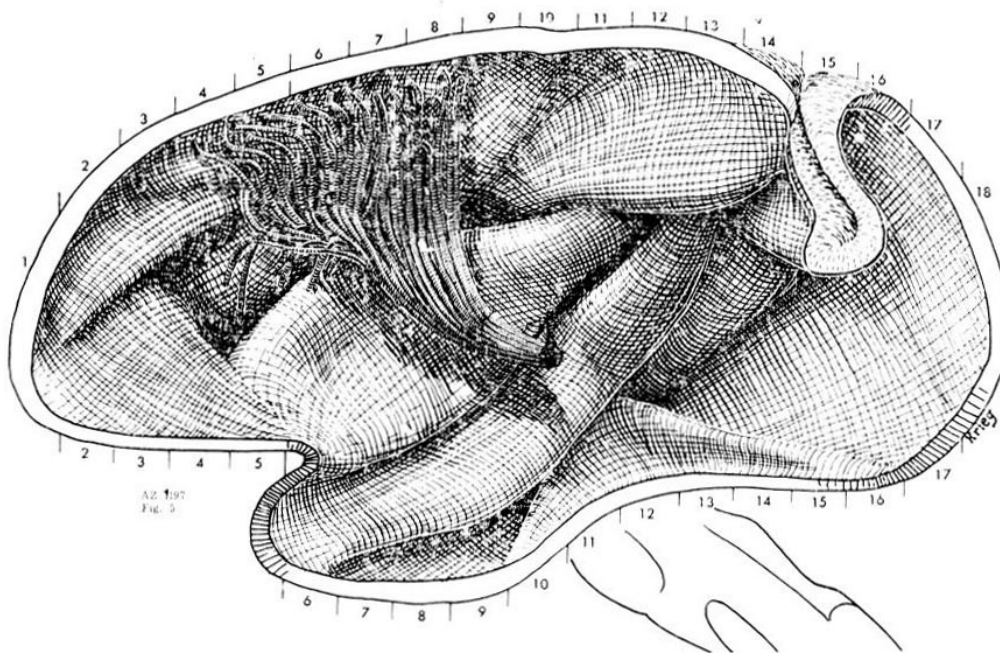


Fig. 5

Lesion 197. One cu. mm. in ventral part of LA destroyed.

possibly continuing into area 8. The ventrolateral component follows the precentral gyrus as far as the lateral fissure, terminating in area 44 and lower 6. An intermediate group ends directly in the arcuate spur and sends fibers forward under the convexity of the arcuate sulcus and into the cortex of its convexity, area 8.

As the bundles run along under the cortex they send off numerous presumptive collaterals at abrupt right angles toward the overlying cortex. Again we see only a mixture of tangential and radial batonnets, never fibers curving to enter cortex. The arrangement is entirely different from anything seen in the entire category of cor-

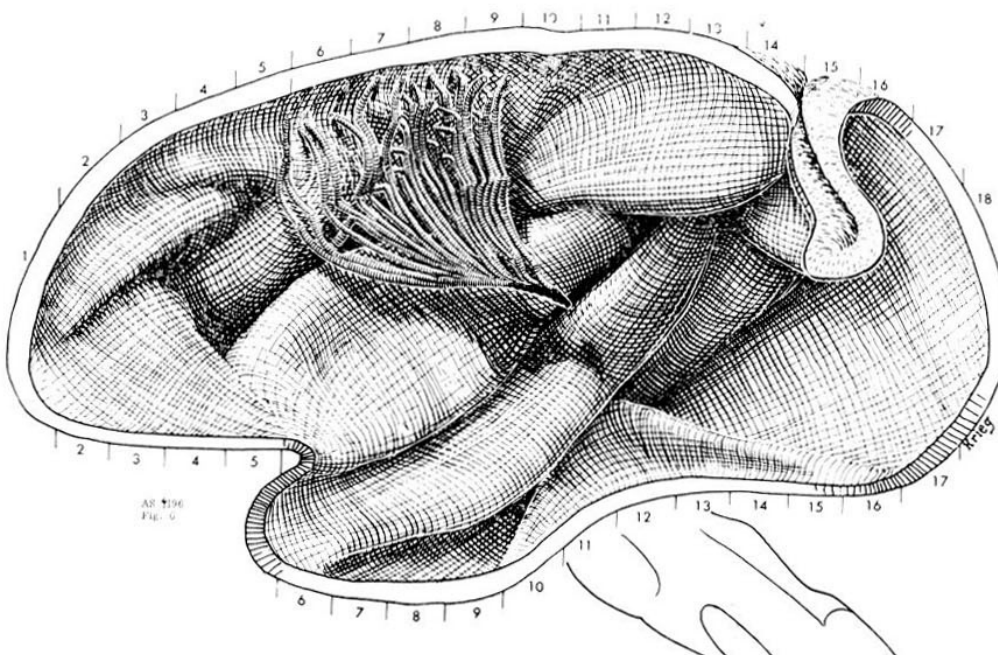


Fig. 6

Lesion 196. Horizontal perforation along upper surface of LA.

ticifugals. Though the lesion is small and is ventrally placed in the nucleus, fibers are widely distributed in areas 6 and 8.

There is another lesion to the lateralis anterior (†196, fig. 6) this one is a fine horizontal line in its dorsal extreme and in the frontal plane. In spite of its restricted size and different position the observed radiation is an extensive one, including the dorsal half of areas 6 and 8, though not their ventral halves, as in the preceding.

One thus gains the impression that there is little point-for-point specificity in the lateralis anterior radiation, and the universal distribution by quasi-collaterals suggests a linear arrangement of thalamic stations here, too.

Medial nucleus

Crouch was unable to find any projection from nucleus medialis, though nearby nuclei in the same lesion showed good connections. The same holds for his predecessor, Sachs, and for our own series, until we permitted an operated animal to survive four weeks, when the medialis radiation was seen fully developed. Unfor-

tunately, only one animal was thus treated, and a well defined though restricted radiation was disclosed. Reconstructed originally by slices, the course of the radiation has been summarized in medial profile in figure 7. The lesion was a nearly horizontal thrust of the cold electrode below the middle of the central part of the medial nucleus. The flat ribbon-like radiation traversed the nucleus anterior to emerge at the frontal pole of the capsule and join the anterior thalamic radiation. Thence it courses with the anterior limb of the internal capsule. On emerging into the alba it trends laterally, not scattering much, and distributes in the inferior frontal and fronto-orbital gyri.

So because we have but one case we cannot say much about the distribution pattern of the medial nucleus. In fact, our case has not confirmed either of the recent views concerning organization of the medialis-frontalis. Mettler¹² divides the medial nucleus into vertical laminae with the prefrontal areas 8-12 arranged in order, roughly speaking, from lateral to medial. Pribram, *et al.*¹⁵ organize the medialis into sagittal laminae, the more medial sending to the more dorsal longitudinal strips of prefrontal cortex, and the more lateral

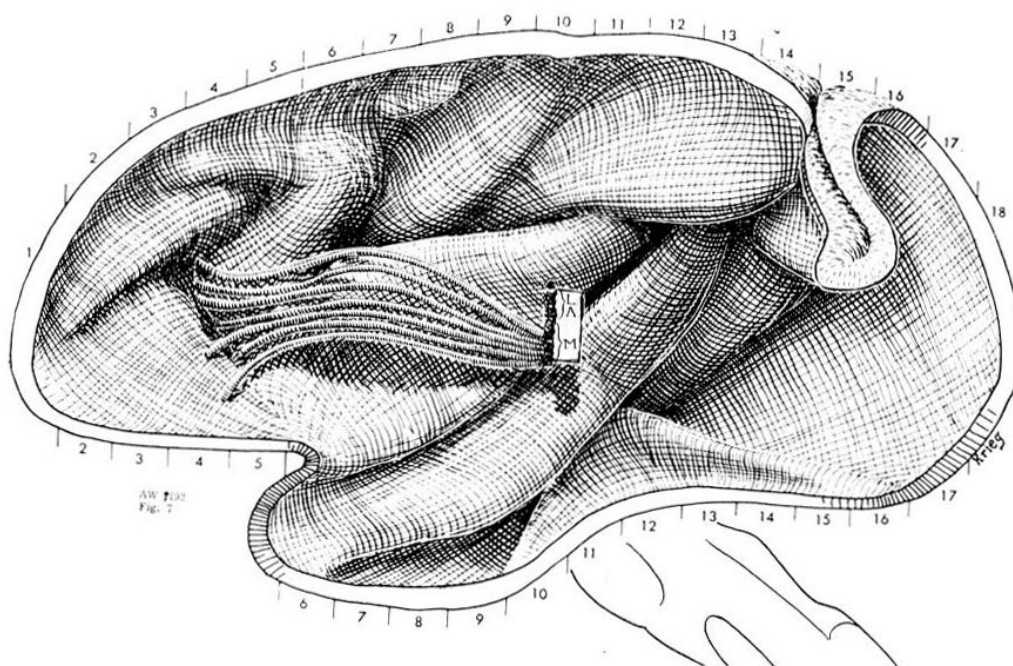


Fig. 7
Lesion 192. Horizontal perforation of medialis.

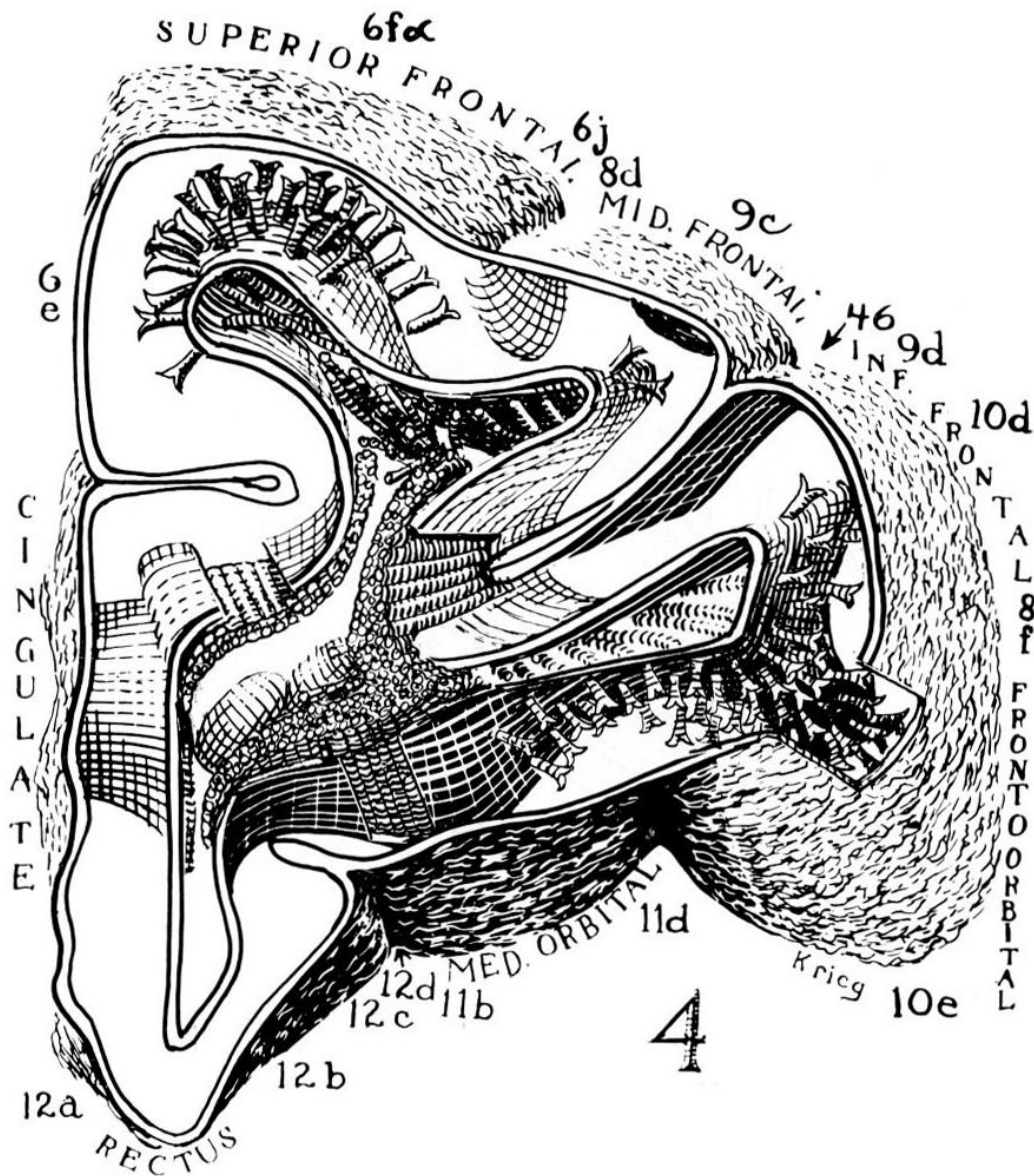


Fig. 8

Lesion 70. Cortical endings and subcortical position of forward running fibers after frontal lobotomy. They arise preponderantly in nucleus medialis thalami.

laminae to the more ventrolateral prefrontal strips. Whichever plan is correct, our lesion should cut through all strips or their radiations and show a scattered distribution in the frontal lobe.

The fiber architectonics of the medialis-prefrontalis radiation can be worked out from the pattern of corticopetal degeneration following prefrontal lobotomy in the monkey. The thalamocortical fibers, once clear of the capsule, show a strong tendency to form a lamina close under the cortex (fig. 8) while running forward and

sending abrupt collaterals into the overlying cortex. The carpet is especially thick under the principal sulcus though none of its cortex here, area 46, seems to receive any endings. Indeed, a distinct clear lamina separates fiber stratum and cortex. The entire gyrus rectus prominence, with its area 12, carries no thalamocorticals. Endings are numerous in certain of the subareas of areas 8, 9, 10 and 11, which we demonstrated long ago. Time is not at hand to detail these; suffice it to point out that the localization is very specific as to parts

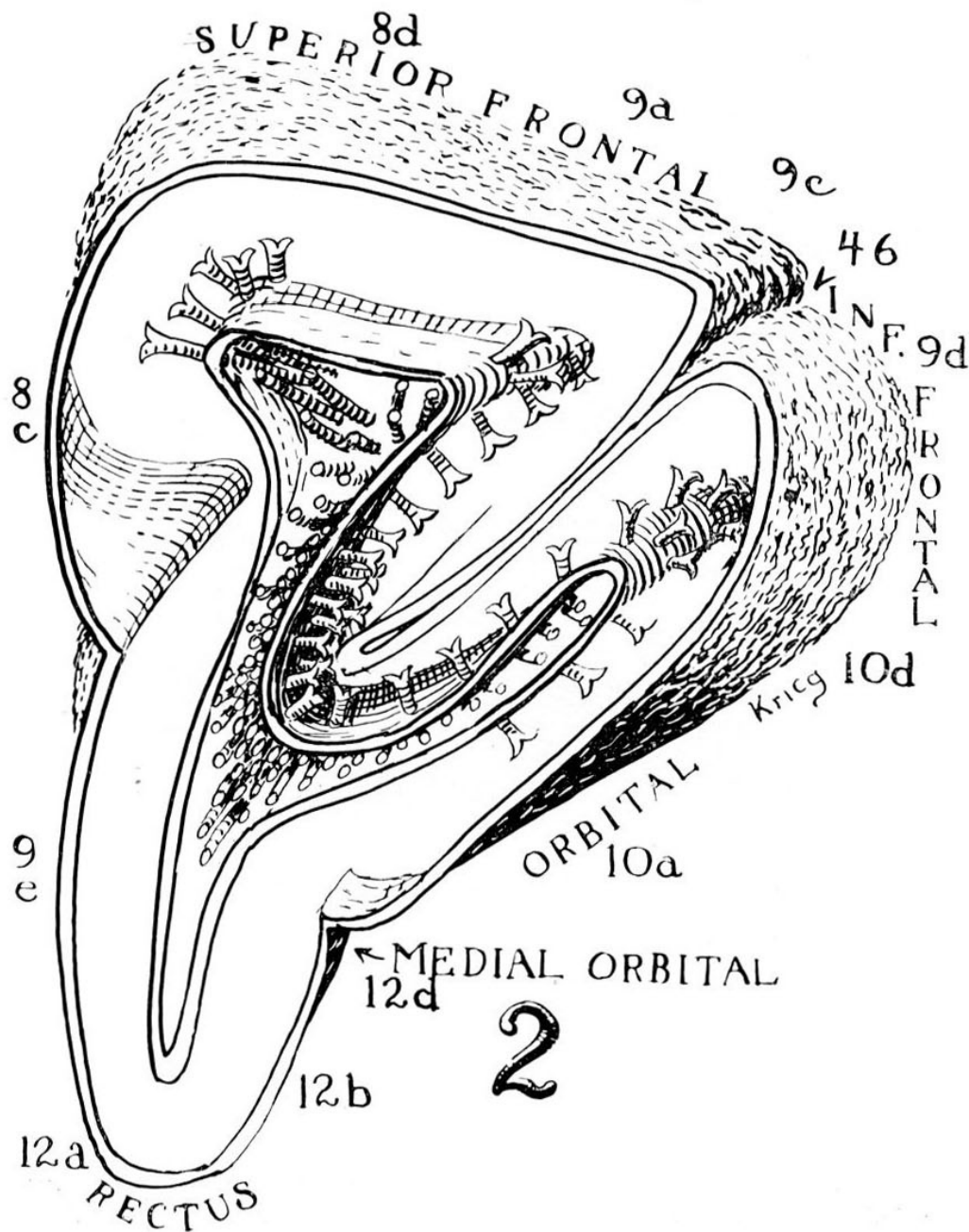


Fig. 9

Lesion 70. Showing the numerous endings around principal sulcus at frontal pole.

of areas. For example, the forward extreme of the principal sulcus receives a great number of endings (fig. 9) though the remainder does not.

It would be possible to adduce further evidence for the generality of the principle of collateralization of the thalamocortical distribution from examples in the posterior half of the cerebrum, but this paper is confined to the frontal lobe. The incredulous may object that surely the visual area is

a region of point-for-point representation. Yet it is here that the branching system seems best organized. The visual radiation is rather compressed between the deep folds of the occipital lobe, leaving little space in the alba. Here the collaterals form a thin lamina, oriented at right angles to the main stalks forming an arrangement which may be likened to a garden lattice.

These findings do not need to oppose the existing system of localization, which

has never been claimed to be broken into mathematical points. Indeed the exquisite work of Hubel and Wiesel⁷ on the evoked activity of individual cells in the visual cortex demonstrates a functional specialization of fantastic specificity which somewhat replaces purely topical identity. It

would perhaps be productive to think of the thalamocortical neurons as a feeder system into a row of cortical cells of differing functions because of differences in their other connections. These cells select what they can use of the data which is presented to them, like a diner in a line at a cafeteria.

S U M M A R Y

Most of our current notions of the thalamocortical radiations are derived from localization of retrograde degeneration in the thalamus after removal of portions of cerebral cortex, with the tacit assumption of unique, uniform, unitary representation on the cortex of points or columns in the thalamus. Closer study shows none of these qualifications is true, and combined with theoretical objections, the resulting quandary demands the tracing of thalamocortical radiations after small stereotaxic lesions within the thalamus. When performed on *Macacus* such studies show the following. 1. The somesthetic nucleus sends the main trunk to motor area 4 and a strong collateral to postcentral areas 3, 1, 2, successively, but in orderly, discrete strips. 2. Small loci in *lateralis anterior* distribute to entire areas 6 and 8, while lesions in different portions of that nucleus show great overlap of cortical field. 3. *Ventralis posterior inferior*

sends only to dorsal part of motor area 4. 4. *Medialis* requires a longer time for its radiation to degenerate, and sends to prefrontal granular cortex only, but not equally (to 9, 10, 11; but not to 12, 46). 5. Thalamocortical radiations perforate the internal capsule, then tend to course tangentially just below the cortex, sending bundles of collaterals into the gyri they pass, and shooting off sharply bending collaterals into overlying cortex, thus furnishing a basis for a linear representation on the cortex of thalamic points, similar to the proved distribution of the somesthetic nucleus.

Corticothalamic connections are quite specific but unequal, and mostly repeat thalamocortical correlations. Regarding thalamocortical neurons as disseminators, and cortical neurons as specific selectors opens the way for a revision of thinking on their relative roles.

R E S U M E N

La mayoría de las actuales nociones acerca de las radiaciones talámocorticales derivan de la localización de la degeneración talámica retrógrada producida por extirpación de porciones de la corteza cerebral y están basadas en la aceptación tácita de una representación única y uniforme en la corteza de puntos o columnas en el tálamo.

Un estudio más minucioso demuestra que estas aseveraciones son erróneas y sumado esto a objeciones teóricas resulta la necesidad de detectar radiaciones talámocorticales a continuación de pequeñas lesiones esterotácticas del tálamo.

Estos estudios se realizaron en *Macacus* y demuestran lo siguiente.

1. El núcleo somestético envía el haz principal al área motor 4 y un fuerte collateral a las áreas postcentrales 3, 1 y 2 sucesivamente pero en franjas ordenadas y distintas. 2. Pequeñas localizaciones en el n. *lateralis anterior* se difunden a la totalidad de las áreas 6 y 8, mientras que lesiones en diferentes porciones de dicho núcleo evidencian que se superponen en el campo cortical. 3. El n. *ventralis posterior inferior* envía solamente a la parte dorsal del área 4 motora. 4. El *medialis* exige un tiempo mayor para que degenere su radiación y abastece solamente la corteza granular prefrontal aunque no en forma uniforme (a 9, 10 y 11 pero no a 12, 46). 5. Las radiaciones

tálamocorticales perforan la cápsula interna, tienden luego a pasar tangencialmente debajo de la corteza, enviando colaterales a los circunvoluciones por las que pasan y despidiendo colaterales acentuadamente inclinados hacia la corteza que se encuentra por encima de esa región; así proporciona una base para la representación lineal de puntos talámicos sobre la corteza similar a la distribución comprobada en el

núcleo somestético. Las conexiones cortico-tálamicas son específicas pero desiguales y mayormente repiten las correlaciones tálamocorticales.

En lo que atañe a las neuronas tálamo-corticales como diseminadores, y a las neuronas corticales como selectores específicos queda abierto el camino para la revisión de lo sostenido sobre la importancia relativa de estas funciones.

R É S U M É

La plupart des notions actuelles sur les radiations thalamo-corticales découle de la localisation de la dégénération thalamique rétrograde produite par l'extirpation de certaines portions de l'écorce cérébrale, étant basée sur l'acceptation tacite d'une représentation unique et uniforme de points ou colonnes dans l'écorce du thalamus.

Une étude plus minutieuse démontre que ces affirmations sont fausses et en associant ceci à des objections théoriques on obtient comme résultat le besoin de détecter des radiations thalamo-corticales après de petites lésions stéréotactiques du thalamus.

Ces études ont été faites sur des *Macacus* et démontrent ce qui suit:

1. Le noyau somestétique envoie la gerbe principale à l'aire motrice 4 et un puissant colatéral aux aires postcentrales 3, 1 et 2 successivement mais en franges ordonnées et distinctes. 2. De petites localisations dans le n. lateralis antérieur se répandent à la totalité des aires 6 et 8, tandis que des lésions sur de différentes portions rendent évident qu'elles se superposent dans le champ cortical. 3. Le ventralis postérieur inférieur envoie

seulement à la partie dorsale de l'aire motrice 4. 4. Le medialis exige un plus longue durée pour la dégénération de sa radiation et fournit seulement l'écorce granulaire préfrontale bien que pas uniformément (9, 10 et 12 mais pas 12, 46). 5. Les radiations thalamo-corticales percent la capsule interne, tendent à passer tangentiellement sous l'écorce, en envoyant des colatéraux aux circunvolutions qu'elles traversent et en lançant des colatéraux extrêmement inclinés vers l'écorce qui se trouve par dessus cette région; de cette façon on offre une base pour la représentation linéale de points thalamiques sur l'écorce, pareille à la distribution prouvée dans le noyau somestétique. Les connexions cortico-thalamiques sont spécifiques bien qu'inégales et en général correspondent à des corrélations thalamocorticales.

En ce qui concerne les neurones thalamo-corticales comme disséminateurs et les neurones corticales comme sélecteurs spécifiques la voie est laissée ouverte pour une révision de ce qu'on a soutenu en rapport avec l'importance relative de ces fonctions.

Z U S A M M E N F A S S U N G

Die meisten unserer gewöhnlichen Kenntnisse ueber die thalamo-corticalen Radiationen haben wir durch die Lokalisierung der retrograden Degenerierung im Thalamus nach der Ablation von Teilen der Hirnrinde, unter der stillschweigenden Annahme der einzigen und einheitlichen

Repraesentation im Cortex von Punkten oder Saeulen im Thalamus. Ein eingehenderes Studium zeigt, dass keine dieser Qualifizierungen richtig ist, und dass zusammen mit theoretischen Einwendungen, die resultierenden Zweifel die Sache nach thalamo-corticalen Strahlungen nach klei-

nen stereotaxischen Laesionen im Thalamus erfordern. Wenn dies beim Macacus geschieht, zeigt sich Folgendes:

1. Der Nucleus somoestheticus schickt die Hauptstraenge nach der Motorzone 4 und einen starken kollateralen Strang nach der postzentralen Zonen 3, 1 und 2 naheinander und in geordneten diskreten Buendeln. 2. Kleine loci im nucleus lateralis anterior verteilen sich in die ganzen Zonen 6 und 8, waehrend Laesionen in verschiedenen Teilen dieses Nucleus groessere Ueberlagerungen im corticalen Feld zeigen. 3. Der Ventralis posterior inferior schickt nur Strange in den dorsalen Teil der Motorzonen 4. 4. Der Medialis braucht mehr Zeit damit seine Strahlung degeneriert und sendet um zum praefrontalen granulaeren Cortex aber nicht gleichmaessig (nach 9, 10, 11; aber nicht nach 12,

46). 5. Die Thalamocorticalen Strahlungen durchbohren die capsula interna, dann verlaufen sie tangentiell gerade unter dem Cortex und senden Buender in die Gyri, an denen sie vorbeikommen und senden scharf abgebeugte Collaterale in die darueberliegende Rinde. So bilden sie eine Base fuer eine lineare Darstellung thalamischer Punkte im Cortex, aehnlich wie die nachgewiesene Verteilung des Nucleus somaestheticus.

Die Corticothalamischen Verbindungen sind spezifisch aber ungleich und wieder holen gewoehnlich die thalamocorticalen Beziehungen. Wenn man die thalamocorticalen Neuronen als Verteiler und die corticalen Neuronen als spezifische Selektoren betrachtet, ist der Weg fuer eine Revision im Denken ueber ihre relativen Rollen frei.

REFERENCES

1. Chow, K. L.: Regional degeneration of thalamic reticular nucleus following cortical ablations in monkeys. *J. Comp. Neur.* 97: 37-59, 1952.
2. Chow, K. L. and K. H. Pribram: Cortical projections of the thalamic ventral group in monkeys. *J. Comp. Neur.* 104: 57-75, 1956.
3. Clark, W. E. Le Gros: An experimental study of thalamic connections in the rat. *Phil. Trans. Roy. Soc. B*, 222: 1-28, 1932.
4. Clark, W. E. Le Gros: The thalamic connections of the parietal and frontal lobes of the brain of the monkey. *Phil. Trans. Roy. Soc. B*, 224: 313-359, 1935.
5. Crouch, R. L.: The efferent fibers of the thalamus of Macacus rhesus. II. The anterior nuclei, medial nuclei, pulvinar, and additional studies of the ventral nuclei. *J. Comp. Neur.* 72: 177-186, 1940.
6. Crouch, R. L. and J. K. Thompson: The efferent fibers of the thalamus of Macacus rhesus. I. Lateral and ventral nuclei. *J. Comp. Neur.* 69: 255-271, 1938.
7. Hubel, D. N. and T. N. Wiesel: Receptive fields of single neurons in the cat's striate cortex. *J. Physiol.* 148: 574-591, 1959.
8. Krieg, W. J. S.: A reconstruction of the diencephalic nuclei of Macacus rhesus. *J. Comp. Neur.* 88: 1-52, 1948.
9. Krieg, W. J. S.: Connections of the frontal cortex of the monkey. 299 pp. Thomas, Springfield, 1954.
10. Krieg, W. J. S.: Connections of the cerebral cortex. 472 pp. Brain Books, Box 9, Evanston, Ill., 1963.
11. Maibenco, E. P.: A Marchi study of the thalamic connections of the monkey. Dissertation, Ph. D., Department of Anatomy, Northwestern University Medical School, 1957.
12. Mettler, F. A.: Extracortical connections of the primate frontal cerebral cortex. I. Thalamo-cortical connections. *J. Comp. Neur.* 86: 95-117, 1947.
13. Minkowski, M.: Etude sur les connexions anatomiques des circonvolutions rolandiques, parietales et frontales. *Schweiz. Arch. f. Neur. u. Psychiatr.* 12: 71-104, 227-268; 13: 255-278; 15: 97-132, 1923 and 1924.
14. Poliak, S.: The main afferent fiber systems of the cerebral cortex of primates. *Univ. Calif. Publ. Anat.* 2: 1-63, 1932.
15. Pribram, K. H.; K. L. Chow and J. Semmes: Limit and organization of the cortical projection from the medial thalamic nucleus in the monkey. *J. Comp. Neur.* 98: 433-448, 1953.
16. Sachs, E.: On the structure and functional relations of the optic thalamus. *Brain* 32: 95-186, 1909.
17. Walker, A. E.: The primate thalamus. 321 pp. Univ. of Chicago Press, 1938.
18. Walker, A. E.: The medial thalamic nucleus. *J. Comp. Neur.* 73: 87-115, 1940.

The Supplementary Motor Area in Man

(Anatomo-functional findings by stereo-electroencephalography in epilepsy)

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I. INTRODUCTION

Since the Supplementary Motor Area was clearly shown to exist in man, between 1948 and 1951, by W. Penfield and his co-workers, in particular Rasmussen, Welch, Jasper and Kristiansen, few works have been devoted to the study of this region especially in epilepsy, because of the difficulty of its neurosurgical approach.

It is known that the anatomo-functional organization of the S.M.A. has been progressively determined by the Montreal School by means of stimulation in the course of open operation on 20 patients under local anaesthesia of the supracallosal median cortex. The responses obtained, from 69 different points, have authorized to situate it on the inner part of F1, in front of the primary motor area, of the foot of which it would be separated by a narrow strip destined to speech, in the dominant hemisphere, above the cingulum but including perhaps its upper lip. Its upper limit would be defined by the median line, except ahead where it could extend on the lateral surface of the hemisphere. As to its ill-defined fore limit, it would not exceed a line passing perpendicularly through the rostrum of the corpus callosum.

Despite its functional heterogeneity Penfield does not attribute any somatotopic organization to it.

Consequently, contrary to the opinion expressed by Foerster in 1936¹⁷ thinking

to confirm, in man, the role attributed by the Vogts³⁶ in 1926 to the areas 6a α and 6a β of the external frontal cortex of macacus, Penfield shows that the postural or adverse movements elicited by stimulation of the S.M.A. have no relation with the precentral gyrus and the primary motor region.

The excisions performed in the internal face, either in the case of tumors or epilepsy, certainly seem to confirm the localization of this area and make it possible to specify its functions.

Its projections, however, remain hypothetical; the schema given by Jasper in 1954 to explain the mechanism of the secondary bilateral synchrony which characterizes, in a large part, the fits of the supracallosal internal face, indicates only the secondary participation of the intralaminar thalamic nuclei from the S.M.A.

In 1951 Erickson and Woolsey¹⁶ find the same type of responses attributed by Penfield to the S.M.A. in three patients.

Bates,⁹ however, in 1953 debates the meaning of the 49 responses obtained in different points of the internal face during 102 stimulations on 9 patients who were anesthetized and had previously undergone a hemispherectomy.

His apparently disconcerting results lead him to think that there is no sufficient argument to confirm the existence of a S.M.A. whereas the lower limb supposes perhaps a double supracallosal cortical re-

presentation regulating the postural movements, and of which homolateral efferent fibers are particularly important.

Since then, no general work seems to have been dedicated to the study of the anatomic-functional organization of this region in man, apart from the papers we published from 1962.

On the other hand, animal experimentation brings us informations of great interest.

Already perceived in 1888 by Horsley and Schaffer¹⁸, by Beevor and Horsley¹⁰ in 1890, then by Sherrington and his pupils in 1917 and by Vogts in 1919, the somatotopic organization of the mesial face of the frontal lobe of anesthetized macacus is established by Penfield and Welch in 1951 on the cercopithecus and in 1952 by Woolsey and his co-workers on the macacus.

Of the work of these last authors, realized from 350 distinct motor points, we

NOMBRE de MALADES=50 - dont 12 exp.multiples

NBRE. D' ELECT⁵. 242 - 766 points

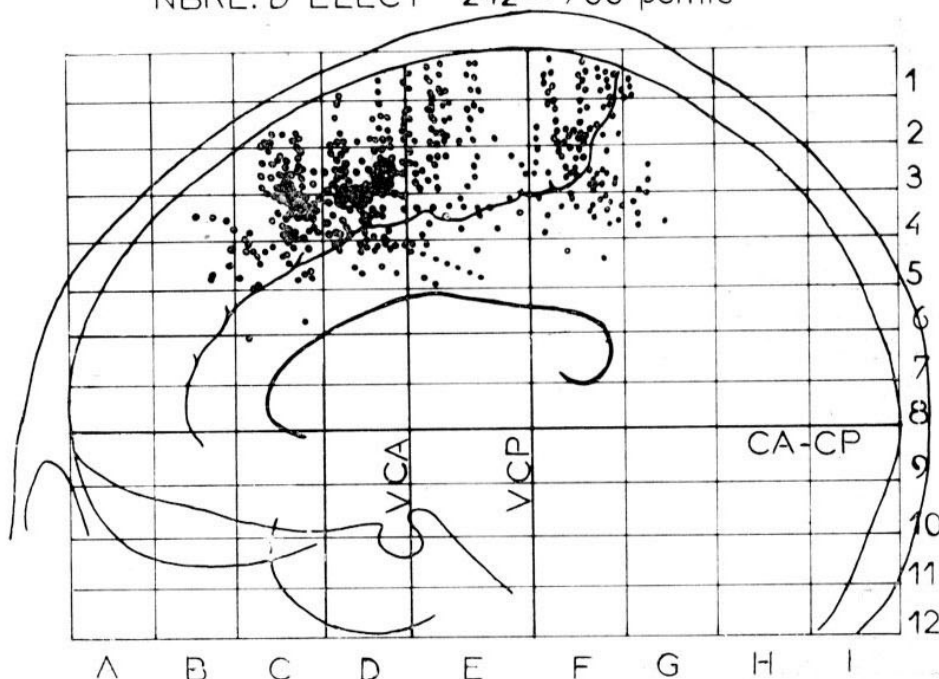


Fig. 1

shall remember only the small dimensions of the semisculus, compared with that of the Rolandic region, its extension to the cingulum, the former position of the head, the median position of the anterior leg and the posterior position of the posterior leg.

In 1957 Coxe and his co-workers describe a similar localization on the *Ateles* which extends, however, ahead of the external face.

In 1958 Showers and Crosby³¹ confirm on the macacus Woolsey's results. Woolsey and his team find in 1960 a similar organization on the chimpanzee and the gibbon.

However from 1959 to 1964 Hughes published several papers on the supracallosal mesial cortex of the cat and the macacus rhesus, explored in chronic conditions. But his conclusions are not identical to those of previous experiments since two felunculi or two semisculi are represented on each internal face set up in mirror fashion on both sides of Rolando's fissure, in apposition at the level of the posterior legs and the tail. Furthermore the cephalic extremities are situated at the level of the *polus frontalis* and *occipitalis* and the cingulum participates altogether to the representation of the homolateral movements. Consequently a

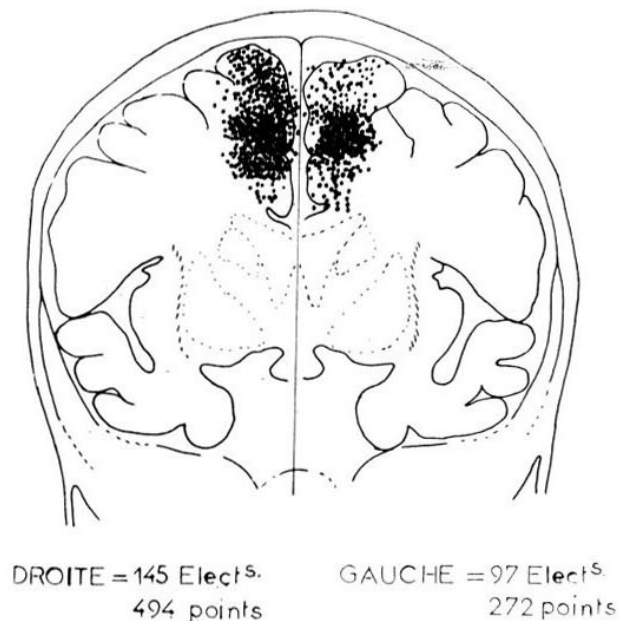


Fig. 2

certain number of difficulties subsist in the definition of the anatomo-functional organization of the supplementary motor area in man still more than in the animal. Several authors still deny its existence, its spatial limits remain unprecised, its functional differentiation is not certain.

As for the projections of the S.M.A. only a number of limited and sometimes contradictory experimental works have been dedicated to this field.

So it was that in 1956 G. Bertrand, while making a comparative analysis of the responses recorded bilaterally at the level of different segments of lateral spinal cord, after stimulation of S.M.A. and of the primary motor area on the macacus, comes to the conclusion that this portion of the mesial face is an integral part of the pyramidal cortex.

Indeed, as far as this author is concerned, the S.M.A. would project directly onto the pyramidal tract and differentiates only from the primary motor cortex by the importance of its ipsilateral fibers.

Yet in 1959 the systematic study of degeneration of the efferent fibers after destruction of the S.M.A. on the macacus forces de Vito and Smith to come to different conclusions. The largest projections concern the homolateral area 4, the S.M.A. and

the area 4 of the contralateral hemisphere through the corpus callosum. At the level of the sub-cortical structures the most important degeneration affects the homolateral capsula interna and the nuclei of the pons on the same side.

The reticular thalamic formations and the sub-thalamic structures are little concerned while the striatum and lateral spinal cord are spared. In these conditions it seems to be a question of a system of multisynaptic projections of double polarity; cortical towards the corresponding primary motor area, axial towards the nuclear formations of the pons.

But many problems arising from the interpretation of clinical events due to stimulation of the S.M.A. in man, outside the field of epilepsy, subsist and deserve to claim attention.

For example, while considering that this region directs essentially the adjustment of postural or tonic movements, Penfield confers it a peculiar role in vocal emission.

Vocalization—considered as a different phenomenon in its determination of arrest of speech, which would be but a suppression of oral movement the same as it would stop a voluntary movement, is excluded from the field of speech.

However in his book with Lamars Roberts, he keeps away from this conception to see in this manner of palilalic expression only the setting into action of the anterior pole of this phasic area, whose pos-

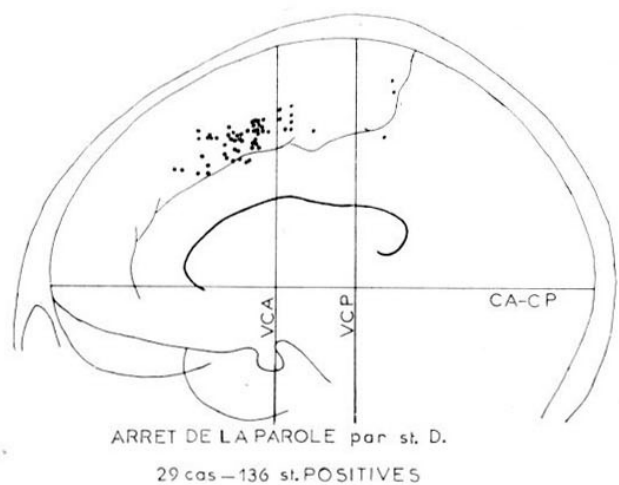


Fig. 3 a

terior portion would be reserved to the understanding.

In this way the S.M.A. becomes in fact a new supplementary area of speech.

The object of this work will therefore be to define the anatomo-functional organization of the supplementary motor area in man.

II. MATERIAL AND METHODS

Our material consists of 50 patients submitted to 62 stereo-EEG explorations, in view of determining the signs and operative procedure of an eventual surgical therapy of epilepsy.

All the cases having been cases of focal cortical epilepsies whose etiology, place of the lesions and seat of origin of the discharges have been established by the clinical, E.E.G. and neuro-radiological examinations, previous to S.E.E.G. investigation and confirmed generally by surgical operations and anatomo-pathological findings.

Ten patients only had a S.M.A. epilepsy but a study of this region was necessary on the other patients because of its eventual setting into action in the course of the fits.

1) Anatomical conditions of the investigation

The laying down of strict anatomo-electro-clinical correlations in the field of epilepsies able to be operated has a meaning only on the basis of strict anatomical location and using a stereotactic technique allowing the setting of a large number of electrodes in the intracranial space.

This precision in the method of reaching the structures, which guarantees the validity of the informations obtained and allows the drawing of anatomo-functional maps, has been defined in previous works given up, in particular, to the diencephalon and to various telencephalic formations.

We can only indicate very schematically here the bases of a new method of location valid for all cortico-sub-cortical structures of the anterior brain. In the sagittal plane

the position of the structures is defined by reference to a system of squaring supported from front to back on the base-line CA-CP and from top to bottom on the verticals which cut it at the level of the two commissures. Its cardinal limits are ensured by the most extreme endocranial bony points at the level of the four lobes.

In this way the position of the different structures is defined by this indirect system of location by reference to the co-ordinates of the squaring which depends, in the case of each brain, on the variable position of the points of support.

As each rectangle of the squaring, varying in dimensions from one patient to another, is a small-scale model, proportional to the large rectangle which embraces it, one can understand that an error in the estimation of the variations of a structure is necessarily limited.

The definition of the structures in the frontal plane is ensured by an identical squaring system, whose lateral limits are ensured by the median line and the extreme endocranial portion of the parietal bone. In the vertical plane their position is estimated by reference to the squaring system placed on the lateral radiography.

In so far as the position of the structures has been defined statistically by a preliminary study of many anatomical serial sections by reference to the squaring system, it becomes possible to report on a common model the position of an electrode introduced into the brain of this or that patient.

In fact this one model can receive with its own coordinates all points of impact of electrodes introduced into the totality of our patients. As a result it is no more a question of an approximate diagram but a means of giving an account on one diagram alone, valid for all explorations, of the variety of concrete informations gathered in each case.

It is a procedure which enables one, without distorting things, to go from the particular to the general.

Of course, the direct locating of certain formation brought to light by fractional

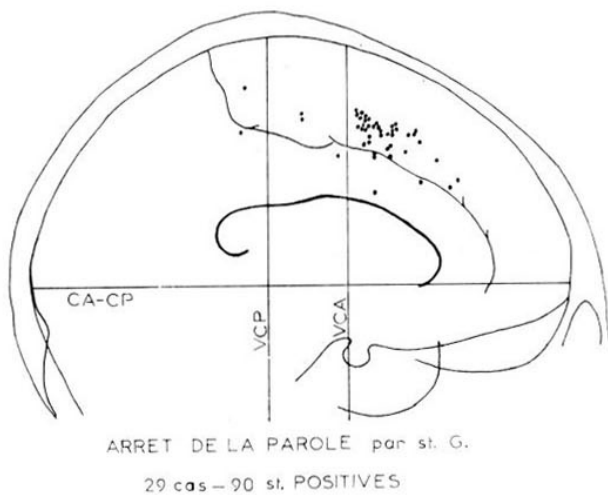


Fig. 3 b

gazeous encephalography, lipiodol ventriculography and angiography, systematically performed in stereotactic conditions on all our patients, adds further precision to indirect locating.

In this particular case the exploration of the cortex of the mesial face is made easier by virtually nearly constant visualization of the calloso-marginal sulcus and corpus callosum, enabling the delimitation of the cingulum.

2) Electro-clinical conditions of investigation

a) S.E.E.G. procedure of investigation.

It is impossible to make a detailed report of an S.E.E.G. investigation into epilepsy.

We had occasion to dwell on this elsewhere.

Let us only say that these 62 operations were performed either in an operating room during some ten hours, on conscious patients, after dissipation of a light anaesthesia or in chronic condition during a fortnight or thereabouts.

These operations required the placing of a large number of intracranial electrodes (more than 4000) in many cortico-sub-cortical structures, which it is pointless to enumerate.

Nevertheless study of the supplementary motor area and the fits which originate there or which secondarily affect it, has compelled us to explore in particular the internal supracallous face from the occipital region to the frontal pole, the gyrus cingulum at the level of its different portions, the corpus callosum at the level of its lateral emergences, the external frontal-central-parietal cortex in particular the areas 4,6 and 8, the orbital face of the frontal lobe, the amygdala and the basal limbic system, the corona radiata, the capsula interna, various thalamic nuclei, in particular VL, the median center, dorsal median, the anterior nuclei group and the reticular pole, the putamen, the pallidum and the nucleus caudatum.

Mostly the investigation of the S.M.A. was bilateral and required placing on the same patient, a large number of electrodes at the level of F1, in order to estimate the manner in which the discharges were propagated and the extent of an eventual epileptogenic zone.

b) Recording and stimulation.

The needles, with multiple contacts, introduced in different planes of the intracranial space, so as to reach in general perpendicularly the mesial face, contain from 5 to 10 electrodes separated by a constant distance of 1mm,5.

The stimulation can be applied conjointly at reception.

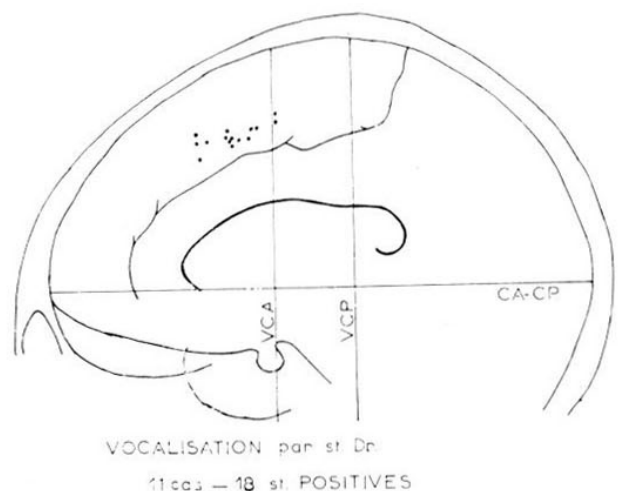


Fig. 4 a

This recording is made permanently on an E.E.G. apparatus with 17 channels which allows to receive simultaneously in bipolar or monopolar derivation 14 different structures, at the same time as are recorded the E.E.G., the E.K.G., the breathing, sometimes the E.D.G. and the muscular activity with coaxial or surface electrodes.

The activity is at the same time received on a cathodic oscillograph. The stimulation is performed in "bipolar" (the distance interelectrodes: 1mm5) using square waves of single direction whose time duration and voltage can be made to vary independently.

These parameters have been standardized according to series in view of obtaining different electro-clinical results in order to test the stimulated region.

Let us simply say that at the level of the S.M.A. the single impulses of long duration (3 ms) and high voltage (up to 15 volts) have been largely used to estimate blow after blow the motor results eventually noted at the setting into action of neighbouring regions.

This kind of stimulus has also been used to determine efferent pathways by studying the latence of the evoked potentials recorded at different levels.

Nevertheless, as in the case of other workers, it has proved mostly indispensable to use train of waves (50 c/s) of 1 ms, of variable voltage and time, working either on the threshold thus avoiding the appearance of after—discharges or continuing the stimulation in order to study the temporal organization of responses.

However we shall come back to this problem when discussing our results.

c) *Observation conditions of the patient.*

Clinical observation of the patient is always made by two neurologists.

The description of the induced phenomena is dictated onto a tape-recorder and repeated on the paper.

The words of the patient, systematically questioned after each stimulation, are recorded and indexed on the E.E.G.

The positive responses are mostly reproduced under the same parameters and under different parameters in identical and different experimental conditions. It is in this way that a disturbance in vocal emission is tested by asking the patient to count, to enumerate objects, to repeat sentences, to read, to describe an event and so on.

Disturbances of motility were estimated in conditions of muscular relaxation or tension, in the course of a spontaneous movement or deliberate action etc. . . .

III. RESULTS

We shall now briefly report our results on the anatomo-functional organization of the supplementary motor area.

Its way of organization will only be determined from the clinical and electrophysiological incidence of central stimulations brought at the level of the cortical structures which sustained its functions, and in their vicinity.

Therefore, in this work, we shall not speak of the disturbances implicated by its excision.

a) *Topographical delimitations.*

1) *Investigation conditions.*

Its topographical delimitation is based on putting on our 50 patients 242 multiple contacts needles representing around 1500 electrodes situated at the level of an extensive region of the two hemispheres. This region embraces from back to front, at the level of the external cortex, the anterior portion of P1 P2, certain parts of the primary sensorimotor region, F1 and F2 to ahead of the area 8, at the level of the mesial face a part of the area said "supplementary sensory" by Penfield, the paracentral lobule, F1 up to the vicinity of the pole and a considerable part of the corona radiata.

One must take note of the fact that the investigation of the mesial face is done by means of some thousand electrodes consi-

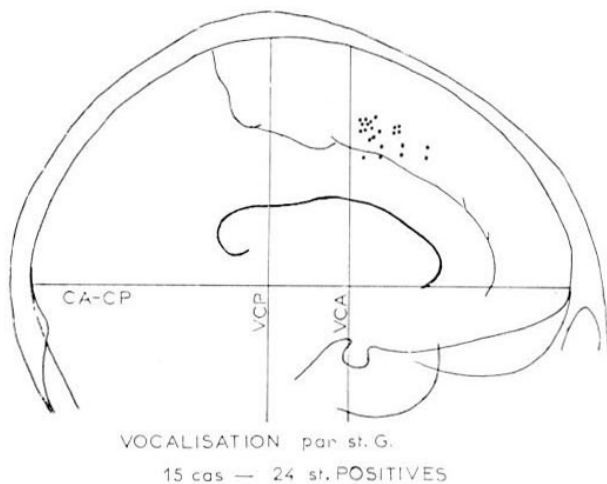


Fig. 4 b

dering the possibility, in the course of operation, of introducing the multiple contact needle, from the external cortex to the median line. 999 stimulations were done, 874 of which at the level of the mesial face.

The stimulation was performed in 378 cases by using single impulses, in 621 cases by using repetitive shocks.

The stimulations of the mesial face touched 766 different points, representing, in fact, two electrodes separated by 1mm5.

The first figure (Fig. 1) shows the position of these points stimulated at the level of the internal cortex and reported onto the grid model of a lateral radiography.

Figure 2 indicates their position in the vertical-frontal plane. It is to be noted only that the stimulated points are more numerous at right than at left and that they cover well a considerable portion of the first frontal gyrus and the cingulum.

2) Modalities of responses at the level of the S.M.A.

Of the 874 stimulations done at the level of the mesial face only 662 induce clinical responses.

The lack of responses during the 212 stimulations is due to stimuli done by means of single impulses.

So, of 662 clinical responses, 482 can be schematically understood, in Penfield's terminology, as speech arrest, vocalization, a raising with abduction of the upper limb,

and a deviation of the head and eyes obtained from more than 300 different points.

Figure 3 shows the position of points whose stimulation induces a speech arrest.

This type of response is obtained 226 times on all our patients.

One observes that the distribution of points is practically identical right and left.

Finally these responses are obtained as frequently on the right as on the left.

On the other hand (figure 4) vocalization is only induced on 26 patients, that is to say only on half of them.

The distribution of points is also the same on the right and on the left.

Neither does there exist any predominance of side.

Important fact-stimulation of the same points can lead to either speech arrest or vocalization.

As for the tonic raising of the upper limb (Figure 5) this is obtained 117 times on 41 patients.

The distribution of points is, of course, identical at right and left but it should be noted that the dispersion is greater than for speech arrest and vocalization.

Especially if one analyzes the parameters of stimulation one notices that the most posterior responses, placed behind the line VcA, are obtained with a small voltage and sometimes without concomitant arrest of speech.

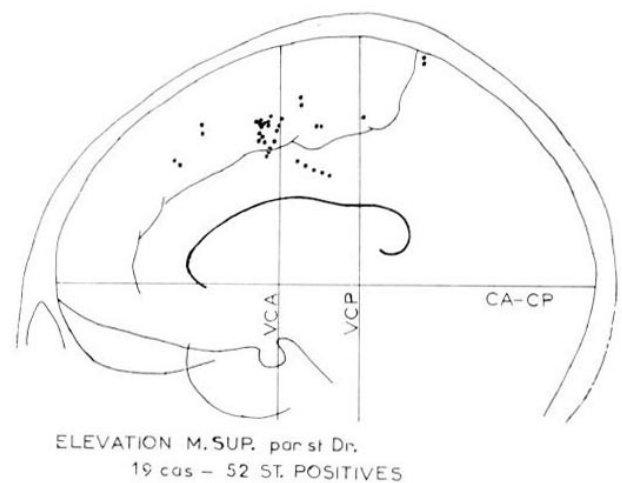


Fig. 5 a

Finally deviation of the eyes and head is obtained (Figure 6) 97 times on most of our patients, as with raising of the arm.

There again the distribution of the responses is the same at right and left, but one notices above all that they extend ahead of the region in which the motor points of the upper limb are placed and probably the one where disturbances of vocal emission are produced.

Figure 7, which receives, in limited number, the points whose stimulation induces clinical responses determining, for Penfield, the essential functions of the S.M.A., makes it now possible to estimate its limits at the level of the mesial face. Let us say, consequently, that it is situated ahead of the primary motor area of the foot, that it extends at the level of F1 right up to the upper lip of the cingulum but without including it—and that its front-back dimensions are small (around 5 cm).

The important density of positive responses over a distance of less than 2 cm immediately ahead of the line VcA makes—important fact—its stereotactic approach extremely easy.

The posterior, inferior and anterior limits once determined, its upper limit remains to be defined by examination of the responses obtained at the level of the external face.

We notice that on the 125 stimulations done—it is true 63 by single impulses—99 remain negative at the level of the area 6. The 25 positive responses are due to the setting in motion of the Rolandic area.

Only once, for a very high voltage, inducing an after-discharge propagated to the mesial face, does one notice an arrest of speech.

Thus, if Penfield's opinion on the role of area 6 is confirmed, it does not seem contrary to this author's hypothesis that the S.M.A. extends onto the lateral face of the hemisphere.

Yet our findings are also in disagreement with his on two important problems.

It was not possible for us, in spite of the great number of stimulations done under nevertheless different parameters to ascer-

tain a supplementary area of speech ahead of the one devoted to the primary motility of the foot.

Furthermore the responses obtained at the level of the mesial face of the parietal lobe, and which we shall report in detail in a later work, do not allow us to confirm the hypothesis of a supplementary sensory area.

In all the cases, the positive stimulations set into action the S.M.A., which seems to us to be the cause of the described manifestations.

Before discussing the eventual somatotopic organization of the S.M.A. two questions deserve comment.

Firstly, this region does not seem to participate in important sensori-vegetative regulations.

Indeed 16 times only the stimulation induced mydriasis on 15 different patients, and once a hastening of the heart, although there is a permanent electro-cardiographical control.

Particularly the fact that it was impossible to reproduce these manifestations during a later stimulation on the same patient, seems to us an important argument in favour of relating them rather to a global emotive reaction aroused by some other cause.

On the other hand the vegetative disturbances are common if the stimulation of the S.M.A. induces an ictal discharge propagated through the cingulum to the limbic basal structures.

We know, at last, that the problem of homolateral responses by stimulation of the S.M.A. has aroused controversy.

Let us say at once that our experience does not confirm the opinion of Bates.

Indeed the lower limb never undergoes isolated ipsilateral tonic modification. Sometimes the motor manifestations involve both extremities almost simultaneously, but precession is in favour of the opposite side.

On the other hand three times, raising the upper limb is homolateral at the time of stimulation but is very quickly followed by an identical movement of the other arm. The three patients were suffer-

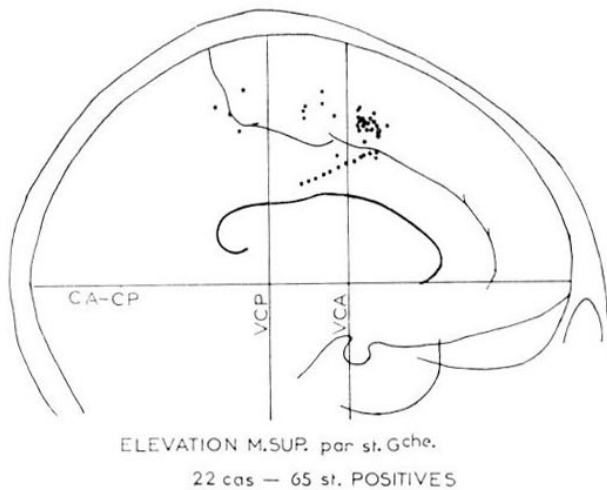


Fig. 5 b

ing from an epileptogenous lesion of the S.M.A. Twenty two times on 8 patients, the eyes were deviated towards the stimulated hemisphere, but on 4 of them this preceded a tonico-clonic fit. The other four were afflicted with epilepsy of the S.M.A.

In other words, our results agree with Penfield's; if the stimulation is done at low voltage or if the S.M.A. has a normal threshold, the results are generally contralateral.

b) "Somatotopic" organization.

The possible somatotopic organization of the S.M.A. raises a complex problem even in animals; considerable differences exist among species, but also among authors. Outside a primary region the establishment of a homunculus presents obvious difficulties due firstly to the necessity of using repetitive stimulations easily propagated in order to obtain progressively installed complex motor phenomena, but also with the different threshold demanded by the varied responses. Furthermore, we were struck by the type of organization of the S.M.A. This organization is such as two identical stimulations done at a distance of 1mm5 are capable of giving different responses. In these conditions the establishment of a somatotopic organization would demand a particularly dense punctiform investigation.

Nevertheless we have already noticed that, in spite of the possible intricacy of

different responses, there is a density of homogeneous points which suggests a somatotopic organization.

Indeed if the arm tonic responses are the most posterior, those relating to vocalization are situated in the middle portion of the area, whereas those representing the eye movements are more anterior.

Once again it is a question only of a greater relative majority of these various types of responses at different levels, but this ought to leave a serious doubt as to the absence of all somatotopic organization.

Moreover study of the clinical manifestations induced by single impulses at the level of the S.M.A. raises a special problem.

Indeed out of 328 stimulations of the supracallosal mesial cortex 116 responses were obtained, 82 of them situated in the supplementary area. 53 times they affected the face and in particular the tongue, the diaphragma oris muscles, the labial commissures and probably the pharyngo-laryngeal muscles. The arm was affected 17 times especially at its rhizomelic level, whilst the hand is never affected. 8 times the responses concerned simultaneously the face and arm, 4 times the arm and leg.

These clonic type responses are perhaps due to the setting into action of fibres belonging to the primary motor area, but their topographical distribution is identical to those of the complex tonic results

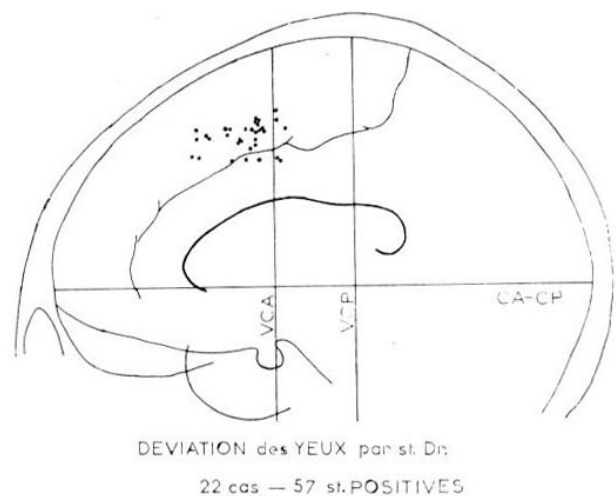
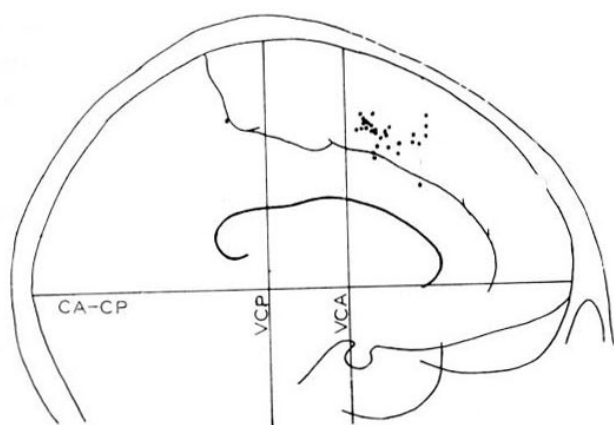


Fig. 6 a



DEVIATION des YEUX par st. G.
20 cas - 40 st. POSITIVES

Fig. 6 b

of the S.M.A. affecting the same segments of the body.

It remains impossible for us to obtain responses from the lower limb with a view to revealing a somatotopic organization.

However, if one thinks that its primary motor delimitation in man covers a small surface and that the supplementary area of the foot limited to a narrow strip on the

macacus is situated just beneath the former, the existence of a truncated homunculus is perhaps explained.

c) Efferent projections.

We shall deal very briefly with the efferent projections of the S.M.A. which will be the object of a later work with Buser—all the the more so since this is a complex problem on which as yet little light has been thrown.

Electro-clinical and electro-physiological studies show however that the S.M.A. projects onto the homologous contralateral area, firstly through the corpus callosum but also towards the extrapyramidal homologous portion of the capsula interna and not in its motor portion, as shown by figure 8, borrowed from Buser.

We see that stimulation of the S.M.A. evokes a brief latency potential at the level of the anterior portion of the posterior arm of the capsula interna, whereas neither the motor fibres nor the pallidum are affected.

Besides, the stimulation of this capsular

VOCALISATION
ARRET de la PAROLE
DEVIATION des YEUX
ELEVATION M.SUP.

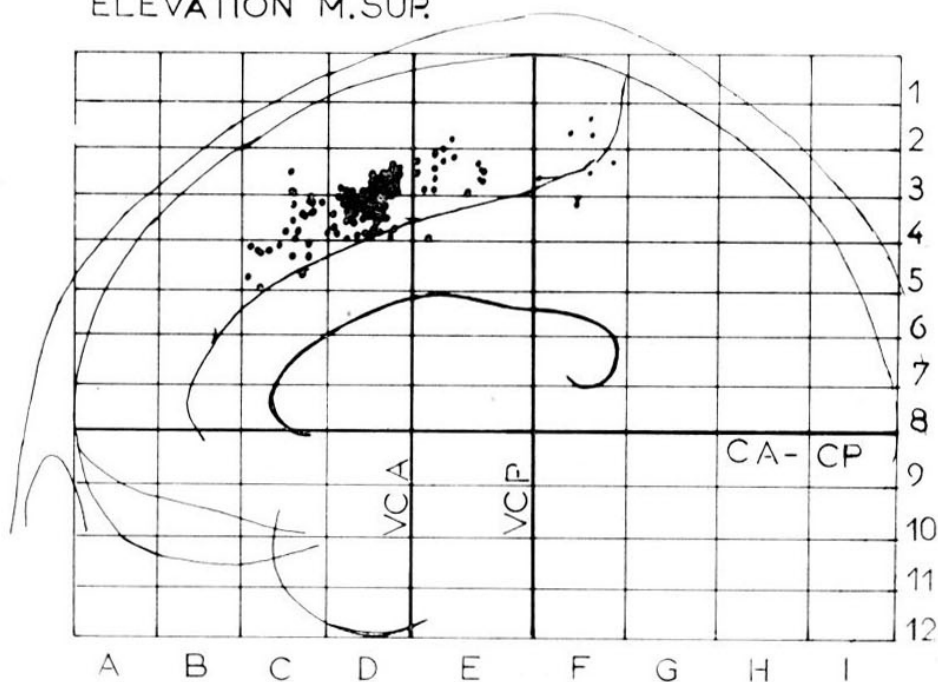


Fig. 7

portion evokes a response in the S.M.A., stimulus of the pallidum remaining ineffective.

The other striated nuclei play a secondary role in the motor regulations which they subtend. Their projections towards the thalamic nuclei are secondary with the exception perhaps of the median centre. Finally, the cingulum in physiological conditions, is not implicated in its sub-cortical efferences, and neither is the basal limbic system. These statements coincide with de Vito's and Smith's conclusions. But the important problem of its relations with the areas 6 and 4 at the cortical level demands further investigation. We have seen, how-

ever, that the S.M.A. probably exercises a direct control on the voluntary motility even if it belongs, without any doubt, to a quite different system.

d) *Functional significance of the S.M.A.*

How can one, in these conditions, envisage the functional significance of the S.M.A. considered first by Penfield as playing an essential part in controlling postural movements and then, in fact, as a quaternary area of speech?

A likely methodological remark is called for; if in order to determine its cortical li-

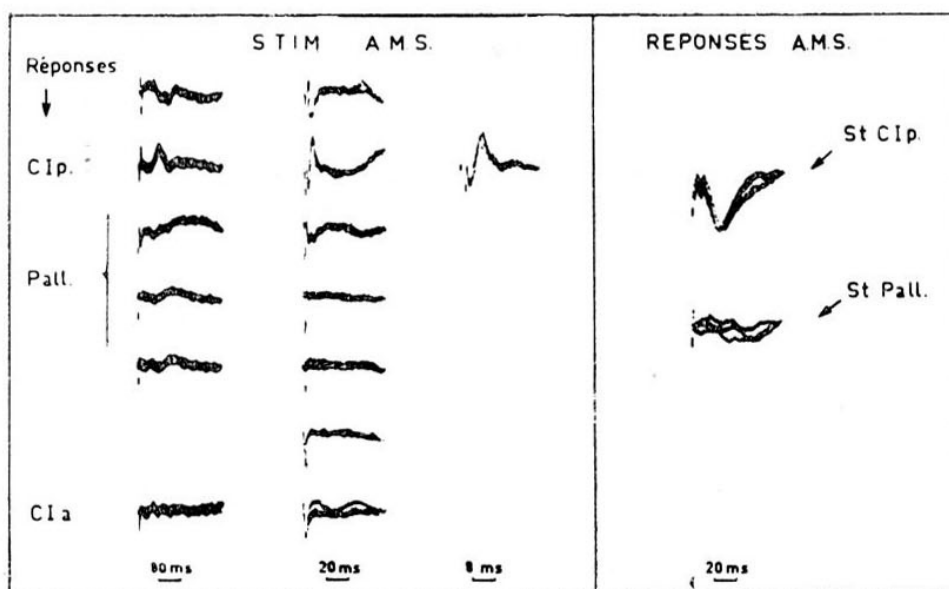


Fig. 8

mits we isolated various clinical manifestations induced by stimulation, it would be naïve to believe that they show the mechanism of its normal functioning. Furthermore the simple statistical analysis of the results, based on the stimulation parameters, is sufficient to convince us of this. Indeed, even if these responses have a different topography, their identical threshold of attainment for a same phenomenon varies considerably from one method to another.

This is why a very low voltage is required for arrest of speech, whereas the rais-

ing of the upper limb, apart from all propagated post-discharge demands a much higher voltage or a current of longer duration.

This difference of threshold of responses, which bears witness no doubt to the variable modalities of recruitment, explains their temporal intricacy when prolonged stimulation is applied to the same point. One understands, in these conditions, why speech arrest precedes progressive raising of the contralateral upper limb whilst deviation of the head and eyes is but beginning.

In this way a complex postural movement is induced, which can moreover secondarily affect the lower limb.

This manner of regulation of the tonic motility cannot but remind one of that which the primary area exercises over the skeletal musculature, although it is subtended by a completely different system and involves a completely different cortical organization.

Speech arrest and vocalization seem to constitute an astonishing enclave in this homogeneous whole. We shall see, however, that this is not the case and that these two closely linked phenomena are but two modalities of faulty motor functioning at the level of the vocal apparatus.

Firstly, we should notice that abrupt arrest of speech may be preceded by a progressive locking of the speech if a low voltage is used. Better still, if the stimulations are applied singly, they will determine the rhythm of counting. Under a higher frequency, for example 3 c/s, speech is literally cut up in rhythm to the stimulations. One notices then, and the E.M.G. recording confirms it, that parasitism is due to often bilateral clonic movements of the buccal-pharyngo-laryngeal apparatus. At 50 c/s its fragmentary jerks are knit together and te-

tanization of the vocal muscles prevents verbal utterance.

Such facts, of course, do not mean that the organization of the S.M.A. is identical to that of the somatomotory area. The mechanisms which control the elaboration of these jerks have yet to be defined.

Moreover, we have already noticed that vocalization was obtained from points identical to those whose stimulation induces speech arrest but a higher voltage is required.

In these conditions it seems to us impossible to dissociate it from speech arrest. We think that it simply represents another modality of motor disturbance of the vocal apparatus, contrary to the opinion of Alajouanine and his co-workers. Moreover its exclusion from the domain of the spoken word is indispensable in so far as the palilalia is also found in different macaci, and that it is possible depending on the stimulation parameters to impose on man a rhythm ring and pitch which are in relation to the tension placed on the buccal-pharyngo-laryngeal muscles.

If one adds to these facts the impossibility of discovering the speech area 4 described by Penfield, we see that the S.M.A. is completely devoted to the organization and control of postural movements and of tonic motility.

SUMMARY AND CONCLUSIONS

1. — Since the time the supplementary motor area was clearly shown to exist in man by W. Penfield and his school (1948 to 1951) few works have been devoted to the study of this region, particularly in epilepsy, due mainly to the difficulty of its surgical approach.

By means of an original technique of anatomic stereotactic locating of the cortical and sub-cortical formations, which made it possible to reach accurately the structures of the supracallosal mesial face, the authors intend to tackle the problem of the functional organization of the S.M.A., in order to get a better idea of the electro-

clinical modalities of the epileptic fits which originate there.

Their material consists of 50 patients who undergo 62 stereo-electroencephalographical investigations in order to determine the signs and operative modalities of an eventual surgical therapy.

The explorations required placing a large number of intracranial electrodes (more than 4000) either in acute or chronic condition on conscious patients.

Some 1000 stimulations, under different parameters, were done at the level of the internal and external cortex of the frontal region, from 766 different points.

II. The anatomo-functional organization of the S.M.A. may be defined as follows:

1) The limits of this region have been defined as corresponding to a small area of the internal cortex of F1, ahead of the foot primary motor area, above the gyrus cingulum and not overlapping onto the external face at the level of area 6. Most of the responses are obtained from a reduced area situated in front of the VCA perpendicular at the bi-commissural base-line.

2) Contrary to Penfield's opinion, the S.M.A. is not separated from area 4 by a strip of cortex which can play the part of integrating the speech at the level of the dominant hemisphere.

3) It is probable that the S.M.A. admits a somatotopic organization: the face is situated ahead of the upper limb; yet the responses at the level of the foot are difficult to prove, probably for technical reasons.

4) The various manifestations obtained at the threshold by electric stimulus are due to an intra-cortical differentiation and with the setting into action of the efferent pathways, composing a system completely different from that of area 4.

5) Electro-clinical and electro-physiological studies show that the S.M.A. pro-

jects onto the homologous contralateral area first through corpus callosum and also to the brain stem through the extrapyramidal portion of capsula interna. On the other hand S.M.A. has no close relations with area 6 at the level of the external face.

The striated nuclei, in peculiar putamen and pallidum, play a secondary part in motor adjustments which the S.M.A. subtends.

Its projections towards the thalamic nuclei are not very important. Finally, in physiological conditions, the gyrus cingulum is not involved in its sub-cortical efferences.

6) From the clinical point of view the role of S.M.A. seems to us to be limited to the adjustment of tonic movements, the trunk, neck, shoulder, upper limb, head and eyes and bucco-pharyngeal musculature. In these conditions the arrest of speech and paroxysmal palilalia, which in our opinion are of identical nature, are but the expression of a tonic modification of variable intensity of the vocal apparatus and seem to us to be the equivalent of a "vocal grasping".

If the postural manifestations contralateral to stimulus are predominant, the homolateral efferent tract has a much greater capsular representation than the one belonging to the pyramidal tract.

RESUMEN Y CONCLUSIONES

1. Desde el momento en que fue demostrada la existencia de un área motora suplementaria en el hombre por W. Penfield y su escuela (1948 a 1951) pocos trabajos han sido dedicados al estudio de esta región, particularmente en la epilepsia, debido a las dificultades de su aproximación quirúrgica.

Mediante una original técnica de localización estereotáxica de las formaciones corticales y subcorticales, que hizo posible llegar en forma adecuada a las estructuras de la cara interna supracallosa, los autores intentan abordar el problema de la organización funcional del A.M.S., a fin de lograr un mejor conocimiento de las particulari-

dades electro-clínicas de las crisis epilépticas que allí se originan.

Para el presente estudio se han explorado 50 pacientes sometidos a 62 investigaciones estéreo-electroencefalográficas con el fin de determinar signos y particularidades operatorias de un posible tratamiento quirúrgico.

Las exploraciones hicieron necesaria la colocación de gran cantidad de electrodos (más de 4000) tanto en casos agudos como crónicos de pacientes concientes.

Fueron efectuadas alrededor de 1000 estimulaciones a diferentes parámetros, a nivel de la corteza interna y externa de la región frontal desde 766 puntos diferentes.

II. *La organización anatómo-funcional del A.M.S. puede definirse de la siguiente manera:*

1) Los límites de esta región fueron definidos como un área pequeña de la corteza interna de F1 delante del área motora primaria del pie, por encima del giro cingulado y no volcada hacia la cara externa a nivel del área 6. La mayoría de las respuestas se obtienen desde un área reducida situada delante de ACV dispuesta perpendicularmente a la línea de base bicomisural.

2) Contrariamente a la opinión de Penfield, el A.M.S. no está separada del área 4 por una banda cortical que puede desempeñar la función de integrar el habla a nivel del hemisferio dominante.

3) Es probable que el A.M.S. admita una organización somatotópica: la cara está situada delante del miembro superior; sin embargo las respuestas a nivel del pie son difíciles de obtener, probablemente por razones técnicas.

4) Las diversas manifestaciones obtenidas en el umbral por estimulación eléctrica se deben a una diferenciación intracortical y con la puesta en acción de las vías eferentes componiendo un sistema completamente distinto al del área 4.

5) Los estudios electroclínicos y electrofisiológicos demuestran que el A.M.S. se proyecta contra el área contralateral homó-

loga primero a través del cuerpo calloso y también contra el tronco cerebral a través de la porción extrapiramidal de la cápsula interna. Por otro lado la A.M.S. no tiene una relación estrecha con el área 6 a nivel de la cara externa.

Los núcleos estriados, el putamen y el pallidum, desempeñan un papel secundario en los ajustes motores que conciernen al A.M.S.

Sus proyecciones hacia los núcleos talámicos son poco importantes. Por último, en condiciones fisiológicas, el giro cingulado no está involucrado en sus eferencias subcorticales.

6) Desde el punto de vista clínico el papel desempeñado por la A.M.S. nos parece estar limitado al ajuste de movimientos tónicos de la musculatura del tronco, cuello, miembro superior, cabeza, ojos, boca y faringe. En estas condiciones la desaparición del lenguaje y la palilalia paroxística, que en nuestra opinión son de naturaleza idéntica, no son sino la expresión de una modificación tónica de intensidad variable del aparato vocal y nos parecen equivalentes a un "grasping" vocal.

Si predominan las manifestaciones posturales del lado opuesto al estimulado, las vías homolaterales tienen una representación capsular mucho mayor que la correspondiente a las vías piramidales.

RÉSUMÉ ET CONCLUSIONS

1. Depuis le moment où W. Penfield et son école démontrèrent l'existence d'une aire motrice dans l'homme (1948 à 1951) peu de travaux ont été consacrés à l'étude de cette région, particulièrement dans des cas d'épilepsie, à cause des difficultés qu'implique leur approche chirurgicale.

Par moyen d'une originale technique de localisation stéréotaxique des formations corticales et sous-corticales, qui a permis d'atteindre convenablement la face interne supracallosum, les auteurs essayent d'aborder le problème de l'organisation de l'A.M.S., afin d'obtenir des connaissances plus précises sur les particularités électro-

cliniques des crises épileptiques qui commencent dans cette région.

Pour cette étude on a examiné 50 patients soumis à 62 investigations stéréoelectroencéphalographiques afin de déterminer des signes et des particularités opératives d'un possible traitement chirurgical.

Les explorations ont demandé le placement d'une grande quantité d'électrodes (plus de 4000) aussi bien dans des cas aigus que dans des cas chroniques de patients conscients.

On a fait près de 1000 stimulations à des paramètres différents, au niveau de l'écorce

interne et interne de la région frontale provenant de 766 points différents.

II. L'organisation anatomo-fonctionnelle de l'A.M.S. peut être définie de la façon suivante:

1) Les limites de cette région ont été définies comme une petite aire de l'écorce interne de F1 devant l'aire motrice primaire du pied, par dessus le gyrus cingulé et non penchée sur la face externe au niveau de l'aire 6. La plupart des réponses sont obtenues d'une aire réduite située devant ACV et disposée perpendiculairement à la ligne de base bicommissurale.

2) Contrairement à l'opinion de Penfield, l'A.M.S. n'est pas séparé de l'aire 4 par une bande corticale qui peut avoir la fonction d'intégrer le langage au niveau de l'hémisphère dominant.

3) Il est probable que l'A.M.S. admette une organisation somatotopique: la figure est située devant le membre supérieur; cependant les réponses au niveau du pied sont difficiles à obtenir; ceci est du probablement à des raisons techniques.

4) Les différentes manifestations obtenues par stimulation électrique dans le seuil sont dues à une différenciation intracorticale avec la mise en marche des voies efférentes composant un système totalement différent de celui de l'aire 4.

5) Les études électrocliniques et électrophysiologiques démontrent que l'A.M.S.

se projette contre l'aire contralatérale homologue, d'abord à travers le corpus callosum, et aussi contre le tronc cérébral à travers la portion extrapyramidale de la capsule interne. D'autre part l'A.M.S. ne garde pas une relation étroite avec l'aire 6 au niveau de la face externe.

Les noyaux striés, le putamen et le pallidum jouent un rôle secondaire dans les ajustements moteurs et sont en relation avec le A.M.S.

Ses projections vers les noyaux thalamiques sont peu importantes. Finalement, dans des conditions physiologiques le gyrus cingulé n'est pas impliqué dans ses efférences sous-corticales.

6) Du point de vue clinique le rôle joué par l'A.M.S. nous semble être limité à l'ajustement de mouvements toniques de la musculature du tronc, du cou, du membre supérieur, de la tête, des yeux, de la bouche et du pharynx. Dans ces conditions la disparition du langage et la palilalie paroxystique, qui à notre avis sont de nature identique, ne sont que l'expression d'une modification tonique d'intensité variable de l'appareil vocal et nous semblent équivalents à un "grasping" vocal.

Si ces manifestations posturales dominent du côté opposé au côté stimulé les voies homolatérales ont une représentation capsulaire beaucoup plus large que celle qui correspond aux voies pyramidales.

ZUSAMMENFASSUNG

1. Seitdem Penfield und seine Schule eindeutig demonstriert haben, dass es ein supplementäres motorisches Feld gibt (1947-1951), haben sich wenige Arbeiten mit dem Studium dieser Region beschäftigt, besonders bei der Epilepsie, und dies hauptsächlich wegen der Schwierigkeit einer chirurgischen Annäherung.

Mittels einer originellen Technik anatomischer stereotaktischer Lokalisation der kortikalen und subkortikalen Formationen, welche es möglich machte genau an die Strukturen der supracalloesen medialen Seite zu gelangen, beabsichtigen die Autoren

des Problems der funktionellen Organisation des S.M.A. Herr zu werden, um einen besseren Einblick in die elektroklinischen Modalitäten der epileptischen Anfälle, die dort entstehen, zu gewinnen.

Ihr Material besteht aus 50 Patienten, die 62 stereo-elektroencephalografischen Untersuchungen unterzogen worden waren, um die Zeichen und die operatorischen Modalitäten bei einer späteren chirurgischen Therapie festzustellen.

Die Exploration bestand darin, eine grosse Anzahl (mehr als viertausend) intrakranielle Elektroden bei akuten oder chroni-

schen Erkrankungen der bei Bewusstsein befindenden Patienten anzulengen. Etwa 1000 Stimulierungen, bei verschiedenen Parametern wurden an der inneren und äusseren Rinde der Frontalregion von 766 verschiedenen Punkten aus ausgeführt.

II — Die anatomisch funktionelle Organisation des S.M.A. sei in folgender Weise definiert:

1) Die Grenzen dieser Region entsprechen einer kleinen Zone der inneren Rinde von F1, vor dem Fuss der primitiven motorischen Zone, ueber dem Gyrus cingulum, wobei sie nicht die äussere Seite teilweise ueberdeckt auf der Hoehe von Feld 6. Die meisten Reaktionen erhaelt man von einer kleinen Zone gegenueber der VCA und senkrecht zur bikommissuralen Basallinie.

2) Im Gegensatz zu Penfield's Meinung, ist die suplementaere motorische Zone nicht vom Feld 4 durch eine Rindenlinie abgeteilt, die die Rolle einer Integrierung der Sprache in der praedominierenden Hemisphaere spielen kann.

3) Es ist wahrscheinlich, dass die suplementaere motorische Zone eine somatotopische Organisation zulaesst; Das Gesicht liegt vor der oberen Gliedmasse; jedoch die Reaktionen in der Gegend des Fusses sind schwer nachzuweisen, wahrscheinlich aus technischen Gruenden.

4) Die verschiedenen Manifestationen, die man an der Schwelle durch elektrische Reizung erhalten hat, sind durch eine intrakortikale differenzierung bedingt und durch das in Aktivitaet setzen der efferenten Pfeiden stellen sie ein System dar, das vollkommen verschieden von Feld 4 ist.

5) Elektroklinische und elektrophysiologische Studien haben gezeigt, dass die suplementaere motorische Zone Wege nach der homologen kontralateralen Zone zuerst durch das Corpus Callosum und dann auch nach den Hirnstamm durch die extrapyramidale Portion der Capsula interna aussendet. Andererseits hat die motorische Zone keine engen Beziehungen mit dem Feld 6 in der Gegend der äusseren Seite. Die Kerne des Nucleus striatus, besonders Putamen und Pallidum, spielen eine sekundaere Rolle bei den motorischen Korrekturen die das S.M.A. unterhaelt.

Ihre Projektion nach den Thalamus-Kernen sind nicht sehr wichtig. Schliesslich, unter physiologischen Bedingungen, ist der Gyrus cingulum nicht an den subkortikalen Efferenzen beteiligt.

6) Vom klinischen Standpunkt aus scheint uns die Rolle der suplementaeren motorischen Zone darauf beschraenkt zu sein, die tonischen Bewegungen von Rumpf, Hals, Schultern, oberen Gliedmassen, Kopf und Auge und die bucco-pharyngeale Muskulatur fein abzustimmen. Unter diesen Bedingungen sind die Stockung der Sprache und die paroxistische palilalie, welche unserer Meinung nach identischer Natur sind, nur der Ausdruck einer tonischen Modifizierung verschiedener Intensitaet, des vokalen Apparates und scheint fuer uns das Equivalent eines "vokal-haltens" zu sein. Wenn die Haltungsmanifestationen Kontralateral zum Reiz vorherrschend sind, hat der homolaterale efferente Trakt eine groessere kapsulaere Repraesentation als diejenige die zum Pyramidaltrakt gehoert.

REFERENCES

1. Alajouanine, Th.; Castaigne, P.; Sabouraud, O. et Contamin, F.: Palilalie paroxystique et vocalisations itératives au cours de crises d'épilepsie par lésion de l'aire motrice supplémentaire. Rev. Neurol., 1959, 101, 6, 685-697.

2. Bancaud, J.: Apport de l'exploration fonctionnelle par voie stéréotaxique à la chirurgie de l'épilepsie. Neurochirurgie, 1959, 5, 55-112.

3. Bancaud, J. et Dell, M. B.: Techniques et méthodes de l'exploration fonctionnelle stéréotaxique des structures encéphaliques chez l'homme. Rev. Neurol. 1959, 101, 220-221.

4. Bancaud, J.; Talairach, J.; Schaub, C.; Bonis A.; Szikla, G. et Colomb, P.: Stereotaxic functional exploration of the supplementary areas of the mesial surface of the

hemisphere. EEG and Clin. Neurophysiol. 1962, 14, 5:788.

5. Bancaud, J.; Talairach, J.; Schaub, C.; Bonis, A.; Szikla, G.; Morel, P. et Bordas-Ferrer, M.: Informations neurophysiopathologiques apportées par l'investigation fonctionnelle stéréotaxique (SEEG) dans les épilepsies. Rev. Neurol. 1963, 108, 2, 81-86.

6. Bancaud, J.; Talairach, J.; Bonis, A.; Schaub, C.; Szikla, G.; Morel, P. et Bordas-Ferrer, M.: La stéréo-électroencéphalographie dans l'épilepsie. Paris, Masson et Cie, 1965, 321 pp.

7. Bancaud, J. et Talairach, J.: L'épilepsie de l'aire motrice supplémentaire: un diagnostic particulièrement difficile chez l'enfant. Rev. de Neuropsych. inf. 1965, 13, 6-7, 483-499.

8. Bancaud, J. et Talairach, J.: Organisation fonctionnelle et physiopathologie de l'aire motrice supplémentaire (enseignements apportés par la SEEG). Neurochirurgie 1966 (sous presse).

9. Bates, J. A. V.: Brain 1953, LXXVI: 405-407.

10. Beevor, C. E. and Horsley, V.: A record of the results obtained by electrical excitation of the so-called motor cortex and internal capsule in an orang-outang (*Simia satyrus*). Philos. Tr. Roy. Soc. London, 1890, 181 B, 129-158.

11. Bertrand, G.: Spinal efferent pathways from the supplementary motor area. Brain, 1959, 79:179-222.

12. Brickner, R. M.: A human cortical area producing repetitive phenomena when stimulated. J. Neurophysiol. 1940, 3: 128-130.

13. Coxe, W. S.; Hirsch, J. F.; Benjamin, R. M.; Welker, W. I.; Thompson, R. F. and Woolsey, C. N.: Precentral and supplementary motor areas of Ateles. Physiologist, 1957, 1:19.

14. Denny-Brown, D.: Selected writings of sir Charles Sherrington. London, Hamish Hamilton, 1939, 532 pp.

15. De Vito, J. L. and Smith, O. A.: Projections from the mesial frontal cortex (supplementary motor area) to the cerebral hemispheres and brain stem of the macaca mulatta. The Journal of comp. Neurol. 1959, 111, 2:262-277.

16. Erikson, V. and Woolsey, C. N.: Observations on the supplementary motor area of man. Trans. Amer. Neurol. Ass. 1951, 50-52.

17. Foerster, O.: The motor cortex in man in the light of Hughlings Jackson's doctrines. Brain, 1936, 59:135-159.

18. Horsley, V. and Schäfer, E. A.: A record of experiments upon the functions of the cerebral cortex. Philos. Tr. Roy. Soc. London, 1888, 179 B: 1-45.

19. Hughes, J. R.: Studies on the supracallosal mesial cortex of unanesthetized, conscious mammals. I. Cat. A. Movements elicited by electrical stimulation. EEG & Clin. Neurophysiol. 1959, 11:447-458.

20. Hughes, J. R. and Mazurowski, J. A.: Studies on the supracallosal mesial cortex of unanesthetized, conscious mammals. II. Monkey. A movements elicited by electrical stimulation. EEG & Clin. Neurophysiol. 1962, 14:477-485.

21. Penfield, W. and Rasmussen, T.: Vocalization and arrest of speech. Arch. Neurol. & Psychiat. 1949, 61, 21-27.

22. Penfield, W. and Welch, K.: The supplementary motor area in the cerebral cortex of man. Trans. Am. Neur. Assoc. 1949, 74:179-184.

23. Penfield, W.: The supplementary motor area in the cerebral cortex of man (Published as part of the 80th and 75th birthday volume for Oskar and Cecil Vogt). Arch. Psychiat. 1950, 185:670-674.

24. Penfield, W. and Rasmussen, T.: The cerebral cortex of Man. New York, McMillan, 1950, 248 pp.

25. Penfield, W. and Kristiansen, K.: Epileptic seizure patterns. Springfield Ill. Thomas, 1951, 104 pp.

26. Penfield, W. and Welch, K.: The supplementary motor area of the cerebral cortex. Arch. Neurol. & Psychiat. 1951, 66: 289-317.

27. Penfield, W. and Jasper, H.: Epilepsy and the functional anatomy of the human brain. London, Churchill, 1954, 896 pp.

28. Penfield, W. and Roberts, L.: Speech and brain mechanisms. Princeton, N. J., Princeton University Press, 1959, 286 pp.

29. Petit-Dutaillis, J.; Guiot, G.; Messimy, R.; Bourdillon, Ch.: A propos d'une aphémie par atteinte de la zone motrice supplémentaire de Penfield, au cours de l'évolution d'une anévrisme artério-veineux Guérison de l'aphémie par ablation de la lésion. Rev. Neurol. 1954, 90, 2:95-106.

30. Robb, J. P.: Effect of cortical excision and stimulation of the frontal lobe on speech. A. Res. Nerv. and Ment. Dis. 1948, 27, 587-609.

31. Showers, M. J. C. and Crosby, E. C.: Somatic and visceral responses from the cingulate gyrus. Neuro. 1958, 8-7:561-565.

32. Talairach, J.; David, M.; Tournoux, P.; Corredor, H. et Kvasina, T.: Atlas d'ana-

tomie stéréotaxique. Paris, Masson et Cie, 1957, 294 pp.

33. Talairach, J.; David, M. et Tournoux, P.: L'exploration chirurgicale stéréotaxique du lobe temporal dans l'épilepsie temporale. Paris, Masson et Cie Ed., 1958, 136 pp.

34. Talairach, J.; Bancaud, J.; Bonis, A.; Szikla, G. et Tournoux, P.: Functional stereotaxic exploration of epilepsy. Conf. Neurol. 1962, 22:328-330.

35. Talairach, J. et Bancaud, J.: Processus de l'investigation fonctionnelle dans la neurochirurgie stéréotaxique. Neurophysiologie et neuropsychophysiopathologie in Actuelles neurophysiologiques, Paris, Masson et Cie, 1963, 137-167.

36. Vogt, C. and Vogt, O.: Die vergleichend-arkitektonische and die vergleichend-reizphysiologische Felderung der Grosshirnrinde unter besonderer Berücksichtigung der menschlichen. Naturwissenschaften, 1926, 14: 1190-1194.

37. Woolsey, C. N.: Organization of somatic sensory and motor areas of the ce-

rebral cortex. Chapitre 4 in Harlow H. F. and Woolsey C.N. Biological and biochemical Bases of Behavior Univ. of Wisconsin Press. Madison, 1958, 476 pp.

38. Woolsey, C. N.; Settlage, P. H.; Meyer, D. R.; Sencer, W.; Ponto Hammy, T. and Travis, A. M.: Patterns of localization in precentral and "supplementary" motor areas and their relations to the concept of a premotor area. Chap. 12 in Patterns of organization in the central nervous system. Res. Publ. Ass. Nerv. Ment. Dis. 1951, 30, 238-64.

39. Woolsey, C. N.; Tasker, R.; Welt, C.; Ladlpi, R.; Campos, G.; Potter, H. D.; Emmers, R. and Schwassmann, H.: Organization of pre-and postcentral leg areas in chimpanzee and gibbon. Trans. Amer. Neurol. Ass. 1960, 85:144-46.

40. Woolsey, C. N.: Cortical localization as defined by evoked potential and electrical stimulation studies, in Cerebral localization and organization, Schaltenbrand G. and Woolsey C.N. Ed. Univ. of Wisconsin Press Madison 1964, 164 pp.

Analysis of Sodium Amytal Effects on Frontal Lobe-Subcortical Interrelations

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Recent neurophysiologic technics, made possible by advances in recording and computing devices, complement long-established anatomic and physiologic methods for study of the brain. In the present investigation several of these technics were applied to the problem of functional relationships between the prefrontal lobes and other regions of the brain during fluctuating behavioral states. Changes in behavior were obtained with administration of sodium amytal. Because our study included human patients as well as rhesus monkeys, we were able to obtain subjective reports of patients to complement physiologic observations and gross changes in behavior.

Electrical activity was recorded from the frontal lobes and overlying scalp, as well as from several subcortical regions. By computer analysis we determined (a) averaged evoked potentials elicited by peripheral-sensory stimuli, as well as single pulse electrical stimulation to subcortical regions, and (b) interrelations of brain regions computed from ongoing EEG activity by cross-spectral analysis technics. By means of these procedures we sought to gain more information regarding the relationship between behavior and frontal lobe function.

METHOD AND PROCEDURE

Electrodes

Two *Macaca rhesus* monkeys and 2 patients, in whom electrodes had been im-

planted for diagnosis and treatment, participated in the study. Electrodes were implanted stereotaxically into precise subcortical regions of the brain, and cortical electrodes were placed under the dura and over the arachnoid⁴. Electrode bundles were constructed of teflon-insulated stainless steel strands, 0.002 in. in diameter, with contact points 2 mm. apart¹⁰. Cortical electrodes were in bundles of three, and subcortical in bundles of 3 to 6, depending on the site of implantation. Patient No. B-12, a man with chronic catatonic schizophrenic reaction, and with a history of epileptic seizures, had 111 leads* implanted 18 months before the study began. Patient No. B-16, a man with temporal lobe epilepsy, had 100 leads** implanted 12 months before the study. Two rhesus monkeys were also implanted using pneumoencepha-

* *Patient No. B-12.* — Electrode Placements: bilateral at several positions in the temporal cortex, occipital cortex, frontal cortex, parietal cortex, centromedian thalamus, hippocampus, hypothalamus, and septal region; unilateral in the right amygdaloid nucleus and left caudate nucleus.

** *Patient No. B-16.* — Electrode placements: bilateral in the occipital cortex, anterior and posterior superior (auditory) temporal cortex, parietal cortex, septal region, hypothalamus, hippocampus, caudate nucleus, amygdaloid nucleus; unilateral in the right frontal cortex, right mesencephalic reticular formation, right globus pallidus, right medial geniculate, left centromedian thalamus, and left posteroventral lateral thalamus.

lography and x-ray verification of stereotaxic electrode placements.

Drug administration and stimulation

Each patient received 500 mg. sodium amytal, diluted to 10 ml. with distilled water and injected intravenously at the rate of 1.0 ml. every 20 sec. except for a 2 minute pause after 1, 5, and 10 ml. These

periods permitted the recording of EEG during sensory stimulation, which consisted of a brief flash of light (Grass PS-2 set at intensity 16) followed 500 msec. later by a loud click about 120 dB)***. The flash-click sequence was repeated 100 times at a rate close to once per second. The patients reclined on a bed partly within a glass-lined enclosure that diffused the light flash. They were instructed to pay attention at all times to light and sound.

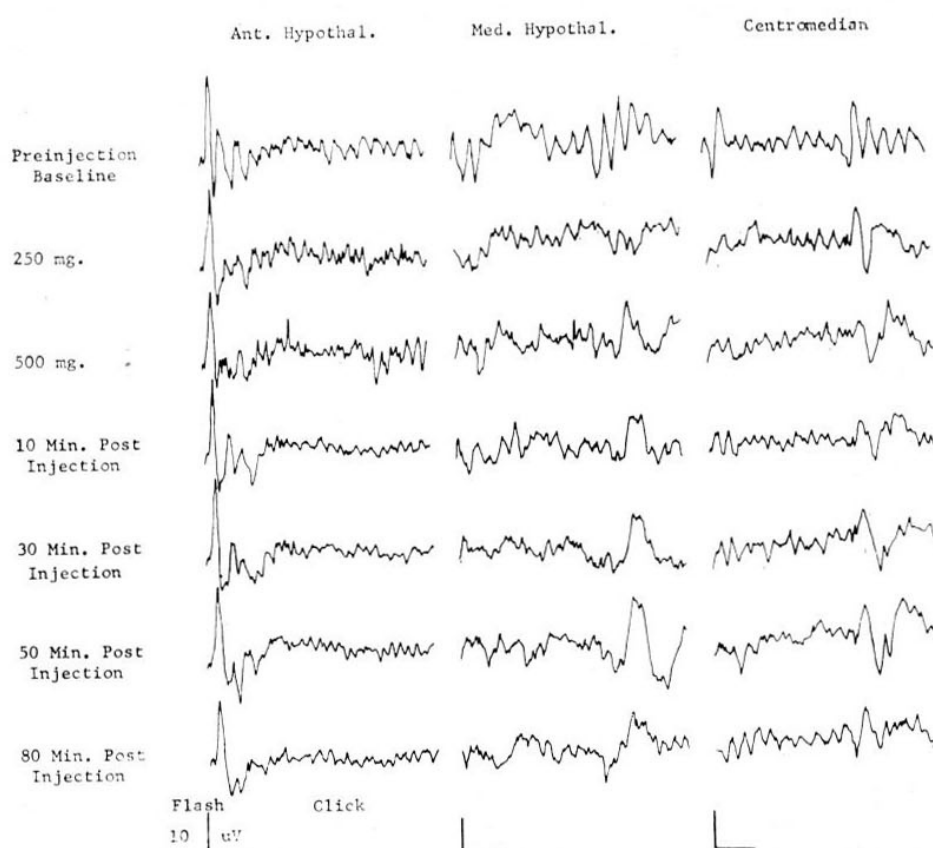


Fig. 1. — Averaged visual and auditory evoked responses (bipolar) recorded from anterior hypothalamus and centromedian nucleus in Patient No. B-16. Responses are shown before, during, and after 500 mg. sodium amytal. Calibrations are 10 μ V. and 200 msec. Averages based on N of 100.

Single pulse electrical stimulation was given immediately before and after drug administration. Biphasic pulses were delivered through stimulus isolation units at a rate of once per sec. Positive and negative components of the pulse were each 0.3 msec. with no intervening delay.

The monkeys received 25 mg. sodium amytal diluted to 10 ml. and injected in-

travenously in a manner identical with the human patients. Recording and stimulating procedures were also identical except that the monkeys were seated in Foringer chairs within the glass-lined enclosure.

*** dB measure relative to 0.002 dynes/cm². Allison Labs. Audiometer Calibration Unit, Model 300.

Recording and computer analysis of data

EEG signals were amplified with capacitance coupled equipment (Grass Model 6) set 2dB down at 1 and 70 cps. These signals were permanently recorded on frequency modulated magnetic tape (frequency response 0-312 cps). Information stored on analog tapes was then processed by two methods.

(a) Evoked responses to both sensory and electrical stimulation were computed on an offline digital summation computer

(Nuclear Data Enhancetron). Responses were read out onto an X-Y plotter for subsequent comparisons.

(b) Analysis of ongoing EEG activity was performed on an IBM 7094 computer using a modified version of an available time series analysis program³. The program provided both autospectral and cross-spectral analysis of the EEG. Digital data tapes, which served as input to the computer, were generated by means of an analog-to-digital converter in the Tulane Biomedical Computing System.

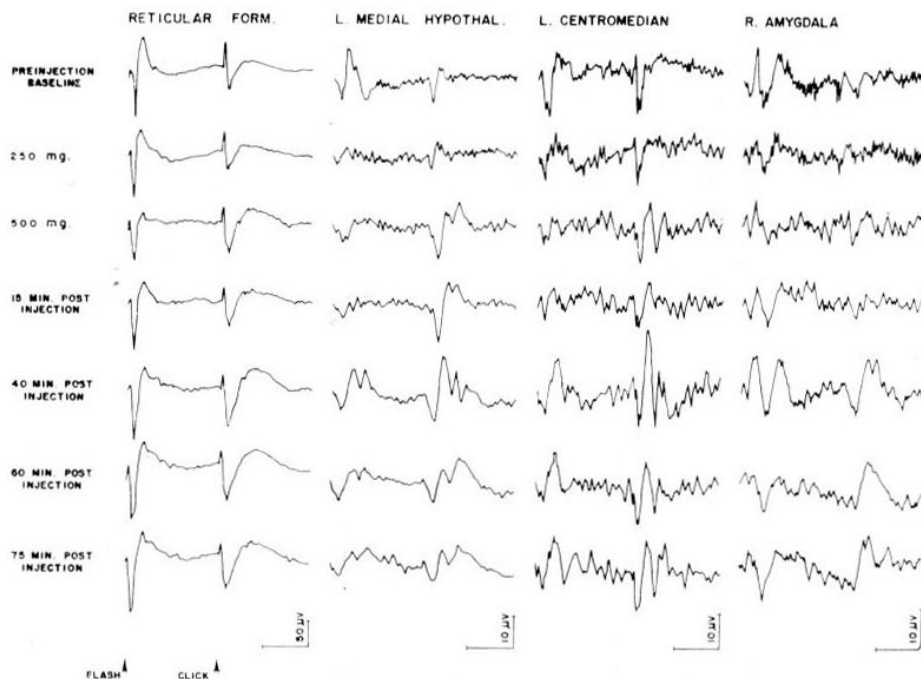


Fig. 2. —Averaged visual and auditory evoked responses (bipolar) recorded from reticular formation, left medial hypothalamus, left centromedian nucleus, and right amygdala in Patient No. B-12. Responses are shown before, during, and after 500 mg. sodium amytal. Calibrations are 10 uV, and 250 msec., except for the reticular formation which is 50 uV. Averages based on N of 100.

RESULTS

Evoked potential analysis

Figure 1 demonstrates the effects of sodium amytal on flash and click responses evoked from subcortical regions from Patient No. B-16. A pronounced visual evoked response (VER) is seen in the anterior hypothalamus which remains stable throughout the experiment. The onset latency of

this response is 30 msec. Since a 30 msec. latency is also recorded at the visual cortex, it seems unlikely that this response depends upon corticofugal projections but suggests instead a more direct pathway. Fibers from the optic tract to the hypothalamus have been described in man by some observers and questioned by others². Both visual and auditory evoked responses (AER) are seen in medial hypothalamus and centromedian thalamus. These two regions show a similar

amytal effect consisting of a depressed VER and a potentiation of the slow secondary components of the AER. This similarity of response pattern between medial hypothalamus and centromedian thalamus suggests a degree of functional equivalence in their response to amytal. The contrasting stable anterior hypothalamic VER, however, suggests that amytal exerts differential effects

on subcortical nuclei. Moreover, the varied effects on VER and AER components suggest that amytal may differentially affect the various sensory systems.

Very similar results were obtained from Patient No. B-12 (fig. 2). Again, the VER in medial hypothalamus and centromedian thalamus decreased (with some recovery later) and secondary AER components

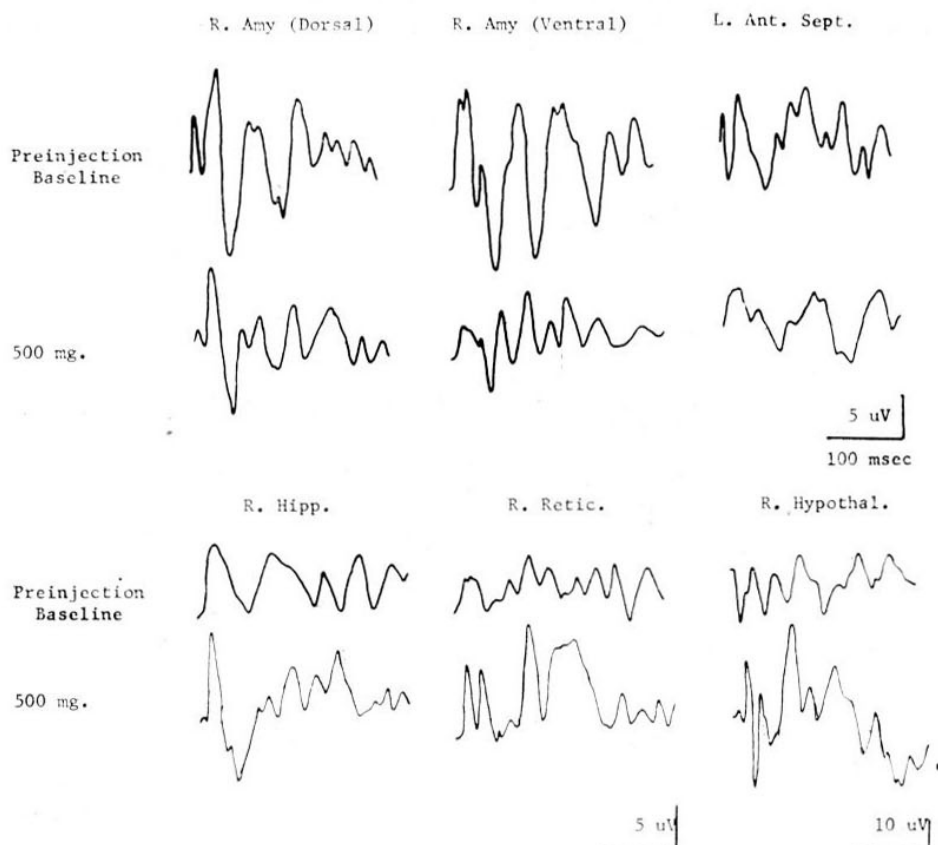


Fig. 3. — Averaged evoked responses in right frontal cortex during electrical pulse stimulation of subcortical regions before and after 500 mg. sodium amytal in Patient No. B-16. Averages based on *N* of 100. — TOP: Depressed cortical response after amytal to stimulation of right amygdala (both dorsal and ventral electrode placements) and left anterior septum. All calibrations are 5 uV. and 100 msec. — BOTTOM: Facilitated cortical response after amytal to stimulation of right hippocampus, right reticular formation, and right hypothalamus. Calibrations are 5 uV. and 100 msec., except for 10 uV. calibration for right hypothalamus.

were potentiated. This general pattern was also reproduced in the amygdaloid nucleus. In contrast, however, the mesencephalic reticular formation response was relatively stable to both flash and click, as it was in the anterior hypothalamus of Patient No. B-16. There is seen in the reticular

formation a reduction of the primary AER, and a potentiation of the slow secondary AER, but these effects are minimal compared with the changes seen in other subcortical areas. The latency of onset in the reticular formation to flash (28 msec.) and click (16 msec.) suggests a discharge

over direct collateral pathways. This is also the case in centromedian thalamus where the onset latency to flash is 32 msec. (best seen in baseline response), and the onset latency to click is 25 msec.

The use of placebo control, with the subject expecting to receive amytal, has demonstrated that the observed changes in evoked responses are not due to a simple habituation effect over time. Using identical procedures of injection, but substituting normal saline for amytal, evoked res-

ponses were found to be stable over long periods of time. Moreover, we were able to reproduce the amytal effect in the same patient on different occasions. This effect was shown to be drug-specific since the use of other pharmacologic agents, including sodium phenobarbital, amphetamine, alcohol (I.V.), and chloralose, did not result in the response patterns described above.

Figure 3 shows the effect of sodium amytal on responses elicited in frontal cortex during one/sec. single pulse electrical

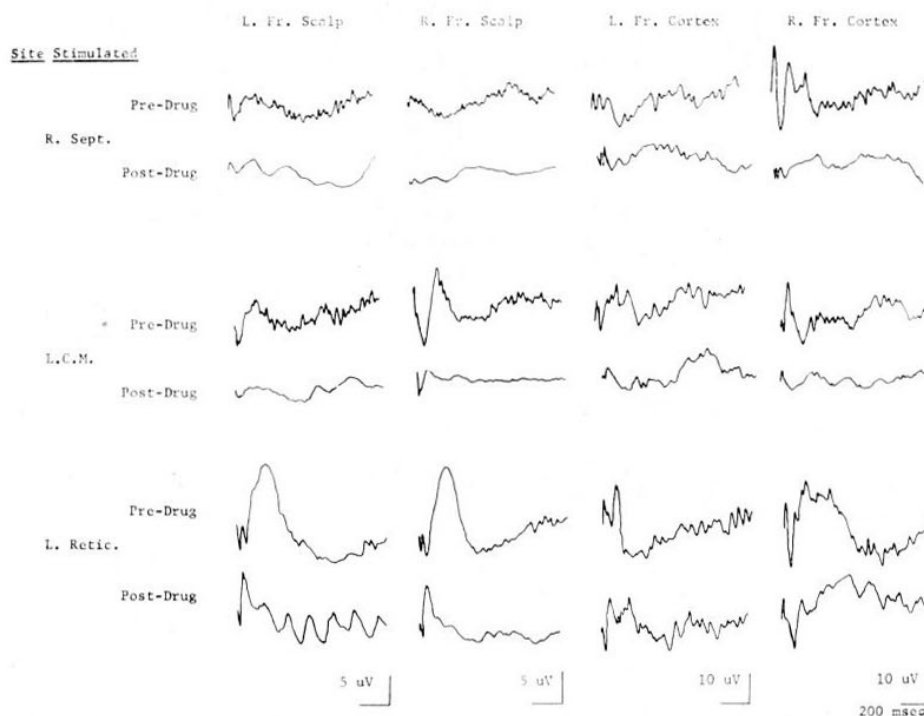


Fig. 4. — Averaged evoked responses recorded in frontal cortex and scalp during electrical pulse stimulation of right septum (top), left centromedian (middle), and left reticular formation (bottom) in the monkey. Pairs of responses are shown before and after 25 mg. sodium amytal. All scalp calibrations are 5 uV. and 200 msec., while the voltage calibration for all cortical responses is 10 uV. Averages based on N of 100.

stimulation of various subcortical regions of Patient No. B-16 before and after administration of the drug. Although the pattern of response varied from region to region, effects of the drug are clearly demonstrated. Amytal suppressed frontal lobe responses to stimulation of dorsal and ventral amygdaloid nucleus, as well as to stimulation of the anterior septal region (upper half of Fig. 3). On the other hand,

there was a facilitation of response to stimulation of the hippocampus, mesencephalic reticular formation, and hypothalamus (lower half of Fig. 3).

Figure 4 presents results obtained from similar experiments conducted in monkeys. Both scalp and cortical recordings are shown. Amytal profoundly depressed the right frontal cortex response to stimulation of the right septum. The relatively

small cortical response on the left side suggests a predominantly ipsilateral projection from the septum. Amytal also depressed the frontal cortex response to left centromedian stimulation. This response appears bilaterally in both scalp and cortex, although the contralateral response is larger. The bilateral response to mesencephalic reticular formation stimulation was depressed, but the effect was minimal by comparison with the depression of the response to stimulation of septum and centromedian thalamus. This is in contrast to the facilitation seen in man during reticular formation stimulation (Fig. 3).

Cross-spectral computer analysis

In evoked potential studies a diminished response following drug administration may be defined as "functional uncoupling" between the frontal cortex and site of stimulation. On the other hand, facilitated responses imply increased functional coupling. Additional techniques are now available which give added information concerning

the functional relations among regions of the brain. The use of cross-spectral time series analysis permits the determination of activity in one region of the brain which is shared by a different brain region. When such shared activity is found, the regions may be described as functionally coupled. Using the coherence function¹¹, which quantifies the degree of shared activity computed at many EEG frequencies, we were able to determine the effect of amytal on functional brain couplings in both patients. By evaluating changes in the magnitude of coherence both before and after amytal, it was possible to assess drug effects. A reduced coherence function after administration of amytal would imply that the drug has acted to decrease coupling at that specific EEG frequency, while an increased coherence value would imply increased coupling. Figure 5 presents a summary of these results in block diagram form. Only predominant effects of increased or decreased coupling are shown. These computed results are based on different recording sessions than the evoked potential data and, hence, recording sites are sometimes

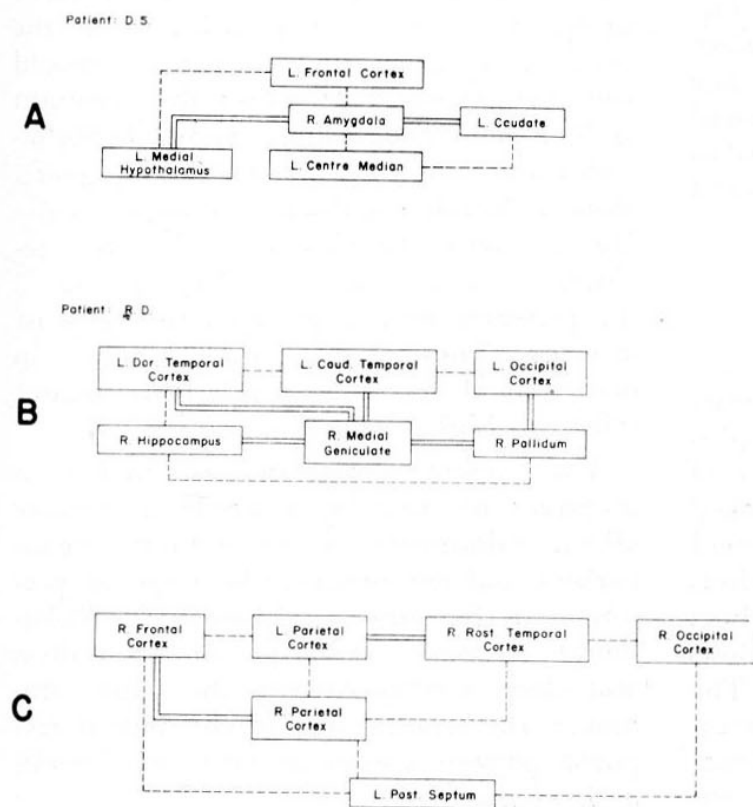


Fig. 5. — Block diagram of cross-spectral coherence analysis showing changes in "coupling functions" as a result of sodium amytal in Patients No. B-12 (A) and No. B-16 (B and C). Broken lines represent reduced coupling following the drug (magnitude of coherence reduced), while double solid lines represent increased coupling (magnitude of coherence increased).

different from those previously described. The broken lines represent a decrease in coupling after use of amytal, whereas the double solid line represents an increase in coupling. Note in Fig. 5A that the frontal cortex became uncoupled from the medial hypothalamus and amygdaloid nucleus, both structures within the limbic system. The uncoupling of frontal cortex and amygdaloid nucleus corroborates the evoked potential data obtained from the patients. Note also in Fig. 5A a general pattern of increased coupling within the limbic system which appears to become uncoupled from both frontal cortex and centromedian thalamus. In Fig. 5C the uncoupling of septal region from the frontal cortex also agrees with the evoked potential data for both patients and monkeys. Moreover, this figure demonstrates that the posterior septum has become uncoupled from at least three cortical regions. Since the septum may be considered as representing a diffuse anterior diencephalic system, these results are in some respects qualitatively similar to the results seen in Fig. 5A involving centromedian thalamus. In contrast, amytal increased coupling between the specific relay thalamus and the cortex (Fig. 5B). This is evidenced by the increased coupling between medial geniculate and contralateral temporal cortex. Increased coupling is also evidenced between medial geniculate and ipsilateral hippocampus and pallidum.

DISCUSSION

Published reports clearly demonstrate that evoked potentials are complex phenomena which depend upon a variety of contributing factors⁸. Although the evoked response is influenced by a wide afferent inflow from many sources, and reflects multisynaptic connections as well as direct anatomic connections, its careful analysis can provide considerable information. The evoked response, however, does not exhaust the entire domain of information inherent in the electroencephalogram. Tonic, on-

going EEG activity recorded in the absence of extraneous stimulation also depends upon a high degree of neural organization. By means of computer analysis of both types of activity, it has been possible to supplement and extend our understanding of brain function. In the present report these techniques were applied to a study of the effects of sodium amytal upon the central nervous system, especially the frontal lobes.

The barbituates, including sodium amytal, are known to depress synaptic transmission¹. There is also evidence that barbituates preferentially depress responses mediated over multisynaptic systems, regardless of the anatomical locations¹². However, in their study of barbituate effects upon afferent transmission through the relay thalamus, King, Naquet, and Magoun⁹ demonstrated that low doses depressed the reticular formation while higher doses (sufficient to produce anesthesia) directly suppress the relay thalamus. Such an effect might account for the results of Figs. 1 and 2. In Fig. 1 the stable anterior hypothalamic VER suggests a pathway not affected by the doses used in the present study. A direct fiber pathway from the optic tract, as mentioned earlier, would thus seem plausible. However, the alteration of VER and AER seen in medial hypothalamus and centromedian thalamus suggests more vulnerable pathways perhaps involving not only the thalamic relay, but reticular formation as well. Yet, in Fig. 2 the reticular formation response was least affected. These results suggest that, in man, amytal may exert a relatively greater effect on higher neuronal centers.

The present results indicate that it is incorrect to describe a single barbituate effect. Administration of sodium phenobarbital did not produce the response pattern seen for amytal, although the behavioral response consisting of drowsiness and sleep was apparently the same. Moreover, the repeatability of the amytal response pattern argues in favor of a well-defined mechanism.

The specific purpose of the present paper was to describe the effects that have particular bearing on frontal lobe function. Although our data do not permit precise conclusions about cellular effects of amytal, it is possible to describe changes in functional relations between certain subcortical structures and the frontal lobes. As evidenced by evoked response (Fig. 3 and 4) and coherence analysis (Fig. 5), a distinct functional uncoupling occurs between frontal cortex and some limbic structures. These data may be related to existing clinical knowledge about frontal lobe function. Clinical studies of patients with frontal lobe lesions, whether accidental or the result of operation, demonstrate that damage to or removal of significant amounts of prefrontal tissue creates a relaxed, carefree attitude⁵. These patients, living almost completely in their immediate environment, have little concern about the future. The anxiety and discomfort of anticipating future difficulties is diminished or abolished. Sodium amytal, the drug we selected for study by the evoked-potential and cross-spectral technics, induces a similar reaction.

Patients who received this drug enjoyed the experience, which they likened to the effects of alcohol; they relaxed, appeared giddy and unconcerned, and said they felt "good". At higher dosages, sleep was the dominant clinical response.

Intravenous injection of sodium amytal in catatonic schizophrenic patients usually alleviates symptoms and produces a clinical response similar to that seen after lobotomy or topectomy⁶. We have previously presented data showing pronounced changes induced by sodium amytal in recordings from parts of the limbic system, principally the septal region where high amplitude fast spindles appear⁷. These effects are uncommon with other barbituates. The demonstrated uncoupling between frontal lobes and limbic system, whose function is related to expressions of emotions, feelings, and levels of attention, provides a basis for understanding this clinical effect. That is, the pharmacological uncoupling of the frontal cortex from subcortical structures is functionally similar to the permanent intervention of lobotomy.

S U M M A R Y

Computer analysis of EEG activity was used to complement existing neuroanatomic and neurophysiologic data concerning function of the frontal lobes. Evoked potential responses to peripheral sensory stimuli and to single pulse electrical stimulation of subcortical brain sites were determined. Cross-spectral time-series analysis of ongoing EEG activity was also per-

formed. The results obtained in 2 patients and 2 monkeys, with subcortical and cortical electrodes implanted for prolonged study, suggest that sodium amytal exerts an uncoupling effect between the frontal lobes and regions of the limbic system. These effects are discussed in terms of existing clinical knowledge about frontal lobe function and effects of sodium amytal.

R E S U M E N

Para complementar los datos neuroanatómicos y neurofisiológicos existentes acerca de la función de los lóbulos frontales se efectuaron análisis por computadores de la actividad electroencefalográfica. Fueron determinadas las respuestas potenciales evo-

cadadas mediante estímulos sensitivos periféricos y mediante la estimulación eléctrica por choques aislados de ciertas regiones subcorticales. También se efectuó el análisis "cross spectral time-series" de la actividad EEG. Los resultados obtenidos en dos

pacientes y dos monos con electrodos implantados por un tiempo prolongado en estructuras subcorticales y corticales sugieren que el amital sódico ejerce un efecto de desconexión entre los lóbulos frontales

y el sistema límbico. Estos efectos se discuten en términos de los conocimientos clínicos existentes acerca de la función del lóbulo frontal y los efectos del amital sódico.

R É S U M É

Comme complément aux données neuro-anatomiques et neurophysiologiques obtenues sur la fonction des lobes frontaux on a fait des analyses par ordinateurs électroniques de l'activité électroencéphalographique. On a déterminé les réponses potentielles évoquées par moyen de stimulations sensorielles périphériques par moyen de la stimulation électrique par chocs isolés de certaines régions souscorticales. On a aussi effectué l'analyse "cross-spectral time-series" de l'ac-

tivité EEG. Les résultats obtenus dans deux patients et deux singes ayant des électrodes placés dans les structures corticales et sous-corticales pendant une longue période suggèrent que l'amythyl sodique exerce une action de déconnection entre les lobes frontaux et le système limbique. Ces effets sont discutés à la lumière des connaissances cliniques qui existent sur la fonction du lobe frontal et les effets de l'amythyl sodique.

Z U S A M M E N F A S S U N G

Man benutzte die Komputernalyse der EEG-Aktivität um die bestehenden neuro-anatomischen und neurophysiologischen Daten bezüglich der Funktion der Frontallappen zu vervollständigen. Man bestimmte die durch periphere sensitive Reize und durch die Reizung mit einzelnen Pulsen von subkortikalen Gehirnstellen hervorgerufenen Potentiale. Man führte auch eine gekreuzte Analyse von spektraler Zeit-Serien der EEG durch. Die bei zwei Patienten und zwei Affen erzielte Resul-

tate, mit subkortikalen und kortikalen Elektroden, die fuer ein laengeres Studium eingesetzt worden waren, lassen daran denken, dass das Amythyl-Natrium einen entkoppelnden Effekt zwischen den Frontallappen und den Gegenden des limbischen Systems ausueben.

Diese Effekte werden diskutiert auf der Basis der bestehenden klinischen Kenntnissen ueber die Funktion des Frontallappens und die Effekte von Amythyl-Natrium.

R E F E R E N C E S

1. Brook, C. M.; and Eccles, J. C.: A study of the effects of anaesthesia and asphyxia on the mono-synaptic pathway through the spinal cord. *J. Neurophysiol.* 10: 349, 1947.
2. Crosby, E. C.; Humphrey, T. and Lauer, E. W.: *Correlative Anatomy of the Nervous System*. New York, MacMillan, 1962, p. 322.
3. Dixon, W. J., Editor: *BMD Biomedical Computer Programs*. Health Sciences Computer Facility, Department of Preventive Medicine and Public Health, University of California School of Medicine, Los Angeles. Program 2T: Autocovariance and Power Spectral Analysis.
4. Heath, R. G.; John, S. and Foss, O.: Stereotaxic biopsy. *Arch. Neurol.* 4:291, 1961.
5. Heath, R. G.; Weber, J. J. and Crandell, A.: "Psychiatry", in *Selective Partial Ablation of the Frontal Cortex by The Co-*

lumbia-Greystone Associates, ed. by Mettler, F.A. New York, Paul B. Hoeber, Inc., Harper & Brothers, 1949, pp. 315-429.

6. Heath, R. G.; Peacock, S. M., Jr.; Monroe, R. R. and Miller, W. H., Jr.: "Addendum E. Electroencephalograms and Subcorticograms Recorded since the June 1952 Meetings," in *Studies in Schizophrenia* by the Tuane University Department of Psychiatry and Neurology. Cambridge, Harvard University Press, 1954, pp. 573-608.

7. Heath, R. G.: "The Problem of the Clinical Evaluation of Sedative and Hypnotic Drugs," in *Sedative and Hypnotic Drugs*. Baltimore, The Williams & Wilkins Company, 1954, pp. 57-80.

8. Katzman, R., Editor: *Sensory evoked responses in man*. Ann. N. Y. Acad. Sci. 112 (Art. 1): 1-546, 1964.

9. King, E. E.; Naquet, R. and Magoun, H. W.: Alterations in somatic afferent transmission through the thalamus by central mechanisms and barbiturates. *J. Pharm. Exper. Therap.* 119:48, 1957.

10. Manning, G. C., Jr.: A new miniature multi-contact electrode for subcortical recording and stimulating. *Electroenceph. Clin. Neurophysiol.* 17:204, 1964.

11. Walter, D. O.: Spectral analysis for electroencephalograms: mathematical determination of neurophysiological relationships from records of limited duration. *Exper. Neurol.* 8:155, 1963.

12. Yamamoto, S. and Schaeppel, U.: Effects of pentothal on neural activity in somatosensory cortex and brain stem in cat. *Electroenceph. Clin. Neurophysiol.* 13: 248, 1961.

Troubles Sensitifs et Sensoriels au Cours des Lésions Préfrontales

Etude comparative

Dr. ROBERT MESSIMY

(Paris).

Henry Head et Gordon Holmes ont clairement pressenti, dès 1920, l'action de contrôle exercée par le cortex sur le thalamus.

Pour eux, les noyaux médians étaient le centre essentiel ("essential center") du thalamus, régularisant la part affective des perceptions sensorielles.

Cette hypothèse de travail fut mise en doute par le fait que l'ablation du cortex sensori-moteur n'entraîne pas de signes de libération sensitive ou sensorielle.

Si on suppose, par contre, que les influx sensitifs ou sensoriels d'un type plus élémentaire, plus archaïque, correspondant à la "sensibilité protopathique" de Henry Head, cheminant par des voies différentes des voies sensitives classiques, aboutissent à d'autres régions du cortex cérébral, l'hypothèse précipitée peut devenir valable. En discutant la physiopathologie nous verrons que la physiologie moderne a établi la réalité d'un système de projection non spécifique des afférences sensitives et sensorielles aboutissant aux noyaux de la ligne médiane du thalamus, se projetant sur différentes régions du cortex et particulièrement sur le cortex préfrontal. On conçoit dès lors que l'ablation préfrontale puisse libérer les impulsions sensitives comme aussi les tendances affectives et instinctives élémentaires.

Ayant eu le privilège, durant l'année 1937, de travailler dans le magnifique laboratoire de J. F. Fulton à l'Université de Yale, j'eus l'attention attirée par de tels

faits, associés à d'autres symptômes que je rappellerai brièvement. Je m'efforcerai ensuite de montrer, à la lumière d'autres travaux, la réalité de l'hyperréactivité sensitive et instinctive au cours des lésions préfrontales.

I. CONSTATATIONS EXPERIMENTALES PERSONNELLES

Méthodes

Les opérations furent pratiquées sur six singes adultes jeunes, dont quatre appartenant à l'espèce mangabey (*Cercocebus torquatus atys*) et deux à l'espèce pithecus (*Macacus rhesus*).

On s'efforça, sur chaque animal, d'extirper tout le tissu situé en avant du bras inférieur du sillon arqué, ce qui inclut les zones 9, 10, 11 et 12 de Brodmann mais épargne la zone 8 (zone du contrôle des mouvements de latéralité oculaire). (Fig. 1 et 2).

Chez un animal, à l'ablation préfrontale, on ajouta l'ablation de la zone prémotrice (area 6 de Brodmann).

Résultats

Les animaux furent étudiés en collaboration avec J. Finan qui, exécutant par ailleurs un travail sur la "delayed reaction" me fit profiter de son expérience de psychologue.

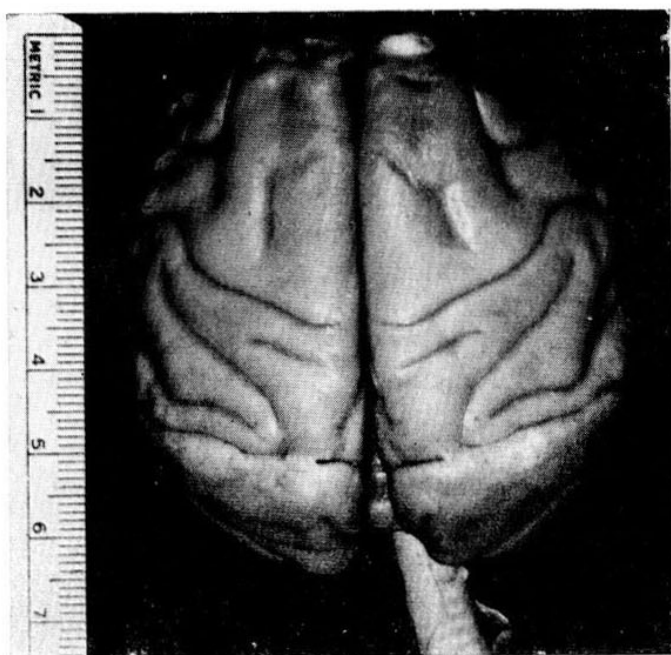


Fig. 1. — Cerveau de singe après ablation préfrontale bilatérale.

Une observation très attentive des animaux, pré-et post-opératoire, nous permit de grouper comme suit les principales modifications observées:

- 1° — Modifications de l'activité.
- 2° — Modifications du mode réactionnel.
- 3° — Modifications du tonus et des réflexes de posture.
- 4° — Modifications des réflexes périostés, tendineux, cutanéomuqueux.
- 5° — Modifications du système autonome.

1° Modifications de l'activité

Déjà observées par les auteurs classiques, notamment David Ferrier (1886), Bianchi (1921), elles furent étudiées par C. F. Jacobsen (seul (1931) ou avec J. F. Fulton et M. Kennard, 1932) qui mit l'accent sur l'*hyperactivité*, par C. P. Richter et M. Hines (1938) qui firent l'étude quantitative de cette hyperactivité.

Nous avons, J. Finan et moi-même, enregistré cette hyperactivité par une méthode d'enregistrement graphique assez rudimentaire et insisté sur son caractère *automatique et stéréotypé*⁵¹.

2° Modifications du mode réactionnel

Très vite après l'opération et persistant au cours de l'évolution, on observe ce que nous avons dénommé une *surréactivité diffuse*. Ces animaux paraissent nettement *hyperesthésiques*; lorsqu'on les prend dans les bras, ils retirent brusquement leurs pattes pour éviter le contact. Dans tous ces cas, les réactions de défense ont un caractère de constance et de brusquerie réflexe très spécial.

L'excitabilité sensorielle est également accrue; les animaux présentent le réflexe d'aveuglement à la lumière avec du larmolement. Ils réagissent exagérément au bruit.

On pourrait penser que cette surréactivité est due à une irritabilité d'origine psychique, à une peur irraisonnée, aussi est-il intéressant d'observer cette hyperesthésie lorsque l'animal est au calme dans sa cage.

Ces symptômes coïncident avec des *troubles paresthésiques* d'un type particulier: dès les premiers jours post-opératoires, l'animal se gratte souvent et spécialement les extrémités.

Ces troubles persistent, semble-t-il, d'une manière permanente. Nous les avons notés

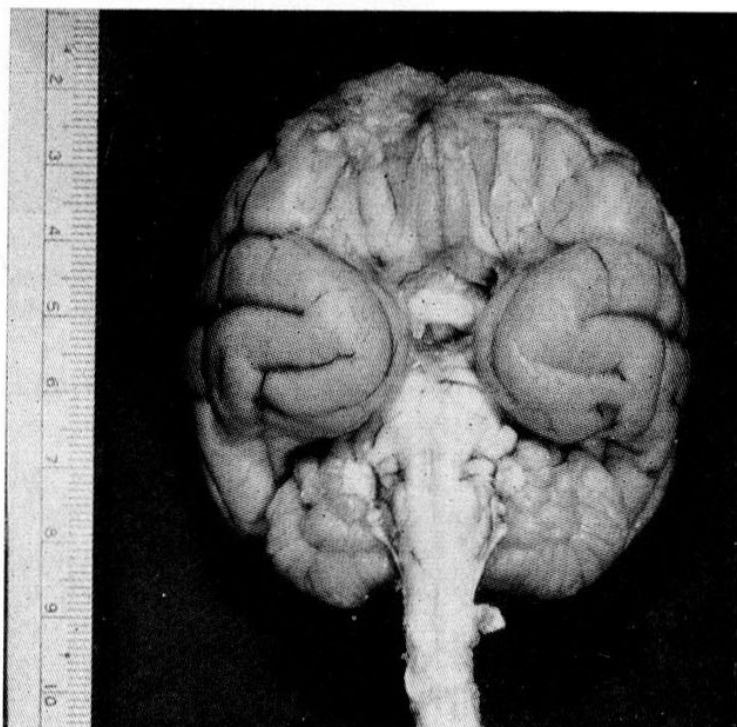


Fig. 2

régulièrement à la fin du jour, dans la période précédant le sommeil. Comme nous l'écrivions déjà, ces faits présentent une certaine analogie avec les troubles sensitifs produits par J. G. Dusser de Barenne et O. Sager (1931) après injection de très faibles doses de strychnine dans le noyaux thalamiques médians du chat. On peut les rapprocher aussi des faits d'hypersensibilité obtenu par Cl. Bernard et bien étudiés par A. Tournay après extirpation de portions du système sympathique.

"*L'exagération des réactions instinctives*", nous paraît un des éléments de cette sur-activité diffuse: exagération des instincts

de défense ou de protection, voracité, colère, peur, sexualité. Là encore, on retrouve la brusquerie et le manque d'inhibition qui aboutissent à une perturbation profonde des manifestations instinctives. Un fait nous paraît capital: *la personnalité affective de chaque animal reste semblable mais exaltée*. Le fait est dû, à notre avis, à la libération de la personnalité neuro-végétative de chaque animal.

Notons ici encore *la modification du cri* qui prend une tonalité plus élevée qu'avant l'opération et le caractère de réponse immédiate, automatique, aux stimulations d'origine externe ou interne".

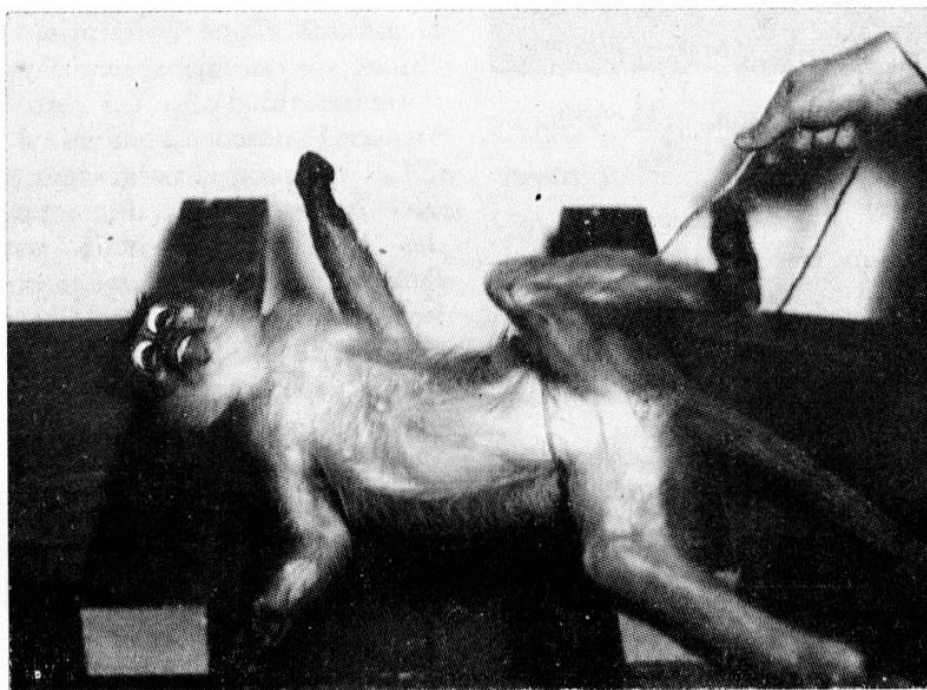


Fig. 3. — *Etat cataleptique: attitude de fakir. L'animal, sur le dos, ne repose que sur deux points d'appui, nuque et région sacrée. Le tronc "fait le pont" entre ces deux points d'appui.*

3° *Modifications du tonus et des réflexes de posture*

Nous ne pouvons détailler ce chapitre et nous dirons seulement qu'après l'ablation préfrontale on assiste au développement d'une *hypertonie extrapyramidale* prédominant sur les muscles de la nuque et du dos, variant aux membres en fonction des réflexes toniques du cou.

Parallèlement à l'hypertonie apparaît une exagération des réflexes de posture qui peut

subsister lors même que l'hypertonie n'est plus nettement perceptible, ainsi qu'une *tendance cataleptique* (Fig. 3).

4° *Modifications des réflexes tendinéo-periodostés et cutanéomuqueux. Réflexes pupillaires*

Après un certain délai suivant l'intervention, on assiste à une exagération de la vivacité des réflexes. Cette exagération est surtout manifeste en ce qui concerne

les *réflexes médians ou axiaux*: réflexe naso-palpébral (qui diffuse au muscle releveur de la lèvre supérieure et au muscle mentonnier) réflexe du menton, réflexes sterno-pectoral et médio-pubien.

Les réflexes pupillaires sont conservés. Dans l'obscurité, les pupilles sont nettement dilatées; sous l'effet de la lumière, elles se contractent modérément mais de manière non soutenue.

L'olfaction persiste après l'intervention.

5° *Modifications du système autonome*

Ces troubles sont constants. Comme nous l'écrivions J. Finan et moi (1937) "on voit survenir diverses manifestations. Les unes peuvent être, qualifiées de sympathiques: signes de colère, tendance à mordre, érection pilomotrice, dilatation pupillaire. Les autres méritent plutôt le nom de parasympathiques: transpiration excessive des extrémités, brusques réactions vaso-motrices, périodes de complète apathie."

Nous avons encore observé chez le singe, après ablation préfrontale, des troubles de la régulation thermique, des modifications évidentes du péristaltisme gastrique (avec E. Clifton) se faisant tantôt vers l'accélération, tantôt vers le ralentissement, des modifications de la régulation cardiaque (avec H. E. Hoff).

Dans le présent article, nous mettons surtout l'accent sur les troubles sensitifs et sensoriels. Si nous avons tenu à rappeler les autres troubles observés après ablation préfrontale, c'est qu'à nos yeux il est difficile de dissocier les uns des autres.

Nous reviendrons sur les mécanisme des symptômes.

En 1939⁵¹, tenant compte des relations anatomiques des lobes préfrontaux et des noyaux médians du thalamus, bien établies par les travaux de Le Gros Clark et Boggon (1932), d'A. E. Walker (1935) entre autres et nous basant sur les relations de ces noyaux médians avec les autres noyaux thalamiques ainsi qu'avec le corps strié et le pallidum, avec l'hypothalamus et les noyaux végétatifs périventriculaires, nous avons cherché à expliquer nos résultats par

une libération des portions phylogénétiquement anciennes du système dit extrapyramidal, par l'intermédiaire de l'archithalamus de Wallenberg.

Cette conception, nous le verrons, reste défendable mais elle mérite d'être rajeunie à la lumière des travaux récents de neurophysiologie.

De retour en France, nous avons pu étudier dans les laboratoires dirigés par A. Gosset, G. Guillaud et I. Bertrand à la Salpêtrière, les effets de l'ablation unilatérale du cerveau préfrontal chez le singe. Nous avons pratiqué, avec la collaboration de R. J. Chevallier, chez cinq animaux (deux mangabeyes, un papio cynocéphale, deux singes callitriches) *l'ablation préfrontale unilatérale*. Afin de préserver les nerfs olfactifs, nous avons laissé en place la partie interne et orbitaire du lobe préfrontal.

Nos résultats, publiés en 1942, furent, d'une manière résumée, les suivants:

1° *Modifications de l'activité*: on observe une augmentation d'activité mesurée par un système pneumatique relié par un cylindre enrégistreur. Elle présentait le même caractère automatique, stéréotype, que chez les animaux ayant subi une ablation bilatérale. Chez ces derniers, l'hyperactivité nous a paru nettement plus marquée, conformément aux observations de C. P. Richter et M. Hines.

2° *Modifications du mode réactionnel*: les réactions aux diverses stimulations deviennent plus vives, mais d'une manière beaucoup moins évidente qu'après ablation bilatérale.

3° *Réflexes*: les réflexes des membres ainsi que les réflexes médians ou axiaux s'exagèrent dès la deuxième ou la troisième semaine post-opératoire. Fait important, pour les réflexes médians dont la réponse peut être dissociée comme le réflexe sterno-pectoral et le réflexe médio-pubien, la réponse est manifestement plus vive du côté opposé à l'ablation préfrontale.

4° *Modifications des réflexes de posture*: l'hypertonie des muscles extenseurs de la tête et du tronc est beaucoup moins marquée qu'après l'ablation bilatérale.

Sur les membres, l'hypertonie débute également pendant la deuxième semaine, puis elle s'atténue. Elle prédomine indiscutablement sur les membres du côté opposé à l'ablation et à la racine du membre. C'est une rigidité du type extrapyramidal, sa recherche donne la sensation de roue dentée.

La tendance cataleptique était à peine décelable chez les callitriches mais nette chez les mangabeys et le papio. Elle était renforcée par l'injection intra-musculaire de substances pharmacologiques possédant une action parasympathicomimétique comme la bulbo-capnine (0,010 g. par kilo) * ou, de manière moins évidente,

l'acétylcholine (0,01 g. par kilo). Elle paraissait plus marquée du côté controlatéral.

5° *Les modifications du système autonome* sont les mêmes qu'après ablation bilatérale, mais beaucoup plus atténuées.

Aussi bien chez les singes soumis à l'ablation bilatérale ou unilatérale, l'étude histologique des coupes sériées des noyaux gris centraux ne montra pas de lésions manifestes.

Nous avons également, avec R. J. Chevallier (1939), étudié chez le lapin les effets de l'ablation de la partie antérieure du cerveau (areas 6 et 8, partie antérieure des areas 4, 24 et 32, d'après l'atlas de

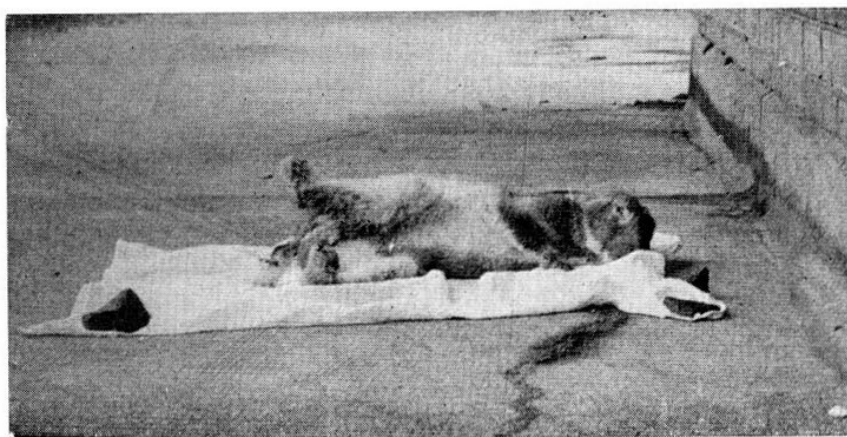


Fig. 4. — Etat cataleptique chez un lapin.

Winkler et Potter) (fig. 4). Après l'ablation les animaux deviennent très excitables, répondant souvent aux stimulations par des grognements et des essais de mordre.

Chez huit sur onze lapins, nous avons pu mettre en évidence une tendance cataleptique (fig. 5) associée à un ralentissement des bruits du cœur, à une respiration ample, un peu ralentie, avec des pupilles peu dilatées. L'ensemble de ces symptômes nous fit penser que la catalepsie fait partie d'un état où prédomine le système vagal. Le rhinencéphale fut trouvé intact lors des vérifications histologiques.

* Note: La coexistence de signes végétatifs de type parasympathique associés à la catalepsie dues à la bulbo-capnine est signalée par W. R. Ingram et S. W. Ranson (1934).

II. TROUBLES SENSITIFS ET SENSORIELS MIS EN EVIDENCE PAR DIFFERENTS OBSERVATEURS

On peut classer, de manière schématique, la répercussion de ces troubles sur l'animal:

- 1° Répercussion sur l'activité.
- 2° Répercussion sur la réactivité, notamment à la douleur.
- 3° Répercussion sur le comportement instinctivo-affectif.
- 4° Répercussion sur les réflexes conditionnés et l'apprentissage.

1° Répercussion sur l'activité

Dès 1874, David Ferrier décrivait les alternatives d'apathie, d'hypocinésie et d'hy-

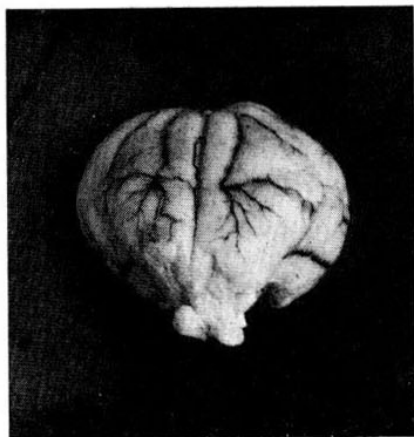


Fig. 5. — Cerveau de lapin après ablation des pôles antérieurs. Les bulbes olfactifs ont été respectés.

peractivité automatique que présentent les animaux sans lobes frontaux.

Bianchi (1921) assimilait les mouvements de manège des singes préfrontaux à des stéréotypies, des tics psychomoteurs.

L'effet stimulant sur l'activité de diverses excitations internes ou externes, notamment de la lumière, après ablation préfrontale, est signalé chez les singes par J. F. Fulton, C. F. Jacobsen et M. Kennard (1932), par C. P. Richter et M. Hines (1938); T. Ruch et Shenkin⁷⁸ signalent aussi l'action favorisante de la lumière sur l'hyperactivité obtenue par ablation de l'area 13 orbitaire chez le singe.

Après ablation de différentes aires du cortex, M. A. Kennard et associés³⁸ constatent une augmentation de l'activité par les "stress" émotionnels et par la lumière.

G. M. French et H. F. Harlow²¹ ont mesuré l'augmentation d'activité des singes: après ablation préfrontale bilatérale, cette activité devint considérable, dépassant dix fois celle d'un singe indemne (G. M. French²²). La lumière joue un rôle certain.

Le rôle stimulant de la lumière a pu être mesuré par W. Isaac et J. L. de Vito³⁷. La lumière serait aussi le concomitant nécessaire des stimulations auditives dans la production de l'hyperactivité. Le degré de l'activité motrice semble refléter le taux de l'impulsion sensorielle totale.

D'après Ch. G. Gross et L. Weiskrantz³¹, l'ablation chez le macaque de lésions limitée au sulcus principalis détermine des modifications de l'activité similaires à celles obtenues par l'ablation de toute la région latérale du cortex frontal.

Les modifications apportées à l'activité par les stimulations d'origine interne sont plus difficiles à mesurer. La faim paraît agir comme chez les animaux normaux, c'est à dire en exaltant l'activité alors que des périodes de pause sont plus volontiers observées après ingestion de nourriture.

2° Répercussion des troubles sensitifs sur les réactions à la douleur

Différents observateurs ont remarqué la plus grande réactivité des singes après ablation préfrontale: M. Kennard et ses associés³⁸, dans le laboratoire de J. F. Fulton, R. J. Campbell et H. F. Harlow¹⁰ qui expliquent la distractibilité de leurs sujets par l'abaissement du seuil d'excitation à tous les stimuli, externes et internes.

On sait que la lobotomie préfrontale, chez l'homme, est susceptible de diminuer la douleur ou tout au moins l'appréhension de la douleur. Différents chercheurs se sont efforcés d'élucider ce problème difficile par l'expérimentation animale. (Lichtenstein⁴⁶, Smith⁸⁶).

Chez les singes rhésus préfrontaux, J. E. Miles et H. E. Rosvold⁶⁰ constatent la persistance des réactions aux stimulations douloureuses.

Waterhouse⁹⁵, également chez des singes lobotomisés préfrontaux, insiste sur la persistance des signes de la peur provoquée par des chocs électriques tandis que la vitesse de leurs réponses aux mêmes chocs est diminuée.

Observant les mêmes difficultés pour éviter rapidement un choc électrique chez les singes écureuils (squirrel monkeys), R. C. Miles⁶² les explique par l'incapacité d'inhiber un acte d'approche habituel.

Signalons encore que B. A. Mayer et R. W. Mac Intire⁴⁸ observant la persistance de la défécation provoquée par les chocs

électriques chez des rats préfrontaux soumis à des chocs électriques mettent en doute, chez cet animal, la diminution de la peur après ablation frontale.

Nous insisterons surtout sur un fait qui paraît reconnu par tous les auteurs: *la persistance de la réactivité ou la plus grande réactivité des animaux aux stimulations douloureuses.*

3° Répercussion des troubles sensitifs sur le comportement instinctivo-affectif

Les troubles du comportement instinctif et affectif, après ablation frontale avaient attiré l'attention des auteurs classiques, aussi bien chez les chiens (Golz, Bechterew) que chez les singes (Bianchi).

Kalisher (1911), chez des chiens dressés auparavant à ne prendre leur nourriture qu'après avoir entendu des sons d'une hauteur déterminée, observe l'impossibilité pour eux, après ablation des lobes frontaux, de réfréner l'impulsion à manger. Afanasev (1913) rapporte une désinhibition des réflexes conditionnés classiques de défense chez des chiens préfrontaux, quand ces réflexes sont renforcés par un choc électrique.

En 1932, J. F. Fulton, C. F. Jacobsen et M. Kennard signalent après lésion frontale une augmentation considérable de l'appétit. J. W. Watts et J. F. Fulton (1934) montrent que l'ablation frontale bilatérale occasionne une faim morbide ("morbid hunger") et parfois une intussusception.

Toute une série de travaux de l'Ecole Russe dont on trouvera un résumé dans une récente étude de S. Brutkowski⁹ ont démontré que chez le chien l'ablation préfrontale détermine des perturbations importantes dans le jeu des réflexes conditionnés par la faim ou par la peur.

A côté des réponses d'attraction pour la nourriture, K. Akert a observé chez deux chats sur trois, après lésions préfrontales extensives en direction caudale sur la région médiane, des réactions de refus de toute nourriture pendant plusieurs jours.

Des troubles du comportement sexuel ont été observés aussi par Brutkowski.

4° Répercussion des troubles sensitifs sur l'apprentissage, le "learning"

Cet apprentissage utilise un conditionnement dit instrumental où les récompenses et les punitions interviennent comme conséquence de la réponse du sujet ou de son échec à répondre.

Nous envisagerons seulement ici deux méthodes bien connues: 1° la "delayed response" introduite par Hunter (1913) et dont la perturbation après lésion préfrontale, soulignée par J. F. Jacobsen (1931), a fait l'objet de très nombreux travaux.

2°, la "delayed alternation" où l'animal a le choix entre deux réponses, l'une de celles-ci étant récompensée aux épreuves alternées.

J. F. Jacobsen (1931-1935) démontre que les singes, après ablation préfrontale, ne sont plus capables de réaliser une action différée (delayed response) alors qu'ils peuvent répondre correctement de manière immédiate. Il signale la distractibilité des animaux, que ce soit par l'observateur ou n'importe quel événement extérieur mais fait surtout intervenir un trouble de la mémoire immédiate pour expliquer le trouble.

Cependant, des collaborateurs de Jacobsen, tels que J. Finan, Nissen, et associés, Malmo, démontrent que d'autres facteurs que le trouble de mémoire sont en cause.

J. Finan¹⁸ prouve par différentes méthodes (Shuttle box, labyrinthe simple) que l'organisation temporelle est conservée; d'après lui, ce qui perturbe surtout les singes préfrontaux au cours de la "delayed response", c'est l'absence de support par un stimulus extérieur au moment du choix.

Malmo⁴⁹, remplaçant dans l'épreuve de "delayed response" les stimuli de nourriture par des stimuli lumineux et variant l'éclairage de la cage où se trouve l'animal, observe que ses performances sont d'autant meilleures que la cage est moins éclairée. Il invoque un processus d'inhibition rétroactive.

Plusieurs travaux ont démontré que la "delayed response" peut être améliorée en réduisant la distractibilité de singes ou de

babouins par des sédatifs, notamment par des barbituriques (M. Wade⁸⁸), (Pribram⁷²). Chez des animaux testés tardivement, J. S. Blum et associés⁶ ne purent observer cet effet mais Mishkin et associés⁶³ confirment l'action favorable des barbituriques chez les babouins préfrontaux, même si l'entraînement a été tardif, aussi bien dans la "delayed response" que dans les tests d'alternation (delayed alternation").

Dans ces expériences, les performances des animaux sont améliorées en réduisant leur réactivité aux stimuli extérieurs, cause de distraction.

Récemment, J. Konorski et W. Lawicka³⁹ ont démontré le rôle capital des distractions dans la "delayed response" des chiens privés de leur cerveau préfrontal. La distraction introduite dans l'épreuve, durant la période de délai, consiste à le libérer ("release").

Suivant les conceptions de Pavlov, la réponse instrumentale (approche de la nourriture à l'endroit approprié) dépend d'un stimulus combiné associant la trace du stimulus de préparation au stimulus actuel de "release". Quand le chien réagit correctement, c'est que le stimulus de préparation ou stimulus de trace est devenu aussi fort ou plus fort que le stimulus de release. Chez les chiens préfrontaux, la force réflexogène du stimulus de préparation est réduite, le stimulus de release devient dominant mais comme il ne suffit pas, à lui seul, à déterminer la direction de la réponse, l'animal se trouve devant une tâche très difficile.

D'après J. Konorski et W. Lawicka, la principale cause du déficit de la "delayed reaction" des animaux préfrontaux est due à l'augmentation de la valeur réflexogène des stimuli externes actuels. Reprenant une expression de K. Goldstein, les auteurs estiment que les animaux frontaux (et aussi les humains) sont plus "stimulus bound", liés au stimulus, que les normaux.

Les difficultés de ces animaux paraissent dues à une incapacité d'inhiber ou de modifier un comportement habituel ou dominant, qui les rend inaptes à contrôler

le jeu des stimuli externes ou internes et à les intégrer en vue d'une action coordonnée.

III. TROUBLES SENSITIFS ET SENSORIELS DANS LA PATHOLOGIE PREFRONTALE HUMAINE

Nous rappellerons ensuite les travaux des auteurs ayant observé des troubles sensitifs au cours des lésions frontales chez l'homme.

Ces troubles ne sont pas classiques. On retrouve cependant, à la lecture des auteurs classiques, des exemples d'hyperesthésie diffuse (Dercum, Berger) ou d'hémihypoesthésie (Feuchtwanger), troubles qualifiés d'hystériques.

K. Goldstein (1927) a insisté sur ces troubles sensitifs: il a observé chez des malades frontaux une hyperexcitabilité des organes sensoriels du côté opposé à la lésion: l'excitation de la peau, des yeux, du nerf auditif détermine des réactions anormales qui aboutissent à des troubles moteurs et à des troubles des perceptions dans l'espace.

Clovis Vincent (1928) remarque aussi l'existence de paresthésies et d'hyperalgésie chez certains malades frontaux.

1^o *Constatations personnelles* — Dans la revue que nous avons faite en 1939⁵¹ de 172 observations de tumeurs frontales du Dr. Harvey Cushing, nous avons insisté sur la fréquence des *paresthésies* du visage ou des extrémités; nous avons retrouvé 10 fois le signe de frottement du nez ("rubbing nose") décrit par Wartenberg au cours de lésions frontales, retrouvé aussi au cours de tumeurs temporales et attribué par Sjöqvist à l'irritation du noyau caudé.

Nous avons relevé des cas d'hypoesthésie mais plus souvent encore, d'*hyperesthésie* (16 cas) associée parfois à des réactions affectives paradoxales.

Parmi les troubles sensoriels, signalons la fréquence relative de la photophobie et la possibilité d'une hyperesthésie auditive. Dollken (1935) observé que les malades frontaux ont une sensibilité excessive pour

les sons très intenses et qu'ils perdent la capacité de leur assigner une tonalité musicale. Au-dessus d'un certain seuil, le son n'est plus perçu que comme un bruit.

Enfin, nous avons retrouvé 11 cas d'*hallucinations* parmi les gliomes, 7 cas parmi les méningiomes (5 méningiomes olfactifs) (1 méningiome sagittal, 1 méningiome des pôles frontaux).

Parmi les autres troubles rencontrés, nous signalerons seulement ceux paraissant causer une perturbation viscérale sensitivo-motrice:

— *troubles urinaires*, classiques. Les stimulations, notamment émotionnelles, exagèrent cette incapacité.

— *troubles génitaux*, variables et d'interprétation difficile.

— *troubles digestifs*, dont 3 cas de "morbid hunger".

Tenant compte de la constatation associée de troubles de l'activité, de modifications du tonus musculaire, avec parfois catalepsie, d'une exagération des réflexes médians, de modifications psychiques paraissant traduire une libération d'instincts élémentaires, nous écrivions: "les lobes préfrontaux chez l'homme comme chez l'animal doivent exercer à l'état normal un rôle inhibiteur sur le système dit extra-pyramidal et vraisemblablement sur les portions archaïques de ce système "et encore: "ils jouent un rôle analogue à celui d'une *résistance* indispensable à la protection des autres zones cérébrales contre l'irruption du potentiel végétatif."

Nous serions tentés aujourd'hui d'ajouter qu'à l'inverse ils doivent pouvoir également mettre en branle le système végétatif, cette dualité fonctionnelle, de stimulation et l'inhibition, leur conférant un rôle régulateur.

En collaboration avec W. J. German (1938), j'ai pu mettre également en évidence des signes de libération extrapyramidale chez trois sujets ayant subi une lobectomie plus ou moins importante pour des tumeurs frontales bilatérales. Ultérieurement, grâce à l'obligeance de Clovis Vincent et de ses élèves, à celle de D. Petit-

Dutaillis, de Jean Guillaume, j'ai pu étudier 18 sujets ayant subi une lobectomie unilatérale. J'ai retrouvé des troubles du même ordre, notamment des paresthésies, du fou rire, souvent plus marqués durant les premiers mois post-opératoires, tendant à s'atténuer par la suite.

Les réflexes des membres et les réflexes paramédians (sterno-pectoral, medio-pubien) sont souvent exagérés du côté opposé à la lobectomie.

Avec M. Feld¹⁷ je pus étudier 20 malades ayant subi une topectomie des aires 9, ou des aires 9 et 10, ou des aires 9, 10 et 46.

Avec D. Petit-Dutaillis et L. Berges⁷⁰, nous avons étudié 50 cas de lobotomie réalisées pour des algies irréductibles (dont 30 lobotomies bilatérales et 20 unilatérales), la plupart suivant le procédé de Poppen.

La fréquence des troubles sensitifs après topectomie des aires 9 ou des aires 9 et 10 ou 9, 10 et 46 ou après lobotomie bilatérale est très grande. Les réactions peuvent être masquées par l'inertie du malade, surtout après lobotomie. Cette réserve faite, nous pensons que la surreactivité est un phénomène constant survenant très tôt (on la constate souvent dès le lendemain de l'intervention), persistant plusieurs mois mais s'atténuant généralement à partir de la 5^e ou de la 6^e semaine.

Chez ces malades, on peut observer des paresthésies et les réactions provoquées par des stimulations simples, telles que le pincement, la piqûre, le chatouillement, le froid, sont généralement vives, immédiates, accompagnées de réactions de défense et souvent associées à des réactions émotives telles que le fou-rire ou une attitude légèrement hostile ("laissez-moi, vous m'embêtez"... etc...). La pression des nerfs (cubitaires et surtout trijumeaux), des testicules chez l'homme, provoque des réactions antagonistes ou des grimaces du visage.

Comme nous l'écrivions en 1952⁵⁴, "chez certains malades, les stimulations paraissent provoquer des réactions érotiques. Nous citerons le cas d'un sujet qui, peu après une topectomie des aires 9 et 10, avait des érections au cours de l'examen et celui d'une femme (une maniaque, il est vrai) qui,

après lobotomie, présentait, quand on la piquait, des attouchements de la région génitale. Plus souvent il s'agit seulement d'une "attitude érotique" avec sourires équivoques."

Ces constatations ne doivent-elles pas être rapprochées par de celles de S. Brutkowski chez le chien?

Dans le premier mois post-opératoire, les malades ont souvent une peur instinctive des piqûres avec parfois réactions de fuite nécessitant deux ou trois personnes pour les immobiliser. Cette peur augmente certainement les réactions mais ne suffit pas à les expliquer: si, après avoir rassuré le malade et lui avoir dit de fermer les yeux on produit une stimulation, on obtient une réponse immédiate, anormale par sa brusquerie, son intensité et sa diffusion. Parfois le sujet gratte avec sa main ou son pied la région irritée, durant quelques secondes, ce qui semble indiquer une persistance anormale de la sensation.

Cependant les sensibilités élémentaires à tous les modes sont conservées et la stéréognosie paraît grossièrement indemne.

Parmi les *troubles sensoriels* nous avons constaté souvent une légère photophobie avec larmolement. L'*bippus* sur lequel Bianchi avait attiré autrefois l'attention est assez fréquent. Cette instabilité des réactions pupillaires paraît l'expression de l'instabilité neurovégétative. L'*irritabilité au bruit* est souvent présente.

Les troubles de l'orientation spatiale signalés dans les lésions frontales par Pierre Marie et dont les recherches de L. Barraquer - Ferré ont démontré la réalité expérimentale sont d'observation difficile chez des opérés.

Les *hallucinations* peuvent être rangées parmi les troubles sensoriels. La fréquence relative des hallucinations auditives au cours des tumeurs frontales avait été soulignée par Courville (1928); H. Baruk (1926) a relevé des hallucinations visuelles oniriques au cours de certaines tumeurs, notamment fronto-calleuses ou de la base; M. David et Puech ont signalé des hallucinations combinées dans les méningiomes de la petite aile du sphénoïde.

Nous avons invoqué^{51, 52, 53, 54, 55} à l'origine de certaines hallucinations, la suppression fonctionnelle préfrontale plus ou moins complète permettant, suivant une théorie développée par R. Mourgue⁶⁴ "*l'intrusion de la vie instinctive (neuro-végétative) dans le domaine de la causalité et de l'orientation (cortical)*".

Nous ne pouvons nous étendre ici sur ce vaste problème, rappelant seulement qu'on peut voir des hallucinations au cours de toutes les lésions frontales bilatérales, tumorales ou non tumorales. Nous en avons signalé des exemples avec D. Petit-Dutailis, au cours de l'hyperostose frontale interne et dans un cas, après lésion par balle, orbito-frontale bilatérale. La survenue d'états oniriques, après topectomie ou lobotomie, a été observée par différents auteurs et nous-même.

H. Krayenbuhl et W. Stoll⁴¹ décrivent une observation d'état hallucinatoire prolongé.

A l'inverse, les mêmes interventions peuvent, après lobotomie, faire cesser ou modifier un état hallucinatoire préexistant.

Rappelons ici l'importance qu'attachait H. Head aux phénomènes d'*hyperesthésie cutanée* chez les hallucinés au cours d'affections viscérales.

Cette hyperesthésie existait chez nos hallucinés frontaux.

En même temps que la désinhibition frontale, la coexistence d'une excitation neuro-végétative paraît nécessaire à la survenue d'un état hallucinatoire: c'est ce qu'ont réalisé M. David, H. Hécaen et J. Talairach¹³ en stimulant les noyaux antérieurs du diencephale après une lobectomie, déterminant ainsi des états maniacoïdes et aussi des états confuso oniriques.

Il faut cependant reconnaître que des états oniriques peuvent survenir à la suite d'autres interventions cérébrales.

Si l'action de contrôle de la région préfrontale sur le système extrapyramidal paraît majeure, d'autres régions du cortex exercent aussi une action.

R. C. Schneider et ses associés⁸² ont récemment invoqué, comme base anatomique des hallucinations au cours de lésions fron-

tales expansives, une irritation étendue aux lobes occipitaux ou temporaux par la voie des fibres éfferentes dans le faisceau inférieur occipito-frontal et le faisceau unciné.

L'importance des *troubles du système autonome* est trop classique pour que nous ayons à y insister.

Parmi les troubles digestifs, on a décrit une "voracité pathologique" après lésion frontale (observ. de Bechterew, Watts et Frazier, Moniz et Lima, Levin). Comme nous l'écrivions⁵² "ces faits peuvent s'interpréter à la fois par l'hyperesthésie coenesthésique (digestive dans ce cas) et par l'hypermotilité. Mais il est probable que des phénomènes d'hypoesthésie et d'hypomotilité peuvent se produire chez certains malades, entraînant du négativisme alimentaire, de l'atonie gastro-intestinale".

De la même manière, nous avons⁵² tenté d'expliquer les troubles génitaux et les troubles urinaires.

Les *troubles psychiques* constituent, de l'avis unanime, l'une des caractéristiques essentielles des lésions frontales. Celles-ci peuvent simuler des syndromes psychiatriques très variés, elles peuvent évoquer la paralysie générale progressive, un syndrome hypomaniaque, un état schizoïde ou même nettement schizophrénique. Des états hystériformes peuvent survenir.

L'*irritabilité* est un signe très fréquent paraissant conditionnée par l'hyperesthésie affective. Sous le nom d'*incontinence émotionnelle*, G. Rylander⁷⁹ a bien exprimé la difficulté, voire l'impossibilité de ces malades à réfréner leurs pulsions affectives. Le manque d'inhibition rend compte également des troubles instinctifs si fréquents. L'activité des malades peut être modifiée, devenir stéréotypée mais l'hyperactivité si spéciale de certaines espèces animales, après lésion préfrontale, paraît transposée sur d'autres plans. C'est ainsi que l'activité verbale peut être tantôt diminuée, tantôt exaltée, d'où un bavardage incessant.

De nombreux auteurs et récemment H. Hécaen³⁴ insistent sur la fréquence des états hypokinétiques au cours des tumeurs frontales.

Les *troubles de la mémoire* sont signalés par la plupart des auteurs. Ce sont des troubles de la mémoire de fixation, de la mémoire immédiate, mais le capital mnésique reste indemne semble-t-il. Ils paraissent surtout dus à la *distractibilité*, elle-même secondaire au défaut d'intégration des stimuli, ceux-ci entraînant une réponse motrice immédiate (verbale ou autre). Un bon exemple de cette modalité réactionnelle est la classique "Witzelsucht" l'Oppenheim, tendance aux jeux de mots, aux coq-à-l'âne avec réponse plus ou moins spirituelle et de caractère immédiat. La rapidité du jeu associatif mental y gagne mais pas la profondeur de la pensée.

L'*euphorie*, de l'avis unanime, reste un excellent signe des lésions frontales chez l'homme.

Le problème de l'action des interventions préfrontales sur la *douleur* est d'interprétation difficile. Comment concilier l'hypermotilité sensitive avec le soulagement, qui paraît souvent réel, de la souffrance?

Nous écrivions nous-mêmes⁵⁴: "les réponses peuvent avoir un caractère ambivalent, le sujet affirmant tantôt qu'il souffre, tantôt qu'il ne souffre pas.

Ces discordances compliquent l'interprétation des résultats. Cependant, l'aspect du visage plus détendu, les périodes d'euphorie entre les accès douloureux constituent un mieux. L'intervention a modifié le mode réactionnel à la douleur, les malades extériorisent davantage leur souffrance par des grimaces, par des cris ou en agrippant ce qui est à leur proximité. Comme nous le disait un infirmier, ils paraissent souffrir d'une manière plus animale... On ne saurait méconnaître que ces modalités réactionnelles, créées par la psycho-chirurgie, vont de pair avec une indifférence idéo-affective, une abolition du côté sublime de la souffrance. Mais certaines riures outrepassent la tolérance humaine et cette considération nous paraît justifier l'intervention."

Depuis R. Leriche, on sait l'importance du système autonome dans la pathogénie de la douleur. Avec D. Petit-Dutaillis⁷⁰

nous écrivions: "C'est en définitive par une action neuro-végétative portant à la fois sur le système vagal et orthosympathique que l'on peut essayer d'expliquer l'action de la psycho-chirurgie sur la douleur.

Les réactions neuro-végétatives se feraient sur un mode plus primitif. De même que les primitifs, de même que les enfants chez qui l'évolution des cancers peut être indolore, les lobotomisés supportent mieux la douleur parce que leur système nerveux végétatif a été modifié, ramené à un niveau plus archaïque. L'action sur l'œdème, que nous avons vérifiée dans trois cas plaide également en faveur d'une action neuro-végétative. Celle-ci rend compte aussi des résultats particulièrement importants obtenus dans les sympathalgies et les causalgies".

2° *Travaux récents* — De différents chercheurs ont observé des troubles sensitifs après lésion frontale chez l'homme (Yacorzinski et L. Davis⁹⁶, L. B. Malmö⁵⁹, W. P. Chapman, A. S. Rose et H. C. Solomon¹², F. A. Mettler et ses associés⁵⁸).

Etudiant les réactions sensorielles, les associés de Columbia-Greystone⁵⁸ n'ont pas observé de modifications visuelles, auditives ou vestibulaires significatives.

En ce qui concerne la sensibilité viscérale, nous signalerons un récent travail de G. Andrew et W. Nathan³ sur les troubles de la miction et de la défécation après lésions frontales.

ESSAI D'INTERPRETATION

Nous ne ferons qu'ébaucher les grandes lignes de ce chapitre qui mériterait une étude extensive. Il faut reconnaître cependant que beaucoup de points d'anatomie et de physiologie susceptibles d'éclairer le problème des troubles sensitifs restent mystérieux, surtout chez l'homme.

I. Bases anatomiques

1° *les connections afférentes* aux lobes préfrontaux sont mal connues (fig. 6).

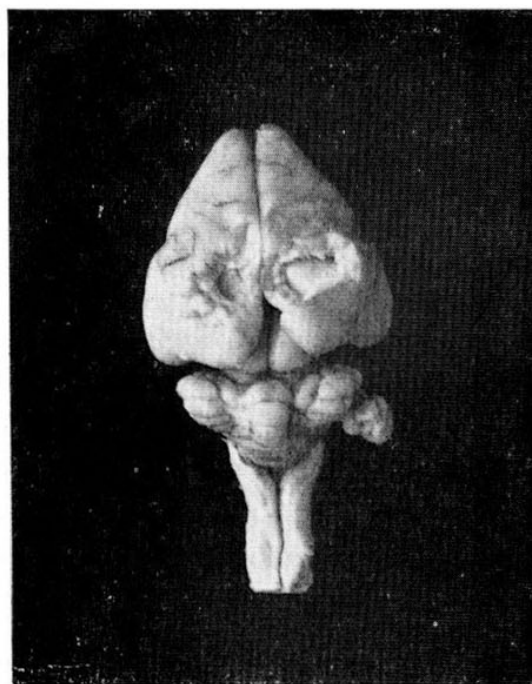


Fig. 6. — Cerveau de lapin après ablation dans la région parieto-occipitale.

2° *les connections efférentes* des lobes préfrontaux ont été particulièrement étudiées chez le singe. Elles ont été surtout décrites avec les noyaux dorso-médians du thalamus. D'autres projections ont été décrites vers les noyaux de la ligne médiane (complexe intralaminaire) et vers le noyau réticulaire.

3° *Fibres d'association*. De multiples fibres d'association corticale reliant les différentes aires préfrontales entre elles ont été décrites, notamment par W. J. S. Kricg⁴² et d'autres.

Le faisceau unciné relie la convexité préfrontale, à sa partie postéro-inférieure, avec la partie antérieure du lobe temporal.

Parmi les voies afférentes au cortex préfrontal, les mieux établies proviennent des noyaux dorso-médians. Les voies efférentes sont nombreuses et paraissent former un lien entre le cortex préfrontal, le striatum, la région limbique, l'hippocampe, l'hypothalamus et la mésencéphale.

II. Bases physiologiques

Nous insisterons seulement ici sur les travaux susceptibles d'éclairer le problème

des troubles sensitifs et instinctivo-affectifs au cours des lésions préfrontales, en soulignant:

1° — l'importance de la représentation du système autonome sur le cerveau préfrontal;

2° les données apportées par la neurographie physiologique.

1° Importance de la représentation du système autonome

C'est surtout sur la *surface orbitaire*, chez le chat et le singe, que des modifications

des réponses autonomes ont été obtenues par la stimulation électrique.

2° Neuronographie physiologique

J. P. Murphy et E. Gellhorn⁶⁵ ont montré chez le chat que l'injection de strychnine dans l'hypothalamus détermine un "firing", c'est-à-dire des potentiels E.E.G. évoqués dans le noyau thalamique dorso-médian et ensuite dans le cortex. Le noyau thalamique ventrolatéral reste constamment négatif. L'injection de strychnine dans le noyau dorso-médian détermine un

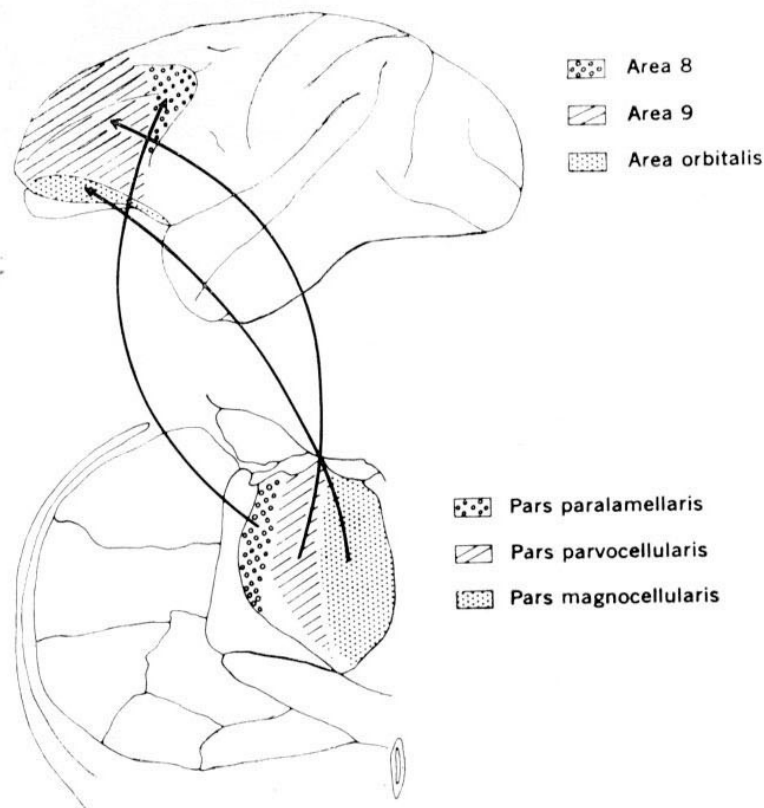


Fig. 7. — Les projections depuis les différentes zones du noyau dorsomédian sur les régions du cortex frontal granulaire (d'après K. Akert, In: *The frontal granular Cortex and Behavior*, 1964).

"firing" dans le cortex ipsilatéral puis contralatéral. En outre, après injection répétée ou après un temps de latence, l'hypothalamus ipsi— et contralatéral, les noyaux ventrolatéraux thalamiques ainsi que le noyau dorso-médian contralatéral sont le siège de potentiels évoqués.

La strychninisation du noyau thalamique ventrolatéral détermine un "firing" dans

l'hypothalamus et dans le noyau thalamique dorso-médian des deux côtés ainsi que dans le noyau thalamique ventrolatéral contralatéral.

La strychninisation d'aires variées du cortex (gyrus proreus, cortex sensori-moteur, aire acoustique primaire, circonvolution cingulée) cause l'apparition de pointes dans l'hypothalamus antérieur et posté-

rieur, dans les noyaux dorso-médians et ventrolatéraux.

Par la méthode de neuronographie physiologique, A. A. Ward et W. S. McCulloch⁹¹ ont montré chez le singe l'existence de projections corticohypothalamiques à partir de la région orbitaire et aussi à partir de la surface latérale de la région préfrontale.

Si les projections hypothalamo-corticales et cortico-hypothalamiques sont d'une importance majeure pour la régulation des pulsions instinctivo-affectives, de l'activité motrice, des sensations d'origine neuro-végétative, il existe d'autres systèmes mis en évidence par les travaux modernes de neurophysiologie, d'une importance également majeure: le système dit de projection thalamique diffuse, et le système de contrôle réticulaire du tronc cérébral.

Le système de projection thalamique diffuse, découvert par Dempsey et Morison (1942) est représenté dans le thalamus par le centre médian, les noyaux intralaminaires, les noyaux antérieurs et ventraux antérieurs, le pôle céphalique du *nucleus reticularis*. L'excitation électrique d'un quelconque de ces noyaux provoque des ondes de recrutement dans les autres noyaux du sys-

tème et dans les régions frontale, cingulée, orbitaire, pariétale et occipitale. Par contre, les zones de réception corticale dite spécifique (somatique, auditive et visuelle) ne sont pas influencées.

La formation réticulaire du tronc cérébral a fait l'objet des travaux de H. W. Magoun qui depuis 1946, avec ses associés (Rhines, Moruzzi, French, Starzl entre autres) a démontré le rôle tant facilitant qu'inhibiteur de cette formation sur l'activité corticale, par l'intermédiaire du mésencéphale et du diencephale.

L'excitation de la formation réticulée du tronc cérébral produit, on le sait, des réactions d'éveil et modifie l'activité. Les afférents sensoriels branchés sur le système réticulaire participent à la réaction d'éveil; qu'il s'agisse de certaines excitations cutanées, d'un fort bruit, d'une lumière brillante, de la distension d'un viscère creux, les messages parviennent par cette voie au diencephale, aux noyaux thalamiques de projection diffuse et au cortex. A l'inverse, comme l'ont montré J. D. French, R. Hernandez-Peon et R. B. Livingston²⁴ le cortex exerce une action régulatrice corticifuge sur le système réticulaire. La perturbation de cette action peut expliquer certains troubles au cours des maladies mentales et après lobotomie.

Il y a lieu de penser que l'action corticifuge influence aussi bien les activités sensorielles que motrices. On conçoit aussi que la douleur puisse être modifiée par ce mécanisme lorsqu'on se souvient des travaux chez le chat et chez le singe par J. M. R. Delgado¹⁴.

Effets produits par lésion des noyaux dorsomédians

J. Hambery et H. Jasper³² ont montré qu'après destruction des noyaux dorsomédians chez le chat, la stimulation du centro-médian, sauf à sa partie inférieure, ne provoque plus les réponses de potentiel évoqué sur le gyrus proreus.

D'autre part, L. Schreiner et ses associés⁸¹, après destruction des noyaux dorsomédians chez le chat constatent une réac-

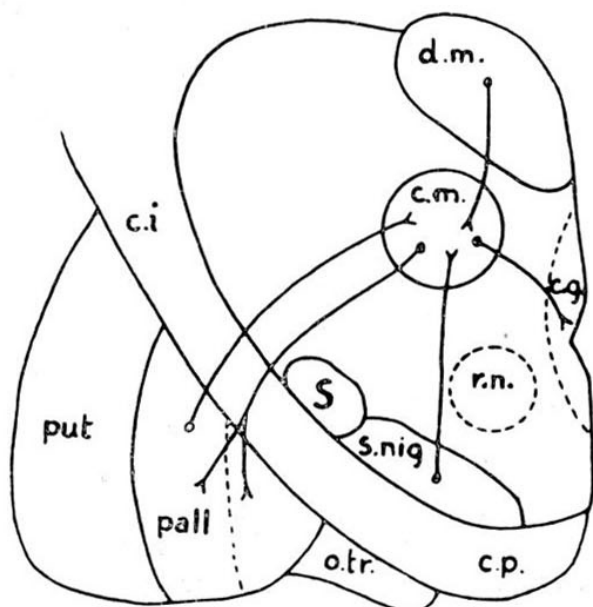


Fig. 8. — Diagramme montrant les connexions suggérées du noyau centro-médian avec d'autres structures (d'après P. Glees, 1946).

tivité accrue aux stimuli tactiles aussi bien nocifs que non nocifs, des réactions d'agressivité, parfois de la voracité, une incapacité d'apprendre.

La destruction des noyaux intralaminaires provoque un état de léthargie, la destruction des noyaux antérieurs du thalamus, une docilité particulière. Devant ces résultats, les auteurs concluent que les noyaux dorso-médians transmettent à l'état normal aux autres noyaux thalamiques l'influence inhibitrice du cerveau préfrontal tandis que les noyaux antérieurs transmettent des influx favorisant un comportement agressif.

C. Pechtel et associés⁶⁸, toujours chez le chat, après lésion des noyaux dorso-médians, constatent des troubles de la mémoire et du learning, une hyperactivité et une absence de crainte; J. M. Warren et K. Akert⁹³ font des observations comparables.

Effets produits par lésion des corps striés

Un grand nombre de travaux ont mis l'accent sur le rôle des corps striés, notamment de la tête des noyaux caudés, pour l'interprétation des effets produits par lésion préfrontale.

Cependant, les recherches d'H. E. Roswold et J. M. R. Delgado⁷⁶ montrent que la stimulation ou la destruction par électrocoagulation du noyau caudé produisent des effets comparables, chez le singe, aux effets des lésions préfrontales: hyperactivité, troubles gastro-intestinaux, troubles de l'apprentissage.

Rubinstein et Delgado⁷⁷ suppriment par excitation caudée la réaction d'évitement, chez le singe, d'un choc électrique. Le même effet avait été obtenu chez le chat par R. L. Thompson⁸⁷.

Ces résultats peuvent s'interpréter par l'intégration des noyaux caudés dans un système où participent les lobes frontaux et aussi l'hippocampe.

L'interaction noyaux caudés - thalamus peut aussi être évoquée.

Dusser de Barenne et Mc Culloch (1938) avaient montré que la stimulation du noyau caudé supprime l'activité thalamo-corticale.

Les travaux récents de D. Albe Fessard et associés² confirmés par A. M. Laurssen⁴³, entre autres, nous apprennent que des stimuli somatiques, visuels et auditifs, évoquent des *potentiels évoqués sur les corps striés, notamment sur la tête du noyau caudé après un relais thalamique*.

G. Krauthamer et D. Albe-Fessard⁴⁰ ont obtenu par stimulation de la partie dorso-latérale de la tête du noyau caudé une inhibition des potentiels sensoriels non spécifiques évoqués par stimuli périphériques.

A côté de leur action inhibitrice bien connue sur l'activité somato-motrice, les corps striés, en particulier les noyaux caudés, ont une action inhibitrice sur les afférences sensitives non spécifiques.

La réalité d'une représentation sensitive d'un mode élémentaire correspondant à la sensibilité protopathique de Henri Head paraît ainsi démontrée. Nous avons vu la complexité de ce système dont les principaux relais, depuis la moelle, se font dans la substance réticulée du tronc cérébral, l'hypothalamus, les noyaux thalamiques de la ligne médiane, les corps striés, le cortex.

A côté de ce système, on peut se demander s'il n'existe pas un système sensitif plus direct, intimement lié au système autonome, reliant la région hypothalamique ventromédiane à la partie médiane des noyaux dorso-médians et au cortex préfrontal, notamment orbitaire.

Les réactions de rage survenant après destruction de la région hypothalamique ventro-médiane ne seraient en effet que la traduction d'une "denervation supersensitivité" d'après Glusman et Roizin²⁸. Des stimuli minimes, insuffisants à évoquer la réaction de rage chez des chats normaux produisent cette réaction après une telle lésion. L'existence de voies de projection hypothalamo-thalamo-orbitaire expliquerait l'électivité des effets obtenus tant sur la douleur que sur certaines réactions autonomes, notamment digestives, par une intervention destinée à interrompre la projection ventro-médiane de la surface orbitaire par lobotomie partielle ou électrocoagulation suivant le procédé de Grantham²⁹ appliqué

en France par Cattan, Frumusan et Bucaille¹¹ à la pathologie digestive, ou encore par voie cingulée basse, comme Le Besnerais et moi-même⁵⁷ l'avons proposé contre les algies irréductibles.

D'importants problèmes concernant les projections exactes de certaines modalités sensitives et sensorielles associées au système autonome restent à résoudre, problèmes aussi ardues que passionnants.

R É S U M É

1° L'auteur rappelle ses constatations expérimentales faites en 1937 avec J. Finan, sur des singes opérés par J. F. Fulton: l'ablation bilatérale du cerveau antérieur, en respectant l'area 8 et l'area 6, détermine des troubles sensitifs et sensoriels que la seule observation montre évidents: paresthésie de la face et des extrémités, larmation anormale, réactivité augmentée à la piqure, au froid, à la lumière, aux bruits, aux émotions.

Il est impossible de dissocier ces troubles sensitifs et sensoriels de l'hyperactivité motrice, au mode souvent automatique et stéréotypé. Si l'hyperesthésie est évidente, elle peut aussi alterner avec des phénomènes d'hypoesthésie coïncidant avec une tendance cataleptique. Celle-ci, décrite pour la première fois par R. W. Barris (1935) chez le chat a été retrouvée par R. Messimy et J. Finan chez le singe (1937) puis, par R. Messimy⁵¹, chez le lapin (1939).

2° Ces réactions excessives aux stimulations extérieures ont été vérifiées par d'autres travaux expérimentaux, après ablation du cerveau préfrontal chez le singe, notamment ceux de M. Kennard et associés (1941³⁸). Parmi ces stimulations, le rôle de la lumière est reconnu par tous, le rôle du bruit associé à la lumière a été démontré par W. Isaac et de Vito (1958³⁷).

La répercussion de la distractibilité sur les réactions conditionnées, en particulier sur la "delayed reaction" fut signalée par C. F. Jacobsen (1935). L'influence des stimulations externes sur cette réaction a été démontrée par J. Finan (1939¹⁸), par R. B. Malmö (1942⁴⁹), par Harlow et ses associés, notamment G. M. French.

De nombreux travaux ont montré que, malgré la persistance d'une réactivité douloureuse, les réponses d'évitement de la

douleur différée par choc électrique, sont perturbées.

Dans tous ces cas, le caractère immédiat des réponses rend compte, au moins partiellement, des perturbations.

3° Chez l'homme, au cours des lésions préfrontales, K. Goldstein avait insisté sur l'hyperexcitabilité sensorielle du côté opposé à la lésion.

En analysant 148 observations de tumeurs frontales opérées par Harvey Cushing ou ses élèves, l'auteur a montré (1939) la fréquence de l'hyperesthésie sensitive et sensorielle. Celle-ci a été retrouvée depuis après lobotomie (W. P. Chapman, Rose et Solomon¹²; Petit-Dutaillis et R. Messimy⁶⁹), après gyrectomie (R. B. Malmö⁴⁹) ou topectomie (F. A. Mettler⁵⁸; M. Feld et R. Messimy¹⁷) des aires 9, 10 et 46. Elle contraste avec la perte d'appréhension de la douleur.

Les modifications de la sensibilité viscérale digestive ou sexuelle sont d'appréciation difficile. Les modifications de la sensibilité viscérale, récemment démontrées par la cystométrie (J. Andrew et P. W. Nathan, 1964³) paraissent expliquer les classiques phénomènes d'incontinence ou de rétention après lésion préfrontale.

Pathogénie. L'auteur invoque une libération de la sensibilité dite protopathique par H. Head mais le mécanisme intime des troubles reste inconnu. Les systèmes thalamo-préfrontal et préfronto-thalamique paraissent impliqués. Il est possible que l'atteinte du système orbito-thalamo-hypothalamique ou encore orbito-hypothalamique, dont l'importance pour la vie émotionnelle, avait été soulignée par J. F. Fulton, entre en jeu. Mais l'action bilatérale des lobes frontaux, agissant comme un tout semble aussi nécessaire.

RESUMEN

1º El autor expone su labor experimental realizada en 1937 con J. Finan en monos operados por J. F. Fulton: la ablación bilateral de los lóbulos prefrontales dejando intactas las áreas 8 y 6 da lugar a notables perturbaciones sensoriales y sensitivas: parestesias faciales y en las extremidades, alteraciones en la secreción lacrimal, hiperreactividad frente a estímulos dolorosos, frío, luz, ruidos, emociones. No se puede disociar estas alteraciones sensitivas y sensoriales de la hiperreactividad motora, que a menudo es estereotipada y carece de un fin determinado.

Se observó una hipoestesia aparente acompañada de una tendencia cataléptica. Esta última, descrita originariamente por R. W. Barris en el gato (1935) fue estudiada por R. Messimy y J. Finan en el mono (1937) y más adelante por R. Messimy en el conejo (1939⁵¹).

2º Otros trabajos experimentales pudieron confirmar la hiperreacción a estimulaciones externas luego de la ablación del lóbulo prefrontal del mono; los de M. Kennard et al. (1941³⁸) reconocen ampliamente la acción de la luz mientras que W. Isaac y de Vito (1958³⁷) demuestran la acción del ruido asociado a la luz.

C. F. Jacobsen (1935) observó que la distractibilidad puede alterar reacciones condicionadas, especialmente la "reacción retardada". La influencia de las estimulaciones externas fue subrayada por J. Finan (1939¹⁸), R. B. Malmö (1942⁴⁹), Harlow y colaboradores, particularmente por G. M. French.

En varios trabajos se demostró que cuando persiste la reactividad a los estímulos dolorosos se ve perturbada la eliminación del dolor retardado (mediante shock eléctrico). En todos estos casos el carácter in-

mediato de la respuesta explica, al menos parcialmente, las perturbaciones.

3º En el hombre K. Goldstein ya hace mucho tiempo hizo notar la hiperexcitabilidad sensorial del lado opuesto a una lesión prefrontal. Luego de analizar 148 casos de tumores frontales, operados por Harvey Cushing o sus colaboradores, el autor pudo demostrar (1939) con qué frecuencia había hiperestesia, sensitiva y sensorial. Este hecho fue confirmado luego de practicarse la lobotomía (W. P. Chapman, Rose y Solomon¹²; D. Petit-Dutaillis y R. Messimy⁶⁹), la girectomía (R. B. Malmö⁴⁹) o la topectomía (F. A. Mettler⁵⁸; M. Feld y R. Messimy¹⁷) de las áreas 19, 10 y 46.

Esta hiperestesia aparece acompañada de la desaparición del temor al dolor.

Son más difíciles de apreciar las modificaciones de la sensibilidad visceral, digestiva o sexual. Los cambios de la sensibilidad vesicular, comprobados recientemente mediante cistometría (J. Andrew y P. W. Nathan 1964³), parecen explicar los síntomas clásicos de incontinencia y retención posteriores a la lesión prefrontal.

Patogenia. El autor sugiere a manera de explicación, la liberación de la "sensibilidad protopática" (H. Head) pero el mecanismo íntimo de las perturbaciones sigue siendo desconocido. Parece existir una relación con los sistemas tálamo-prefrontal y prefrontotalámico.

Es muy probable que la lesión de los sistemas órbito-tálamo-hipotalámico, cuya importancia en la vida emocional fue subrayada por J. F. Fulton desempeñe un papel importante; también parece revestir gran importancia la acción bilateral de los lóbulos prefrontales funcionando como un todo.

SUMMARY

1º The author reviews his experimental work done in 1937, with J. Finan, on monkeys operated by J. F. Fulton: the bilateral

ablation of prefrontal lobes, sparing area 8 and area 6 gives rise to evident sensitive and sensorial disturbances: Paresthesias of

the face and of the extremities, abnormal lacrymation, overreactivity to pinprick, to cold, light, noises, emotions.

One cannot dissociate these sensitive and sensorial disturbances from the motor hyperactivity, frequently purposeless and stereotyped.

An apparent hypoaesthesia was also observed, coexisting with a cataleptic tendency. This tendency, first described by R. W. Barris on the cat (1936) was seen by R. Messimy and J. Finan on the monkey (1937) and later by R. Messimy on the rabbit (1939⁵¹).

2° Other experimental works could verify overreaction to external stimulations, after ablation of the prefrontal brain of the monkey: namely those of M. Kennard and al. (1941³⁸). The action of light is widely recognized, the action of noise associate to light was demonstrated by W. Isaac and de Vito (1958³⁷).

The distractibility can disturb the conditioned reactions, especially the "delayed reaction" as it was seen by C. F. Jacobsen (1935). The importance of external cues was stressed by J. Finan (1939¹⁸), by R. B. Malmö (1942⁴⁹), by Harlow and co-workers, specially G. M. French.

In several works, it was demonstrated that, if the reactivity to painful stimulations persists, avoidance of delayed pain (by electric shock) is perturbed.

In all these eventualities, the immediate character of the response explains, at least partially, the disturbances.

3° By *man*. K. Goldstein has, a long

time ago, stressed the sensorial hyperexcitability on the opposite lesion of a prefrontal lesion.

Analysing 148 cases of frontal tumors, operated by Harvey Cushing or his co-workers, the author could show (1939) how frequent was the hyperaesthesia, sensitive and sensorial. The fact was verified after lobotomy (W. P. Chapman, Rose and Solomon¹²; D. Petit-Dutaillis et R. Messimy⁶⁹), after gyrectomy (R. B. Malmö⁴⁹), or topectomy (F. A. Mettler⁵⁸; M. Feld and R. Messimy¹⁷) of the area 19, 10 and 46.

This hyperaesthesia appears in contrast with the loss of fear of the pain.

More difficult to appreciate are the changes of visceral sensibility, digestive or sexual. The changes of the vesical sensibility, recently demonstrated by cystometry (J. Andrew and P. W. Nathan 1964³), seen to explain the classical symptoms of incontinency or retention after prefrontal lesion.

Pathogeny. The author proposed, as an explanation, a release of the "protopathic sensibility" (H. Head) but the intimate way of disturbances remains unknown.

The thalamo-prefrontal and prefronto-thalamic systems seem to be concerned.

It is quite possible that the lesion of the orbito-thalamo-hypothalamic systems, of which J. F. Fulton has stressed the importance for emotional life, plays an important part. But the bilateral action of prefrontal lobes, acting as a whole, seems also very important.

ZUSAMMENFASSUNG

1) Der Autor führt auf seine Befunde aus dem Jahre 1937 zurück welche er mit J. Finan auf Grund von Studien an von J. F. Fulton operierten Affen ausführte.

Bilaterale Ablation des Stirnhirnes, unter Erhaltung von Area 6 und 8 verursacht sensitive und sensorielle Störungen welche schon allein durch folgende Beobachtung auffallen: Parästhesien des Facies und der Extremitäten, abnormale Tränenbildung,

erhöhte Reaktivität bei Stechen, Kälte, gegenüber Licht, Lärm und Emotionen.

Es ist unmöglich diese sensitiven und sensoriellen Störungen von der motilen Überaktivität zu trennen, welche oft in automatischer und stereotypischer Weise auftritt.

Die evidente Hyperaesthäsie kann auch abwechselnd mit einer Hypoaesthäsie, zugleich mit kataleptischer Tendenz auftreten.

ten. Diese wurde zum ersten Male von R. W. Barris (1935) bei Katzen gezeigt und wurde von Messimy und Finan beim Affen und später von Messimy⁵¹ beim Kaninchen aufs Neue beschrieben.

2) Diese übermässigen Reaktionen auf äussere Reizungen haben sich auch bei anderen experimentalen Versuchen, nach Ablation des Stirnhirnes beim Affen bewahrt, (M. Kennard und seine Mitarbeiter (1941³⁸)).

Bei diesen Reizungen spielt das Licht eine grosse und allgemein bekannte Rolle, ebenso wie der Einfluss von Lärm, zusammen mit dem des Lichts, wie es von W. Isaak und de Vito (1958³⁷) beschrieben wurde.

Die Einwirkung der Zerstreuung auf die konditionellen Reaktionen, insbesondere die "delayed reaction" wurde von Jacobsen (1935) beobachtet.

Der Einfluss äusserer Reizungen auf diese Reaktionen wurde von J. Finan (1939¹⁸), Malmo (1942⁴⁹), Harlow und Mitarbeitern, insbesondere von G. M. French beschrieben.

Zahlreiche Arbeiten haben gezeigt dass, obwohl die Reaktivität für Schmerzempfindung erhalten blieb, die Reaktivität bei differierter Schmerzvermeidung (elektr. Schock) gestört ist.

In allen diesen Fällen ist die Unmittelbarkeit der Reaktionen, zumindest teilweise, eine Erklärung für die Störungen.

Beim Menschen, in den präfrontalen Läsionen hat K. Goldstein auf die sen-

sorielle Hyperexzitabilität der der Läsion gegenüberliegenden Seite hingewiesen.

In 148 Beobachtungen von Hirntumoren, welche von Harvey Cushing und seinen Schülern operiert wurden, hat der Autor die Häufigkeit der sensitiven und sensorischen.

Hyperesthäsie festgestellt. Man fand diese von neuem nach Lobotomie (W. Chapman, Rose u. Solomon¹²; Petit-Dutaillis et Messimy⁶⁹), nach Gyrectomie (R. B. Malmo⁴⁹) oder Topectomie (F. A. Mettler⁵⁸; Feld et Messimy¹⁷) der Areas 9, 10 und 46. Sie steht im Gegensatz zum Verlust des Angstgefühls vor Schmerzempfindung.

Die Veränderungen der viszerale Sensibilität (Verdauung oder Sexualität) sind schwer zu ermessen.

Die Veränderungen der vesikalen Sensibilität welche letzthin durch Zystometrie gezeigt wurden (J. Andrew u. P. W. Nathan, 1964³) scheinen Inkontinenz oder Retention nach präfrontaler Läsion zu erklären.

Pathogenie. Der Autor vermutet eine Freimachung der sogenannten protopathischen Sensibilität (H. Head). Das thalamopraefrontale und das praefronto-thalamische System scheinen in Mitleidenschaft gezogen.

Es ist möglich dass die Läsion des orbito-thalamo-hypothalamischen Systems, dessen Bedeutung für das Gefühlsleben von J. F. Fulton hervorgehoben wurde, eine wichtige Rolle spielt. Aber die beidseitige Action der Stirnlappen welche als global anzusehen ist, erscheint ebenso wichtig.

REFERENCES BIBLIOGRAPHIQUES

(à partir de 1939)

Dans le but d'alléger la bibliographie, nous avons supprimé certaines références que le lecteur trouvera facilement dans les ouvrages suivants:

— *The frontal Granular Cortex and Behavior* A Symposium edited by J. M. Warren and K. Akert.
Mc Graw-Hill Book Company.
New-York 1964.

— *Columbia Greystone Associates*

Selective partial ablation of the frontal Cortex — F. A. Mettler editor. — Paul B. Hoeber, Inc. Medical Book. New-York 1949.

— *The frontal lobes*

Assoc. for Research in nervous and Mental Disease. Vol. XXVII — The Williams and Wilkins Company — 1948.

Frontal lobes and schizophrenia. Edited by M. Greenblatt and H. C. Solomon — Springer Publishing Company. New-York 1953.

— J. F. Fulton — Physiologie des lobes frontaux et du cervelet Masson et Cie, éditeur Paris, 1953.

1. Akert, K.: Comparative Anatomy of the Frontal Cortex and Thalamocortical Connections in the frontal Granular Cortex and Behavior, p. 372-396, 1964.

2. Albe-Fessard, D.; Rocha-Mirando, C. and Oswaldo-Cruz, E.: Activités évoquées dans le noyau caudé du chat en réponse à des types divers d'afférences. E.E.G. Clin. Neurophysiol. T. 12, 649-661, 1960.

3. Andrew J. and Nathan, P. W.: Lesions of the anterior frontal lobes and disturbances of micturition and defecation. Brain. Vol. 87. Part. II. June 233-262, 1964.

4. Bailey, P.; Bonin G. von and McCulloch, W. S.: The Isocortex of the Chimpanzee. 1950. Urbana III University of Illinois Press, 440 pages, 1950.

5. Beach F. A.: Effects of lesions to corpus striatum upon spontaneous activity in the male rat. Journal of Neurophysiology. T. 4. N° 2, 191-195, 1941.

6. Blum, J. S.; Chow, K. L. and Blum, R. A.: Delayed response performance of monkeys with frontal removals after excitant and sedative drugs. Journal of Neurophysiol. T. 14, 197-202, 1951.

7. Borrel, A.; Petit-Dutaillis, D.; Messimy, R. et Janny, P.: Délire onirique avec fabulation fantastique, consécutif à une lésion orbito-frontale par projectile. Revue Neurologique. T. 81, N° 4, 1949.

8. Bowsher, D.: Les relais des sensibilités somesthésiques et douloureuses au niveau du tronc cérébral et du thalamus. Toulouse Médical, 64 è Année, N° 9, 965-984, 1963.

9. Brutkowski S.: Prefrontal Cortex and Drive Inhibition in: The frontal Granular Cortex and Behavior, p. 242-270, 1964.

10. Campbell, R. J. and Harlow, J. F.: Problem solution by monkeys following bilateral removal of the prefrontal areas. V. Spatial delayed reactions. Journal of Experimental Psychology, Vol. 35, N° 2, 110-126, 1945.

11. Cattani, Frumusan et Bucaille: L'infiltration novocaïnique préfrontale en pathologie digestive. Arch. des Maladies de l'Appareil Digestif, T. 43, 137-158, 1954.

12. Chapman, W. P.; Rose A. S. and Solomon, H. C.: Measurements of heat stimulus producing motor withdrawal reaction in

patients following frontal lobotomy. In: The frontal lobes, 1948.

13. David, M.; Hécaen, H. et Talairach, J.: Les troubles psychiques de type expansif au cours des interventions sur la région du 3^e ventricule. Revue Neurologique Nov-Déc., T. 78, 541-560, 1946.

14. Delgado, J. M. R.: Cerebral structures involved in transmission and elaboration of noxious stimulation. Journal of Neurophysiology, T. 18, 261-273, 1955.

15. Denny-Brown, D.: The frontal lobes and their functions. In A. Feiling Edit. Modern trends in Neurology. New-York. Paul B. Hoeber Inc.

16. Elithorn, A.; Piercy, M. F. and Crosskey, M. A.: Prefrontal leucotomy and the anticipation of pain. Journal of Neurology, Neurosurgery and Psychiatry, Vol. 18, N° 1, 34-43, 1955.

17. Feld, M. et Messimy, R.: Contribution à l'étude de la topectomie Presse Médicale (20 avril), T. 57, 358-360, 1949.

18. Finan, J. L.: Effects of frontal lobe lesions in temporally organized behavior in monkeys. Journal of Neurophysiology, T. 2, N° 3, 208-226, 1939.

19. Freeman, W. and Watts, J. W.: Retrograde degeneration of the thalamus following prefrontal lobotomy. The Journal of Comparative Neurology, T. 86, 65-93, 1947.

20. Freeman, W. and Watts, J. W.: Psychosurgery. 2^e Edit. Springfield III. Charles C. Thomas, 598 pages, 1951.

21. French, G. M. and Harlow, H. F.: Locomotor reaction decrement in normal and brain-damaged monkeys. The Journal of Comparative and physiological Psychology, T. 48, N° 6, 496-501, 1955.

22. French, G. M.: Locomotor effects of regional ablations of frontal cortex in rhesus monkeys. The Journal of comparative and physiological Psychology, T. 52, 18-24, 1959.

23. French, J. D.; Von Amerongen, F. K. and Magoun, H. W.: Effects of chronic lesions in central cephalic brain stem of monkeys. A.M.A. Archives of Neurology and Psychiatry, Vol. 68, N° 5, 577-590, 1952.

24. French, J. D.; Hernandez-Peón, R. and Livingston, R. B.: Projections from cortex to cephalic brain stem (reticular formation) in monkey. Journal of Neurophysiology, T. 18, N° 1, 74-95, 1955.

25. Glees, P. and Wall, P. D.: Fiber connections of the subthalamic region and the centro-median nucleus of the thalamus. Brain, T. 69, 195-208, Sept. 1946.

26. Glees, P.: The interrelation of the strio-pallidum and the thalamus in the

macaque monkey. *Brain*, T. 68, Part. 4, 331-346, 1945.

27. Gjone, R. and Seteklew, J.: Excitatory and inhibitory bladder responses to stimulation of the cerebral cortex in the cat. *Acta physiologica Scandinavica*, T. 59, fasc. 4, 337-348, 1963.

28. Glusman, M. and Roizin, L.: Role of the hypothalamus in the organization of agonistic behavior in the cat. *Trans. Amer. Neurol. Assoc.*, 85, p. 177, 1960.

29. Grantham, E. G.: Prefrontal Lobotomy for relief of pain, with a report of a new operative technique. *Journ. of Neurosurgery*, T. 8, 405-410, 1951.

30. Goldstein, K.: The mental changes due to frontal lobe damage. *Journ. of Psychol.*, T. 17, 187-208, 1944.

31. Gross, C. G. and Weiskrantz, L.: In: *The frontal cortex and Behavior*, p. 74-101, 1964.

32. Hambery, J. and Jasper, H.: Independence of diffuse thalamocortical projection system shown by specific nuclear destructions. *Journal of Neurophysiology*, T. 16, 252, 1953.

33. Harlow, H. F.: *Références bibliographiques in Frontal Granular Cortex and Behavior*, 1964.

34. Hécaen, H.: Mental symptoms associated with tumors of the frontal lobe. In *Frontal Granular Cortex and Behavior*, 335-352, 1964.

35. Hillemand, B.: *Manifestations digestives au cours des atteintes du système nerveux central*, 1955. Paris, Imprimerie R. Foulon, 29 rue Deparcieux.

36. Hoff, E. C.; Langford, H. G.; Vester, J. W. and Thomas, P. R.: Strychnine facilitation of pressor responses evoked from cerebral cortex. *Journ. of Neurophysiol.*, T. 14, p. 167-174, 1951.

37. Isaac, W. and de Vito, J. L.: Effect of sensory stimulation on the activity of normal and prefrontal lobectomized monkeys. *The Journal of Comparative and physiolog. Psychology*, T. 51, 172-174, 1958.

38. Kennard, M. A.; Spencer, S. and Fountain, G.: Hyperactivity in monkeys following lesions of the frontal lobes. *Journ. of Neurophysiol.*, T. 4, N° 7, 512-524, 1941.

39. Konnorski, J. and W. Lawicka: Analysis of errors by prefrontal animals on the delayed - response test. In: *The frontal Granular Cortex and Behavior*, 1964.

40. Krauthamer, G. and Albe-Fessard, D.: Inhibition of non specific sensory activities following striopallidal and capsular stimu-

lation. *Journ. of Neurophysiol.*, Vol. 28, N° 1, 100-124, 1965.

41. Krayenbuhl, H. et Stoll, W.: Prefrontal leucotomy and topectomy for relief of intractable pain. *Rapport au IVE Congrès Neurol. International*. Paris 5-10 sept. 1949.

42. Krieg, W. J. S.: *Connections of the frontal cortex of the monkey*. Charles C. Thomas Publ. Springfield, Illinois, 1954.

43. Laursen, A. M.: *Corpus striatum*. *Acta Physiologica Scandinavica*, Vol. 59, Supplementum 211, 1963.

44. Le Beau, J.: *Psychochirurgie et fonctions mentales*, Paris, Masson et Cie Edit, 1954.

45. Le Gros Clark, W. E.: The connections of the frontal lobes of the Brain. *The Lancet*, Londres, 353-356, 6 Mars 1948.

46. Lichtenstein, P. E.: Studies of anxiety II. The effects of lobotomy on a feeding inhibition in dogs. *Journ. of Comparative and Physiol. Psychology*, T. 43, 419-427, 1950.

47. Mc Lardy, T.: Thalamic projections to frontal cortex in man *Journ. of Neurol. Neurosurg. and Psychiatry*, T. 13, N° 3, 198-202, 1950.

48. Mayer, B. A. and Mc Intire, R. W.: The extinction of the C.E.R. following frontal ablation. *Journ. of comparative and Physiol. Psychology*, T. 53, N° 6, 549-562, 1960.

49. Malmö, R. B.: Interference factors in delayed response in monkeys after removal of frontal lobes. *Journ. of Neurophysiol.*, T. 5, N° 4, 295-308, 1942.

50. Malmö, R. B.: In: *The frontal lobes*, p. 537-564, 1948.

51. Messimy, R.: Les effets, chez le singe, de l'ablation des lobes préfrontaux. *Revue Neurologique*, T. 71, N° 1, p. 1-37, 1939.

52. Messimy, R.: Les effets chez l'homme des lésions préfrontales. *Annales de Médecine*, T. 45, N° 5, 321-360, 1939.

53. Messimy, R.: Faits expérimentaux et cliniques concernant les fonctions des lobes préfrontaux. *Annales de Médecine*, T. 49, N° 1, 69-84, 1948.

54. Messimy, R.: Sur les troubles sensitifs et sensoriels observés après lobotomie ou topectomie préfrontales. *Arquivos de Neuro-Psiquiatria*, Vol. 10, N° 3, 305-314, 1952.

55. Messimy, R.: Les hallucinations dans la pathologie préfrontale. *Essai d'interprétation*. *La Presse Médicale*, T. 61, N° 3, 52-54, 1953.

56. *Messimy, R.*: Où en est la psychochirurgie? La Semaine des Hôpitaux de Paris, 33^e année, N° 51-52, 1957.
57. *Messimy, R. et Le Besnerais, Y.*: Lobotomie préfrontale sélective par cingulotomie. Revue Neurologique, T. 96, N° 3, 234-238, 1957.
58. *Mettler, F. A.*: Bibliographie in: Columbia - Greystone associates. Selective Partial Ablation of the Frontal Cortex, 1949.
59. *Meyer, A. et Beck, 1954*: Prefrontal leucotomy and related operations. Anatomical aspects of success and failure. Edinburgh and London, Oliver and Boyd, Ltd. 1954.
60. *Miles, J. E. and Rosvold, H. E.*: The effect of prefrontal lobotomy in rhesus monkeys on delayed-response performance motivated by pain-shock. Journ. of comparat. and physiol. Psychology, T. 49, 286-292, 1956.
61. *Miles, R. C. and Blomquist, A. J.*: Frontal lesions and behavioral deficits in monkey. Journ. of Neurophysiol., T. 23, N° 4, 471-484, 1960.
62. *Miles, R. C.*: Learning by squirrel monkeys with frontal lesions In: The frontal Granular Cortex and Behavior, p. 149-167, 1964.
63. *Mishkin, M.; Rosvold, H. E. and Pribram, K. H.*: Effects of nembutal in baboons with frontal lesions. Journ. of Neurophysiol., T. 16, N° 2, 155-159, 1953.
64. *Mourgue, R.*: Neurobiologie de l'hallucination, Bruxelles, M. Lamertin, 58-60 rue Coudenberg V., 1932.
65. *Murphy, J. P. and Gellhorn*: Further investigations on diencephalic-cortical relations and their significance for the problem of emotion. Journ. of Neurophysiol., T. 8, N° 6, 431-447, 1945.
66. *Nauta, W. J. H.*: Some efferent connections of the prefrontal cortex in the monkey. In: The frontal Granular Cortex and Behavior, p. 397-409, 1964.
67. *Newman, P. P. and Wolstencroft, J. H.*: Influence of orbital cortex on blood pressure responses in cat. Journ. of Neurophysiol., T. 23, N° 2, 211-217, 1960.
68. *Pechtel, C.; Masserman, J. H.; Schreiner, L. and Levitt, M.*: Action des lésions des noyaux médio-dorsaux du thalamus sur le comportement du chat. The Journ. of Nervous and Mental Disease. Baltimore, T. 121, N° 1, 26-33, 1955.
69. *Petit-Dutaillis, D.; Borel, A.; Messimy, R. et Bouvet, M.*: Psychose hallucinatoire chronique avec hypertension artérielle. Guérison des troubles psychiques et de l'hypertension après lobotomie préfrontale bilatérale. Revue Neurologique, T. 84, N° 2, 1951.
70. *Petit-Dutaillis, D.; Messimy, R. et Bergès, L.*: La psychochirurgie des algies irréductibles. Etude basée sur 57 cas. La Semaine des Hôpitaux de Paris, T. 29, N° 75, 1-11, 1953.
71. *Pribram, K. H. and Weiskrantz, L.*: A comparison of the effects of medial and lateral cerebral resections on conditioned avoidance behavior of monkeys. The Journ. of comparat. and psychol. Physiol., Vol. 50, N° 1, 74-80, 1957.
72. *Pribram, K. H.*: Some physical and pharmacological factors affecting delayed response performance of baboons following frontal lobotomy. Journ. of Neurophysiol., T. 13, N° 5, 373-382, 1950.
73. *Pribram, R. H.; Chow, K. L.; Semmes, J.*: Limit and organization of the cortical projection from the medial thalamic nucleus in monkey. Journ. of comparat. Neurol., T. 98, 433-448, 1953.
74. *Pribram, K. H.; Alumada, A.; Hartog, J. and Ross, L.*: A progress report on the neurological processes disturbed by frontal lesions. In: The frontal Granular Cortex and Behavior, p. 28-55, 1964.
75. *Rose, J. E.; Woolsey, C. N.*: The orbitofrontal cortex and its connections with the mediodorsal nucleus in rabbit, sheep and cat. In: The frontal lobes. Res. publ. Assoc. Nerv. Mental Dis., T. 27, p. 210-232, 1948.
76. *Rosvold, H. E. and Delgado*: The effect on delayed-alternation test performance of stimulating or destroying electrically structures within the frontal lobes of the monkey's brain. Journ. of comparat. and physiol. Psychology, T. 49, 365-372, 1956.
77. *Rubinstein, E. H. and Delgado, J. M. R.*: Inhibition induced by forebrain stimulation in the monkey. Amer. Journ. of Physiology, Vol. 205, N° 5, 941-948, 1963.
78. *Ruch, T. C. and Shenkin, H. A.*: The relation of area 13 on orbital surface of frontal lobes to hyperactivity and hyperphagia in monkeys. Journ. of Neurophysiol., T. 6, N° 5-6, 349-360, 1943.
79. *Rylander, G.*: Personality changes after operations on the frontal lobe: a clinical study of thirty-two cases. Acta Psychiat. Neurol. Copenhagen, Suppl. 20, 1939.
80. *Rylander, G.*: Personality analysis before and after frontal lobotomy. Res. Publ. Assoc. Nerv. Mental Dis., T. 27, 691-705, 1948.
81. *Schreiner, L.; Rioch, D. Mck.; Pechtel,*

C. and Massermann, J. H.: Behavioral changes following thalamic injury in cat. *Journ. of Neurophysiol.*, T. 16, N° 3, 234-246, 1953.

82. Schneider, R. C.; Crosby, E. C.; Bagchi, B. K.; Calhoun, H. D.: Temporal or occipital lobe hallucinations triggered from frontal lobe lesions. *Neurology*, T. 11, 172-179, 1961.

83. Soulaire, A.; Soulaire, M. L. et Teyssere: Modifications de l'activité spontanée du rat à la suite de lésions du cerveau antérieur. *Journ. de Physiol.*, T. 47, 278-282, 1955.

84. Starzl and Magoun, H. W.: Organization of the diffuse thalamic projection system. *Journ. of Neurophysiol.*, T. 14, 133-146, 1951.

85. Starzl, T. E.; Taylor, C. W. and Magoun, H. W.: Ascending conduction in reticular activating system, with special reference to the diencephalon. *Journ. of Neurophysiol.*, T. 14, 461-477, 1951.

86. Streb, J. M. and Smith, K.: Frontal lobotomy and the elimination of conditioned anxiety in the rat. *Journ. of comparat. and physiol. Psychology*, Vol. 48, N° 2, 126-129, 1955.

87. Thompson, R. L.: Effects of lesions in the caudate nuclei and dorsofrontal cortex on conditioned avoidance behavior in cats. *Journ. of comparat. and physiol. Psychology*, Vol. 52, N° 6, 650-659, 1959.

88. Wade, M.: The effect of sedatives upon delayed response in monkeys follow-

ing removal of the prefrontal lobes. *Journ. of Neurophysiol.*, T. 10, N° 1, 57-61, 1947.

89. Walker, A. E.: A cytoarchitectural study of the prefrontal area of the macaque monkey. *Journ. of comparat. Neurol.*, T. 73, 59-86, 1940.

90. Walcker, A. E.: The medial thalamic nucleus. *Journ. of compar. Neurol.*, T. 73, 87-115, 1940.

91. Ward, A. A. and Culloch, W. S. Mc: The projection of the frontal lobe on the hypothalamus. *Journ. of Neurophysiol.*, T. 10, 309-314, 1947.

92. Warren, J. M.; Warren, H. B. and Akert, K.: Orbitofrontal cortical lesions and learning in cats. *Journ. of comparat. Neurol.*, T. 118, N° 1, 17-41, 1962.

93. Warren, J. M. and Akert, K.: Impaired problem solving by cats with thalamic lesions. *Journ. of comparat. and Physiol. Psychology*, Vol. 53, N° 2, 207-211, 1960.

94. Warren, J. M.: The behavior of carnivores and primates with lesions in prefrontal cortex. In: *The frontal Granular Cortex and Behavior*, 168-191, 1964.

95. Waterhouse, I. K.: Effects of prefrontal lobotomy on conditioned fear and food responses in monkeys. *Journ. of comparat. and physiol. Psychology*, Vol. 50, N° 1, 81-88, 1957.

96. Yacorzinski, G. K. and Davis, L.: Evidence for cortical areas in inhibition and mediation of Tickle. *Arch. of Neurol. and Psychiat.*, T. 53-54, 355-357, 1945.

L'Agraphie Secondaire aux Lésions du Lobe Frontal

par H. HECAEN et R. ANGELERGUES *

I. RAPPEL HISTORIQUE

L'existence d'une agraphie frontale fut déduite des patientes recherches anatomo-cliniques d'Exner (1881) qui confrontant méthodiquement tableaux cliniques et topographies lésionnelles dans les observations de lésions corticales de la littérature, remarqua une relative prévalence des atteintes de la deuxième circonvolution frontale gauche lorsqu'une agraphie était présente et en inféra l'existence d'un centre graphique au niveau du pied de F2, homologue du centre de Broca au niveau du pied de F3 — Henschen (1922), qui devait confirmer cette hypothèse par ses études personnelles, attribuait au pied de F2 la valeur d'un centre psychique superposé au centre moteur de la main et des doigts.

En fait, en dehors de la relation de fréquence établie par Exner, seul le cas de Gordinier (1899) s'inscrit en faveur d'un centre graphique. Rappelons qu'il s'agissait d'un gliome de 2 cms. de long siégeant au niveau du pied de F2, s'enfonçant en direction du ventricule latéral et intéressant la substance blanche de F1; la malade était incapable d'écrire de l'une ou l'autre main et l'on ne pouvait identifier, dans ses productions graphiques, que quelques lettres; il n'existait aucun trouble du langage parlé, ni de la lecture; secondairement, l'auteur observa un ralentissement du débit oral, sans symptômes aphasiques.

Wernicke, puis Déjerine rejetèrent vigoureusement la notion d'un centre graphique autonome, sur le double argument que

l'écriture restait entièrement sous la dépendance du langage en général et qu'elle n'était pas, quoiqu'habituellement effectuée avec la main dominante, la fonction privilégiée d'une partie du corps comme la phonation était celle des muscles bucco-velo-laryngés. Cependant, l'agraphie frontale demeure dans ces conceptions, puisqu'elle existe à la suite de l'atteinte du centre de Broca, mais elle est étroitement liée au trouble de la parole. Avec Pierre Marie au contraire disparaît la notion d'une agraphie frontale, puisque l'agraphie est toujours secondaire à la lésion de la zone de Wernicke et que, d'une façon générale d'ailleurs, pour cet auteur, le lobe frontal ne joue aucun rôle dans la réalisation du langage. Avec ce qu'il nomme la "graphoplégie" (agraphie totale), par opposition aux agraphies du pli courbe (écriture copiée) et temporale (écriture sous dictée). Pitres réhabilite l'agraphie frontale. Plusieurs auteurs, en acceptant une "agraphie motrice", notion généralement distinguée de celles d'"agraphie optique", "agraphie aphasique", "agraphie apraxique", etc..., demeurent aussi implicitement ou explicitement fidèles à l'agraphie frontale. Nielsen, reprenant les conceptions de Henschen, en distinguera deux variétés: l'agraphie frontale type F3 et l'agraphie frontale type F2.

Penfield et Roberts (1959) ont rapporté

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un cas d'agraphie observée après excision d'une cicatrice épiléptogène d'origine traumatique siégeant au niveau des 2^{ème} et 3^{ème} circonvolutions frontales. Alors que le langage parlé était normal et que l'on notait seulement une petite difficulté à la lecture à voix basse, l'écriture spontanée et sous-dictée était très altérée au 9^{ème} jour après l'intervention, mais à un examen pratiqué trois mois plus tard, l'agraphie avait disparu.

En vérité, si l'on excepte l'agraphie intégrée dans le cadre de l'aphasie motrice corticale des classiques ou de l'aphasie de Broca et le rôle que la lésion frontale peut jouer dans le déterminisme de ces syndromes, l'agraphie par lésion frontale est d'observation extrêmement rare, constatation qui nous paraît peu compatible avec la notion d'un centre graphique frontal.

II. SITUATION DES SYMPTOMES AGRAPIQUES DANS LES DESORGANISATIONS SECONDAIRES AUX LÉSIONS FRONTALES

1^o L'agraphie dans la symptomatologie d'ensemble des lésions corticales

Si nous comparons, sans tenir compte de la localisation lésionnelle, les tableaux cliniques observés chez 257 sujets droitiers porteurs de lésions hémisphériques gauches, selon que l'agraphie était présente (121 cas) ou absente (136 cas), nous constatons une nette augmentation de fréquence de certains symptômes lorsque l'on passe du groupe sans agraphie au groupe avec agraphie: alexie (de 19,85 % à 66,66 %), alexie des chiffres (de 6,5 % à 50,45 %), anarithmétique (de 19,83 % à 77,47 %), apraxie idéatoire et idéo-motrice (de 2,94 % à 33,88 %), apraxie constructive (de 17,05 % à 45,33 %), aphasie de Broca (de 9,55 % à 40,49 %), aphasie sensorielle (de 18,38 % à 48,76 %), troubles sensitifs (de 19,85 % à 38,97 %), détérioration intellectuelle (de 13,97 % à 26,44 %) et réactions de catastrophe (de 19,85 % à 34,71 %).

Si l'on excepte donc la détérioration intellectuelle et les réactions de catastrophe à l'origine desquelles une atteinte frontale peut éventuellement être invoquée, et qui représentent d'ailleurs les symptômes dont l'augmentation de fréquence est le moins marqué, les associations symptomatiques les plus remarquables ne tendent pas à relier l'agraphie à l'atteinte frontale, si l'on s'en tient à la fréquence du trouble de l'écriture.

Si l'on considère les symptômes purement moteurs de l'aphasie, nous les voyons au contraire remarquablement diminuer de fréquence du groupe sans agraphie (22,05 %) au groupe avec agraphie (3,50 %).

2^o Agraphie et trouble de la parole

Cette disjonction entre aphasie motrice et agraphie est confirmée par une étude que nous avons conduite sur 214 cas de lésions hémisphériques gauches dont la topographie a été établie avec précision par vérification opératoire ou nécropsique. Pour cette étude, nous avons attribué à chaque symptôme aphasique une valeur numérique allant de zéro (intégrité totale) à 4 (disparition complète). Dans chaque groupe topographique, nous avons pu ainsi déterminer un indice moyen de désorganisation pour chaque modalité de trouble du langage en divisant le total des valeurs numériques des cas du groupe par le nombre de cas.

Si agraphie et troubles de l'articulation sont sensiblement au même niveau au cours des lésions fronto-temporales (respectivement 1,15 et 1) et relativement d'un degré analogue au cours des lésions fronto-pariétales (respectivement 1,18 et 1,45) et fronto-pariéto-temporales (respectivement 2,33 et 1,85), nous observons une dissociation très nette en faveur de l'agraphie lorsque le centre de gravité de la lésion devient plus postérieur (3,66 contre 0,15 lors des lésions pariéto-temporo-occipitales), mais aussi une dissociation en faveur des troubles de l'articulation lors des lésions

frontales (0,30 contre 0,05) et rolandiques (0,44 contre 0,22).

La première de ces dissociations confirme seulement un fait d'évidence, à savoir la multiplicité des formes de l'agraphie et la relation étroite de certaines d'entre elles avec la désorganisation totale du langage ou la désorganisation plus particulière du langage écrit; la deuxième tendrait à disjoindre l'agraphie d'expression des phénomènes moteurs de la parole.

Si nous comparons, selon qu'il existe ou non une lésion frontale, l'indice des troubles articulatoires à celui des troubles de l'écriture, nous voyons le premier s'élever de 0,316 dans le groupe sans lésion frontale à 0,766 dans le groupe avec lésion frontale alors que l'indice de l'agraphie diminue du groupe sans lésion frontale (1,379) au groupe avec lésion frontale (0,846).

Considérée dans son ensemble, l'agraphie n'apparaît donc pas essentiellement comme un symptôme d'origine frontale, mais ce fait ne permet nullement de rejeter, aussi rare soit-elle, l'existence d'une variété frontale de l'agraphie et sa spécificité neuropsychologique. Il conduit simplement à une certaine réserve quant à l'existence d'un centre spécialisé directeur ou coordinateur des mouvements de l'écriture au niveau des circonvolutions frontales, sans cependant impliquer que l'agraphie présumée frontale ne représente qu'un aspect contingent et rare de l'aphasie motrice.

Si l'agraphie représente en effet un des éléments de l'aphasie d'expression dont l'origine lésionnelle dépend d'une lésion antérieure frontale ou rolandique basse, nous voyons aussi que l'atteinte de l'écriture n'est pas strictement parallèle à celle du langage parlé. Une certaine autonomisation de l'écriture par rapport à l'expression orale se manifeste donc. Est-il des cas où cette absence de parallélisme est telle qu'elle justifie la conception de l'agraphie pure de Exner? Ils sont certainement exceptionnels et nous avons dit que seul le cas de Gordinier parmi ceux auxquels il est fait classiquement référence, mérite d'être retenu, encore qu'avec quelques réserves, puisqu'il ne comporta qu'une vérification anatomique macroscopique.

III. L'AGRAPHIE COMME SYMPTÔME PRIVILEGE AU COURS DES LÉSIONS FRONTALES

Nous avons eu l'occasion d'examiner un sujet ne présentant aucun trouble du langage parlé ni de la lecture mais atteint d'agraphie très accusée. Il existait aussi chez lui une anarithmétique quasi-totale. La seule réserve provient du niveau mental et scolaire prémorbide de ce sujet, très certainement peu élevé. L'observation nous a paru néanmoins valable pour deux raisons: parce qu d'une part le malade, comme son père, soutenait que ses difficultés d'écriture étaient apparues après le traumatisme et que d'autre part, dans la phase suivant immédiatement un équivalent épileptique, les difficultés graphiques s'accroissaient considérablement, en accusant la même forme de désorganisation.

On doit admettre semble-t-il l'origine lésionnelle frontale de cette agraphie mais sans autre précision malgré l'ablation de la zone épileptogène sur la face interne droite, malgré aussi la porencéphalie frontale droite constatée à l'encéphalographie gazeuse, étant donné la dilatation ventriculaire et le léger syndrome pyramidal droit.

Observation N° 1. — G. Jean-Alain. 28 ans sujet fruste sans CEP, gaucher écrivant de la main droite (indice 0,3 - 2 frères gauchers).

Epilepsie post-traumatique ayant nécessité une ablation de la zone épileptogène dans la région prémotrice parasagittale droite trois ans après le traumatisme.

A l'examen 5 ans après l'intervention, on ne note qu'une hémihyperextensibilité et hémihyperreflectivité tendineuse droites. Aucun trouble des gnosies et praxies.

Aucun trouble du langage en dehors de l'écriture.

Agraphie: le malade ne peut écrire correctement que son nom et encore sous forme de signature. Dans l'écriture de l'adresse les dysorthographies sont considérables: 60 bouvars jean jores bon broncen (60 Boulevard Jean Jaurès Bordeaux).

Si les lettres sont en général bien écrites sous-dictée sauf V pour W, J pour K, gu

pour q, à l'écriture des mots dictés apparaissent immédiatement des erreurs par ex: chaise: hesen, crayon: creilon; coq: goce; arbre: abre; village: l'ilge...

Dans la dictée des courtes phrases, outre les dysorthographies on remarque que les blancs ne sont pas placés aux endroits corrects par ex: *il febau, il fait baus au jourduin, je vous dret meu promenet.*

L'écriture avec des cubes alphabétiques donne les mêmes résultats, ainsi les mots dictés maison, village, bateau, océan, vent... sont écrits metxon, vilage, bateus, aucean, vems...

La phrase *il fait beau aujourd'hui et je voudrais aller me promener* est composée: *Il fetbeut ot joudui je vouldret alet meu pruat meunet.*

La copie est beaucoup plus satisfaisante et on ne constate que peu d'erreurs (d pour de, metson pour maison).

L'épellation est troublée comme l'écriture: chaise: H.A....; crayon: reiylon; bague: bace; soulier: coulier...

Lorsqu'il doit choisir parmi plusieurs orthographes d'un même mot celle qui est correcte, il y réussit 6 fois sur 10.

De courtes phrases écrites par l'observateur avec une orthographe défectueuse sont considérées comme sans signification par le malade.

Au cours de l'examen le malade présente un équivalent comitial et immédiatement après les performances graphiques sont encore plus perturbées. Ainsi, (entre parenthèses la performance avant la crise) cheval (cheval) chauene; maison (maisons) encans; lampe (lampe) lasipans...

L'écriture des chiffres isolés ou des nombres de 3 chiffres au plus est en général correcte mais pour les plus grands nombres les erreurs sont constantes et du type suivant 1510: 100050010, c'est à dire respectant les chiffres mais en y intercalant des 0, ce qui oralement correspond à la prononciation du nombre.

Le calcul est également très troublé. Si la lecture des nombres est possible jusqu'à 5 chiffres, le calcul mental, les opérations arithmétiques sont impossibles. Le malade ne peut également apprécier la valeur de

position des chiffres que jusqu'aux unités de mille.

Examen psychométrique:

QI verbal 75.

QI performance 88.

Indice de détérioration 49 %.

PM. 38:22 en temps libre.

Test de Benton: 1/10.

E.E.G. foyer de pointes rapides dans la région prérolandique droite; après une crise séquences de pointe-ondes irrégulières bifrontotemporales.

Encéphalographie fractionnée: dilatation des ventricules dans leur ensemble avec image de porencéphalie frontale droite.

Cette observation paraît donc témoigner en faveur de la possibilité d'une agraphie isolée très voisine de l'agraphie constatée lors des aphasies d'expression: désorganisation du graphisme, mot avec choix aléatoire et non phonétique de ses constituants, agrammatisme, relative préservation de l'écriture copiée, absence de difficulté de réalisation des graphèmes, troubles de l'épellation et de l'écriture avec des cubes alphabétiques.

Nous rapprocherons de ce cas l'observation d'un sujet atteint de tumeur fronto-diencéphalique gauche, observation assez sommaire en raison de l'état du sujet. L'écriture copiée est ici également conservée et on ne note aucun trouble de la réalisation des graphèmes. Le trouble du langage oral existe ici mais n'est représenté que par une aphasie amnésique importante.

Observation N° 2. — P. Léonce - droitier - 55 ans - chauffeur de car.

Etat de subobtusion avec bradypsychie très marquée et akinésie. Le langage spontané ne révèle aucune déformation arthrique. La compréhension verbale est conservée, bonne exécution du test de Head d'imitation des mouvements main, oeil, oreille. Pas de trouble de la lecture.

Aphasie amnésique très marquée.

Ecriture: s'il peut écrire correctement ses nom, prénom et adresse des paragraphes

considérables surviennent dès qu'il essaie de décrire sa maladie "c'est toujours dimanche au (2 mots raturés) jour de suite de sante".

L'écriture sous-dictée montre les mêmes troubles: alors qu'il lui est dicté "à l'ombre du protocole leurs regards"... il écrit d'abord "à leur eur couper", puis rature ces mots et écrit de nouveau "à leur ordre du Coupavage du e". Prié d'écrire "il fait beau aujourd'hui et je voudrais aller me promener" il trace "il faut (un mot raturé) oublier et je vous aller aller (raturé) embrasser peur nous restrer".

La copie d'une courte phrase est par contre bien exécutée.

Calcul: Bonne lecture et écriture des chiffres et nombres. Calcul mental non troublé mais anarithmétique totale, les nombres sont bien posés mais le principe de l'opération est totalement absent. Aucun trouble des *praxies*.

Pas de troubles de la *somatognosie* à l'exception d'une certaine confusion entre annulaire et auriculaire et annulaire et index dans la désignation sur ordre verbal.

Pas de troubles des *gnosies visuelles*.

Bonne reproduction des *structures rythmiques*.

Hémihyperextensibilité droite.

Intervention: gliome préfrontal gauche infiltrant les faces orbitaire et interne et s'infiltrant en profondeur en direction de la région diencéphalique.

Cette observation n'est pas sans rapport aussi avec celle de Penfield et Roberts où l'agraphie apparut transitoirement après excision frontale gauche.

Une troisième de nos observations si elle se présente comme dissociée de tout trouble du langage oral et de la lecture et, par certains de ses caractères, comme proche de nos premiers cas, ne peut être considérée comme témoignant uniquement d'une lésion frontale. Il s'agit en effet d'une démence pré-sénile où l'atrophie cérébrale pour prédominer dans la région frontale n'en est pas moins généralisée. On la retiendra surtout en raison des troubles de l'écriture encore que dans ce cas existent quelques difficultés

de réalisation des lettres et que la copie soit loin d'être intacte.

Observation N° 3. — R. Clotaire - droitier - 58 ans - magasinier pas de CEP.

Adressé au Centre Neurochirurgical Saint-Anne pour céphalées frontales et oedème papillaire, troubles de la mémoire et de l'attention, inertie, apragmatisme, survenus depuis 18 mois. Cependant il n'a cessé son travail qu'une semaine avant l'hospitalisation.

Le sujet est bien orienté dans le temps et l'espace, est au courant des faits du monde extérieur; son comportement témoigne avant tout d'un manque d'initiative.

A l'examen: le langage oral ne présente aucune perturbation, l'inertie extrême aboutissant souvent à des réponses monosyllabiques, à une pauvreté phrasique considérable et à des persévérations dans les tests de transformation.

Dans la *lecture*, on note des oublis de parties de mots ou de syntagmes dépendant des troubles de l'attention et de l'appréhension d'un message tant soit peu complexe. Par contre, les ordres présentés par écrit sont bien exécutés.

Ecriture: l'écriture spontanée est très réduite en raison de l'inertie du sujet. Dès les noms et prénoms les erreurs se manifestent (Clotaire pour Clotaire), l'adresse est illisible: 52 BRU (mot illisible barré) Jole... tr (5, rue Salengro) nom de village illisible, pour le département (Oise) écrit quatre O bien séparés.

Dans l'écriture sous-dictée il tend à renoncer rapidement à la tâche, il trace des lettres correctement soit en cursives soit en majuscules sauf R.C.B. Pour bol écrit bobolaver: laves; leberté: diofilili; vase: vonot; Paris: voinovoré, etc...

La dictée des syntagmes est caractérisée par la séparation des éléments du syntagme (blancs graphiques en place) par le volume graphique conforme à l'usage du mot correct (fils est écrit fifi et femme est indiquée par une ligne ondulée, par l'absence d'hésitation quand le mot est remplacé par la ligne ondulée, par la présence de paragraphes dues à l'oubli des graphèmes

mo pour mon, par la présence de schémas inverses pour certaines lettres (f, d).

Dans la dictée des monosyllabes sans sens, l'erreur est constante mais le graphème initial qu'il met en majuscules, est en général correct de même que les voyelles. Dans les disyllabes l'erreur est constante, il débute presque toujours par C ou Ch et met 2 syllabes. Il refuse tout essai aux trisyllabes.

La copie des lettres majuscules est servile mais relativement exacte avec cependant quelques traits idéographiques indiquant le passage par la verbalisation. Il en est de même dans la copie des mots et de quelques dissyllabes sans signification. A noter de grandes difficultés à engager le schéma: le b de bol et le L de liberté sont surchargés et on constate une absence de ligature entre les graphèmes.

L'écriture avec des cubes alphabétiques aboutit à des erreurs aussi marquées à l'exception de son nom qui est bien composé: par exemple Table est écrit B.L.O.P.E.; Poste: R.P.L.O. etc... ces erreurs sont d'ailleurs reconnues du malade quand il se relit. Si on ne lui donne que les lettres entrant dans le mot qu'il doit écrire l'échec est également total.

L'epellation manifeste aussi des perturbations très importantes même pour son nom et prénom (CLOTEUHL).

Calcul: s'il parvient à écrire les chiffres et les nombres de 3 chiffres, les erreurs sont constantes pour les plus grands nombres ($1748 = 1348$; $10632 = 1042$). La lecture des nombres est bonne. L'anarithmie est totale et le calcul mental très troublé.

Aucun trouble des *praxies*, *buccolinguo-faciales*, *idéomotrices*, *idéatoire* et de l'*abillage*.

Praxie constructive: le dessin sur ordre de formes simples est bien réalisé de même que la copie d'un modèle de maison et de bicyclette mais celle d'un cube ou d'une pyramide est impossible.

Aucun trouble de la somatognosie ni des gnosies visuelles.

Examen neurologique: hémihyperextensibilité droite, hypotonie faciale droite.

Examen psychométrique: affaiblissement intellectuel global.

Wechsler-Bellevue:

QI verbal: 76.

QI performance: 81.

Test de Benton: 0 sur 10.

Cubes de Krox: 3 réussites sur 18 épreuves.

Examen EEG: bouffées d'ondes lentes rythmiques bilatérales à maximum antérieur et altérations plus polymorphes prédominant en frontal gauche.

Encéphalographie gazeuse: atrophie généralisée corticale et sous corticale prédominant nettement dans les régions frontales.

Une 4ème observation s'inscrit dans la ligne des précédentes en même temps qu'elle montre la liaison avec les aphasies d'expression. D'ailleurs la lésion ne peut être considérée comme strictement frontale, atteignant lors de l'examen clinique au moins les circonvolutions rolandiques, l'extension pariétale pouvant par contre n'avoir pas encore existé à cette époque. Les troubles du langage oral sont ici présents: dysprosodie, léger agrammatisme, accidents phoniques, léger trouble de la compréhension, mais leur intensité est sans rapport avec celle de la désorganisation de l'écriture qui est totale à partir de morphèmes. L'écriture copiée est par contre presque conservée.

Observation N° 4. — Petitb... Lucien - 53 ans - Droitier - Tourneur; interné à la suite d'un état confuso-onirique d'origine alcoolique et adressé au Centre Neurochirurgical en raison d'un foyer EEG temporal gauche.

Le langage spontané est caractérisé par une pauvreté de l'énoncé mais avec adéquation de la réponse, avec interruptions continuelles du débit par une dysprosodie légère avec tendance à l'agrammatisme, par de rares et minimes fautes articulatoires et par un trouble de l'évocation verbale.

La répétition et surtout la lecture à haute voix mettent en évidence des accidents

phoniques (mutations phoniques, bafouillage, télescopages).

Léger degré d'*aphasie amnésique* (12 réponses exactes sur 15 objets présentés).

La compréhension verbale est relativement peu troublée (échecs aux ordres complexes mais bonne réussite aux tests de Kleist). Bonne exécution des tests grammaticaux.

La lecture des lettres et mots est bonne. Il exécute bien les ordres simples et semi-complexes mais échoue aux ordres complexes. Paralexies considérables dans la lecture à haute voix.

Écriture: il parvient à écrire son nom et adresse mais paraphrasies considérables dès qu'il tente de décrire sa maladie: "quel point (mot rayé) boul qui mede blesser" ou de rédiger une lettre à sa femme: "chérie (rayé) femmes je se le compredre de 2 gosses de la (2 mots rayés) boucher. "Tendant de se relire il déclare "je ne croyais pas être aussi malade que ça".

Sous-dictée il écrit bien 9 lettres sur 10 (w transcrit u), 3 mots sur 7 (roue = ruoe; liberté: libertie; Bordeaux: Bordaut; microphone: monnigero).

Aucune syllabe sans signification n'est bien transcrite: vera pour vara, torva pour gobi, tuque pour lorn, repa pour ropa, chedot pour chokabé, delesque pour takopi.

Une courte phrase *je mange* est bien transcrite mais la phrase *le livre est ouvert* est écrite "tu te envoimen" et pour *il fait beau aujourd'hui et je voudrais aller me promener* il trace "il se firai pour elle qui reporet que réperont répere".

Avec des cubes alphabétiques il parvient à écrire son prénom, *bol*, *col* et *vrai*, mais pour *monarchie* écrit monarche, pour *annoncer* anicnone.

Aucune transcription de logatome n'est correcte: ainsi vori pour vara, minon pour mifo, ropain pour ropa, lur pour loru, etc. La copie ne montre que de légères erreurs: que pour *qui*, votrer pour *voter*, rearmrem pour *réarmement*.

L'épellation est à peu près totalement impossible: Bol: b... H, table: TABS, règle CCEA, etc....

Calcul: Si la lecture des chiffres isolés ne donne lieu qu'à une erreur, la lecture des nombres est constamment erronée.

L'écriture des chiffres isolés est correcte et on ne note que 3 erreurs sur 9 nombres de 2 à 6 chiffres.

Les opérations arithmétiques sont bien exécutées mises à part quelques erreurs de calcul. Les signes arithmétiques sont bien reconnus, la valeur de position des chiffres dans un nombre bien appréciée.

Les problèmes simples d'arithmétique sont bien réussis. Le calcul mental est bien exécuté lorsqu'il s'agit de la table de multiplication.

Aucun trouble des *praxies* et des *gnosies*. Impossibilité de reproduire des rythmes de plus de deux éléments.

Examen neurologique: hémihyperextensibilité droite - parésie faciale droite.

Astéréognosie main droite avec abolition de la dermolexie et élargissement des compas de Weber. Extinction à la piqure simultanée en faveur de l'hémicorps gauche.

E.E.G. foyer polymorphe temporopariétal gauche.

Artériographie carotidienne gauche paraissant normale.

Aggravation brutale deux mois plus tard des troubles de la parole, hémiplegie droite.

Intervention: Tumeur kystique affleurant au cortex au niveau du pied de F2.

Décès 2 mois plus tard. A l'autopsie: foyer opératoire au niveau de F2-F3, avec formation tumorale intéressant la partie basse des circonvolutions rolandiques, la circonvolution pariétale inférieure et se prolongeant en profondeur.

Ces 4 observations, à des degrés divers, témoignent de la possibilité d'une agraphie dissociée ou d'intensité non parallèle à celle des troubles du langage oral au cours des lésions frontales. Le caractère général des troubles de l'écriture les rapproche de l'agraphie des aphasies d'expression.

Au contraire, l'observation suivante tend à évoquer la possibilité d'un agraphie d'un type différent au cours des lésions de ce

lobe et à le rapprocher de l'apraxie frontale telle que décrite par Denny-Brown.

Observation N° 5. — Mme. T. Cécile - 51 ans - gauchère, écrivait de la main droite (hérédité familiale de gaucherie).

Adressée le 15.10.1948 pour des équivalents comitiaux, une bradypsychie, des céphalées et des vertiges évoluant depuis deux ans. L'examen met en évidence un léger syndrome pyramidal gauche avec paralysie faciale gauche de type central mais surtout une hypertonie de type oppositionniste des extrémités gauches. Grasping reflex de la main gauche avec groping. Stase papillaire. L'étude du psychisme révèle un état de bradypsychie avec obtusion légère sur lequel se manifestent des tendances euphoriques.

L'intervention (3.II.48) permet l'ablation d'un méningiome frontal de la convexité droite.

Les jours suivants, l'obtusion persiste et même s'accroît pour s'atténuer progressivement, la réaction de préhension persiste du côté gauche.

L'examen le 17-II-48 révèle qu'il n'existe pas de troubles du langage parlé à l'exception d'une impossibilité de croiser à l'imitation du test main-oeil-oreille de Head, alors qu'elle précise à haute voix les mouvements de l'observateur. Par contre les troubles de l'écriture sont extrêmement importants: alors que vraisemblablement persiste la forme des lettres et des mots, le résultat est illisible en raison de la superposition des lignes, des mots et des lettres avec multiplication des jambages et d'une façon générale itération de toutes les formes graphiques en particulier des arrondies. Il s'ensuit un gribouillage illisible dont émergent cependant quelques mots presque corrects à quelques répétitions de jambages ou à une itération de lettres prés.

Le 26-II-48 le grasping gauche a disparu, de même que l'hypertonie; la malade est lucide, mais présente une labilité de l'humeur variant de l'euphorie à la sensibilité avec pleurs et attendrissement sur son sort. A l'examen on ne note qu'une parésie faciale, une hémihyperextensibilité et un signe de Rossolimo gauches. L'écriture est

améliorée, mais les troubles sont du même type: itérations et multiplications des jambages.

Le 4-3-49 les troubles de l'humeur sont nettement améliorés, mais il existe toujours un puérilisme important. L'écriture est maintenant quasi-normale, cependant on constate encore une tendance à multiplier les jambages.

Chez cette malade gauchère il n'existait pas de troubles du langage oral et les troubles de l'écriture sont avant tout caractérisés par des itérations avec multiplication des jambages des lettres, telles qu'on les rencontre, mais en général de façon moins marquée, lors des lésions du carrefour postérieur de l'hémisphère mineur chez le droitier. Le grasp reflex ne peut en rendre compte puisqu'il n'existait que du côté gauche, mais une liaison entre ces deux phénomènes pathologiques doit être au moins suspectée lorsqu'on envisage cette question en fonction des 3 observations qui vont suivre.

Dans la première d'entre elles, due à un méningiome de la face interne du lobe frontal, le trouble de l'écriture ne revêtait pas le même aspect que dans l'observation précédente et témoignait d'un trouble de type praxique: difficulté à tracer les lettres et à respecter les espaces entre les mots avec cependant copie presque conservée. D'autre part, bien que la réaction de préhension ne fut pas présente, on constatait une très nette apraxie idéomotrice unilatérale gauche. Trouble de l'écriture et apraxie unilatérale disparurent après ablation de la tumeur.

Observation N° 6. — P. Henri-Julien - 71 ans - droitier - menuisier.

Début des troubles par une impossibilité de l'écriture et même de la signature, ainsi qu'une impossibilité des gestes fins de la main droite en même temps que une difficulté pour trouver les mots.

A l'examen du langage 6 mois après le début des troubles, on ne constate qu'un certain ralentissement du débit, une certaine tendance écholalique et une certaine difficulté à trouver les mots inhabituels. Il n'existe pas de troubles de la compréhens-

sion ni de la lecture; à la répétition des mots et logatomes, les erreurs sont minimes: affaiblissement des finales, quelques persévérations. Il échoue à dénommer 2 des 15 objets présentés.

Écriture: Il ne parvient à écrire, et de façon peu lisible que son nom et son prénom, mais ne réussit pas à écrire son adresse.

Sous-dictée, l'écriture est encore plus difficile: pour *il fait beau aujourd'hui* il écrit *il fat ba*; une autre phrase est écrite de façon illisible, les espaces entre les mots n'étant pas respectés. Les noms des objets présentés sont écrits de façon correcte mais peu lisible. Avec des cubes alphabétiques il compose sans erreur les mots dictés.

La copie d'une courte phrase est bien réalisée, mais avec beaucoup de difficultés; il ne peut terminer une seconde phrase, *le temps est à l'or* (orage).

Il transcrit bien en cursive des mots écrits en majuscules et copie bien des mots écrits en caractères russes ou grecs.

L'épelation est bien exécutée.

Calcul: pas de troubles de la lecture et de l'écriture des chiffres et des nombres. Parmi les opérations arithmétiques, seule l'addition est bien exécutée et encore avec une légère erreur. Les signes arithmétiques sont bien reconnus, la valeur de position des chiffres dans un nombre bien appréciée.

Praxies: *Apraxie buccolinguofaciale* légère — *Apraxie idéomotrice unilatérale gauche* — *Praxies mélokinétique, idéatoire, de l'habillage et constructive* normales.

Aucun trouble des gnosies.

Examen: hémiparésie droite légère (légère diminution de la force musculaire des doigts et de la flexion avant-bras sur bras) avec parésie faciale droite. Absence de toute réaction de préhension. Absence de troubles sensitifs.

Intervention: Méningiome parasagittal de la région prémotrice gauche.

Un mois plus tard disparition de tous les symptômes préopératoires.

Nous avons constaté un tableau clinique très voisin dans deux autres observations.

Rien que la lésion frontale interne, pour très probable qu'elle fut, ne représente que la prévalence d'un processus beaucoup plus diffus, nous les présenterons en soulignant l'intensité et le caractère nettement apraxique des phénomènes agraphiques, la présence d'apraxie de l'habillage et constructive, l'agnosie spatiale unilatérale si accusée dans un cas qu'elle perturbe la lecture et légère dans l'autre. En effet, l'apraxie unilatérale avec réaction d'esquive ou de préhension forme avec ce type d'agraphie un syndrome dont l'origine nous paraît devoir être recherchée dans les lésions frontales, si on se réfère aux deux cas de tumeurs plus haut présentés.

Observation N° 7. — Gr — Adolphe - 64 ans - droitier - cultivateur.

Il est adressé au Centre Neuro-chirurgical Sainte-Anne pour trouble de la mémoire, céphalées, difficultés motrices du membre supérieur gauche apparus depuis deux ans ainsi qu'une impossibilité d'écrire et des difficultés de la lecture.

On ne constate aucun trouble du langage parlé.

La lecture est troublée en raison d'une impossibilité de passer d'une ligne à l'autre dans un texte et d'une négligence de la partie gauche du texte et même des mots dès qu'ils sont un peu longs. Les lettres et les mots courts sont par contre bien lus.

Écriture: le malade précise de lui-même "depuis un an je ne peux même pas signer". L'agraphie est en effet totale: il ne peut tracer que des boucles lorsqu'il tente d'écrire son nom. S'il doit copier un mot il tente de repasser sur le contour des lettres (closing in), il parvient à peine à copier une ou deux lettres mais U est transformé en O et T est accolé au modèle.

Avec des cubes alphabétiques il ne parvient pas à construire son nom (GB pour GRU... et échoue totalement pour son prénom.

Lorsqu'il doit choisir parmi des lettres en désordre celles nécessaires à la composition de mots dictés les résultats sont les suivants, il construit bien après quelques corrections *BOL*, *TROU*, *LIT*, mais *BANC* est construit *BAT*; *nuit*: *NUI*; *papa*: *AP-*

PA. Si on ne lui donne que les lettres entrant dans le mot, les résultats sont également erronés, même pour son nom: RCU... pour GRU... et son prénom PAEODHL (Adolphe), *papa* est construit PPAA et relu comme Papa.

L'epellation montre également des perturbations importantes: *Adolphe*: ADF...; *lunette*: PU...; *cigarette*: SE...SR.G; *baguette*: BA; *montre*: M...P; *lampe*: L...P... etc.

Calcul: l'écriture des chiffres est impossible, il trace des traits et des boucles non identifiables sauf 4 et 12.

La lecture n'est possible que jusqu'aux nombres de deux chiffres. Toute opération arithmétique est impossible, même si on lui en écrit les termes et si on lui fournit des cubes chiffrés pour écrire les résultats.

Le calcul mental n'est possible que pour les opérations très simples.

Praxies: *Apraxie idéomotrice gauche* très accusée, *apraxie mélokinétique du membre supérieure gauche*. Impossibilité d'imiter les mouvements coordonnés sans signification des deux mains. *Apraxie de l'habillage*, *Apraxie constructive avec phénomène de closing in*.

Absence d'apraxie bucco-linguo-faciale et d'apraxie idéatoire.

Aucun trouble de la *somatognosie*.

Pas de troubles des *gnosies visuelles*, en dehors des symptômes d'agnosie spatiale, *agnosie spatiale unilatérale gauche* très nette, *trouble des notions topographiques* et de la *mémoire topographique*.

A l'examen neurologique il n'existe aucun trouble parétique ni sensitif, ni atteint du champ visuel. Il existe une *disposition de résistance du membre supérieur gauche* constamment gardé en flexion sur la poitrine et une *réaction d'esquive* de cette main avec retrait de l'avant-bras. A droite on constate au contraire une *réaction de préhension et d'aimantation*.

Réflexe de la moue très accusé. Limitation des mouvements oculaires volontaires.

Etat mental: affaiblissement intellectuel très léger.

Encéphalographie gazeuse: dilatation ventriculaire prédominant au niveau du ventricule droit. Dilatation des espaces sous-arachnoidiens, en particulier de la face interne du lobe frontal droit.

Observation N° 8. — D... Jeanne - 74 ans - droitière - caissière.

Adressée pour raideur progressive du membre supérieur gauche, difficultés de l'habillage et de l'écriture apparues depuis deux ans. On ne constate *aucun trouble du langage oral ni de la lecture*.

Ecriture: elle ne parvient pas à écrire son nom correctement ni son prénom (Jane puis Janes pour Jeanne).

Grandes difficultés à écrire des lettres isolées "je ne peux pas fermer la lettre", dit-elle, ne fermant pas les boucles des lettres telles que d ou g ou écrivant o pour f, e pour l. La copie de lettres en cursives révèle les mêmes difficultés, par exemple la copie d'un d aboutit à deux ovales concentriques avec un appendice supérieur. Le plus souvent, qu'il s'agisse d'écriture copiée ou dictée, le phénomène fondamental est *l'inversion des mouvements*: elle hésite sur la direction (droite ou gauche, haut ou bas) à prendre, se trompe et cherche à corriger, aboutissant à un graphisme illisible.

Si elle doit copier son nom écrit en cursives, elle le transcrit correctement, mais, s'il est écrit en majuscules, elle copie servilement les premières lettres avec des inversions puis termine correctement en cursives. Elle copie plus aisément des mots écrits en cursives, mais en séparant les syllabes.

Avec des cubes alphabétiques, elle parvient à écrire quelques mots: table, cigarette, cheval, liberté...

Dans de courtes phrases les erreurs apparaissent (il fait beau; il fai beau; le livre te beu pour *le livre est beau*).

Epellation: elle parvient à épeler correctement chaise, justice, bol, mais échoue à *fauteuil* (FAUTEUL), *monarchie* (MONAUI), *fenêtre* (FEUTRE), *république* (REPUBUE), etc....

Calcul: bonne lecture des nombres jusqu'à 4 chiffres. L'écriture des chiffres et des nombres à deux chiffres est bien réalisée.

Dans les plus grands nombres apparaissent des erreurs: 148: 14 puis un gribouillage; 264: 26 puis forme intermédiaire entre 9 et 4; 1233: 1333; 120457: 12457.

Avec des cubes numériques les résultats sont bons à l'exception de 7532: 70532.

Dans les *opérations arithmétiques*, elle parvient à poser les termes, semble avoir conservé le principe de l'opération mais se trompe dans les calculs et néglige les retenues.

Quelques erreurs dans l'appréciation de la valeur de position des chiffres dans un grand nombre et dans la reconnaissance des signes arithmétiques.

Calcul mental: relativement conservé.

Praxies: net degré d'*apraxie-buccolin-guo-faciale*.

Apraxie idéomotrice gauche avec quelques erreurs dans l'exécution des gestes avec la main droite.

Impossibilité de reproduire les mouvements coordonnés des deux mains exécutés devant elle par l'observateur.

Absence d'*apraxie idéatoire*.

Apraxie de l'habillage très accusée.

Apraxie constructive quasi-totale avec conscience de l'échec.

Aucun trouble de la *somatognosie*.

Bonne reconnaissance des *objets, images, couleurs et physionomies*.

Données spatiales: Bonne orientation chez elle, dans son quartier et dans le service. Les *notions topographiques* apparaissent conservées mais perturbées par une certaine négligence de l'espace gauche qui ne se manifeste d'ailleurs que dans cette tâche.

Impossibilité de reproduire en tapping la moindre *structure rythmique*.

L'examen neurologique est négatif à l'exception d'une disposition de résistance extrêmement marquée du membre supérieur gauche avec réaction d'aimantation très accusée et réaction de préhension de cette main. A noter que la préhension n'apparaît que sous contrôle visuel et cède sur ordre.

Faible tendance à la réaction de préhension du côté droit.

Grasp-reflex bilatéral du pied.

L'examen psychométrique montre un niveau très inférieur à la moyenne (QI 76 au W.B. niveau IV au P.M. 38) mais les résultats à l'échelle de performance (*apraxie*) abaisse considérablement le Q.I. Le niveau verbal est cependant inférieur à la moyenne (échecs aux chiffres et problèmes). Indice de détérioration pathologique non significatif au Benton, hautement significatif au W.B. mais l'échec massif à l'échelle performance ne permet pas d'en tenir compte de façon absolue.

A l'encéphalographie gazeuse légère dilatation ventriculaire prédominant à droite avec sillons plus marqués dans la région suscallosale antérieure droite.

IV. COMMENTAIRES

L'agraphie "frontale", dans la mesure où ce qualificatif établit une lésion stricte avec la désorganisation isolée de ce lobe, est donc d'une extrême rareté. Cependant, on ne peut en contester radicalement l'existence car certains cas plaident très fortement en faveur de sa réalité.

Si l'agraphie n'apparaît d'autre part qu'exceptionnellement dans sa variété strictement frontale, le rôle privilégié de la lésion frontale dans le cadre d'une désorganisation plus globale doit être retenu dans le déterminisme des troubles de l'écriture, comme en témoignent nos observations.

Le mécanisme de l'agraphie frontale, pure ou non, n'en est pas pour autant univoque. Ainsi avons nous pu en distinguer deux variétés: une agraphie plus ou moins intégrée dans une aphasie d'expression et une agraphie située dans le cadre d'une désorganisation du geste.

La première éventualité, que nous semble d'ailleurs la moins directement liée à l'atteinte frontale étant donné le rôle des lésions rolandiques souvent associées, concerne spécifiquement l'utilisation du code graphique. Il nous paraît à ce sujet indispensable de rappeler que, dans le cadre général des troubles du langage, le rôle désorganisateur de la lésion frontale sur l'en-

codage graphique reste quantitativement mineur par rapport à celui de la lésion pariétale; mais la lésion frontale, conjointement à la lésion rolandique, produit une qualité différente du trouble de l'écriture. Aucun argument décisif ne permet d'admettre ou de rejeter un rôle privilégié du pied de F2.

La deuxième éventualité nous paraît en fait plus caractéristique de l'agraphie frontale et semble bien ressortir aux mécanismes de l'apraxie d'aimantation, telle que l'a décrite Denny-Brown, sans que le trouble du graphisme puisse être directement expliqué par les phénomènes toniques.

R É S U M É

Après un bref rappel historique de la question et une étude statistique sur la fréquence du trouble de l'écriture lors des diverses lésions cérébrales qui montre la rareté de l'agraphie frontale, 7 observations sont présentées qui à des degrés divers plaident cependant en faveur de l'existence de troubles de l'écriture en rapport avec les lésions du lobe frontal.

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R E S U M E N

Luego de una breve reseña histórica acerca del problema de la agrafía frontal y de una estadística acerca de la frecuencia con que se producen modificaciones en la escritura como consecuencia de diversas lesiones del cerebro, que demuestran que la agrafía frontal es poco común, son presentados algunos casos que confirman sin embargo la existencia de perturbaciones de la escritura relacionadas con lesiones frontales. Si bien la agrafía frontal pura se da

excepcionalmente debe tenerse presente la importancia de la lesión frontal dentro del cuadro de una desorganización global que da lugar a perturbaciones de la escritura, como lo comprueban nuestras observaciones.

Sin embargo ya se trate de un mecanismo puro o no, la agrafía frontal puede manifestarse de diversas formas. Hemos distinguido hasta ahora dos tipos: la agrafía integrada en mayor o menor grado a una

afasia expresiva y la agrafía dentro del cuadro de la desorganización de los gestos.

El primer tipo, que parecería ser el menos directamente vinculado a una lesión frontal teniendo en cuenta la frecuencia con que se acompaña de lesiones rolándicas, se refiere específicamente al uso del código gráfico. A este respecto debe tenerse presente que dentro del cuadro de las perturbaciones del lenguaje, el papel desorganizador de las lesiones frontales es cuantitativamente menor que el de una lesión parietal; mientras la lesión frontal acompa-

ñada de la rolándica da lugar a una perturbación de otra naturaleza. Ningún argumento decisivo permite aceptar o dестerrar la posibilidad de que el pie de F2 desempeñe un papel preponderante.

El segundo tipo de agrafía parece ser más característico de la agrafía frontal y parecería corresponder al mecanismo de la apraxia magnética descrita por Denny-Brown aunque las perturbaciones gráficas no pueden ser directamente atribuidas a fenómenos tónicos.

S U M M A R Y

A brief reminder of the history of the problem of frontal agraphia is given, together with statistics concerning the frequency of writing disorders connected with different cerebral lesions and showing that frontal agraphia is rare. Several cases are then presented which do, however, plead for the existence of writing disorders connected with frontal lesions.

Although actual frontal agraphia is exceptional, it can hardly be denied as cases prove that a frontal lesion is most important, as far as a more global disorganization is concerned in determining disorders of writing.

Nevertheless the mechanism of frontal agraphia whether this be pure or not, is not of a single sort. We have so far distinguished two sorts: agraphia, more or less an integral part of an expressive aphasia and agraphia, part of a gestural disorganization.

The former kind of agraphia, which would seem to be the less directly related to a frontal lesion (considering the frequently associated rolandic lesions) concerns specifically use of the graphic code. Here it must be borne in mind that, in the general framework of disorders of language, the role of a frontal lesion is lesser, in quantity than that of a parietal lesion, as far as the disorganization of graphic encoding is concerned: whereas the frontal lesion in conjunction with the rolandic lesion, produces a different quality of writing disorder. No decisive argument has been found for or against a major role of the foot of F 2.

The second kind of agraphia seems more characteristic of frontal agraphia and would seem to correspond to the mechanisms of magnetic apraxia as described by Denny-Brown although tonic phenomena may not be held a direct explanation of graphic disorders.

Z U S A M M E N F A S S U N G

Es wird eine kurze Geschichte ueber das Problem der Frontalen Agraphie gegeben zusammen mit einer Statistik ueber die Haeufigkeit der Schreibstoerungen bei verschiedenen Hirnschaedigungen. Es wird so

gezeigt, dass die frontale Agraphie selten ist. Es werden verschiedene Faelle vorgefuehrt welche indessen fuer die Existenz von Schreibstoerungen bei frontalen Schaedigen sprechen.

Obwohl die frontale Agraphie selten ist, kann sie schwerlich abgeleugnet werden, da ja Faele beweisen, dass die frontalen laesionen sehr ernst sind, in so weit als es sich um eine ausgedehntere Deorganisation handelt, die die Schreibstoerungen verursacht.

Immerhin ist der Mechanismus der einfachen oder kombinierten frontalen Agraphie, nicht einfacher Art. Bisher haben wir zwei Arten unterscheiden koennen: die Agraphie als einem mehr oder weniger integralen Teil einer expressiven Agraphie und die Agraphie als einem Teil der Deorganisation der Gesten.

Der erstere Typ der Agraphie, welcher weniger direkt mit frontaler Läsion in Verbindung stände (wenn man die haeufig vergesellschafteten Laesionen der regio Rolandica in Betracht zieht) bezieht sich hauptsächlich auf den spezifischen Ge-

brauch eines graphischen Schluessels. Man muss dabei wissen, das im allgemeinen Geruest der Sprachstoerungen, die Rolle der frontalen Laesion quantitativ weniger wichtig ist, als eine parietale Laesion, soweit es sich um die Deorganisation der graphischen Schlüsselung handelt. Dagegen erzeugt die frontale Laesion verbunden mit der rolandischen Laesion eine andere Art der Schreibstoerungen. Es ist kein entscheidendes Argument fuer oder gegen eine groessere Rolle des Fusses von F2 gefunden worden. Die zweite Art von Agraphie scheint mehr charakteristisch fuer frontale Agraphie zu sein und entspraech dem Mechanismus der magnetischen Apraxie wie sie von Denny-Brown beschrieben worden ist, obwohl die tonischen Phaenome nicht als direkte Erklaerung der Schreibstoerungen angesehen zu werden brauchen.

Psychological Deficits Associated with Frontal Lobe Lesions

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Defects following injury to the frontal lobes have traditionally been sought in the highest intellectual operations of the human mind, and in some cases have indeed been found^{1, 2, 4, 5, 10}. But in many others they undoubtedly have not^{13, 27}. The reasons for this inconsistency are many and varied. The age at which the patient sustains his brain damage is undoubtedly one factor, though its precise significance is far from easy to assess^{24, 28}. Another may well be the extent to which actual loss of cerebral tissue is complicated by more extensive neurophysiological dysfunction^{6, 13}. Then, too, methodological snags of all kinds abound. Teuber²⁷ has recently reminded us of the hazards inherent in the study of single cases and the no less serious—if less widely recognised—hazards that arise in the study of groups of cases. But even when we make every allowance for such hazards, it still cannot be said that any clear and consistent effect of frontal lobe damage upon intellectual performance has as yet been convincingly demonstrated.

I do not wish in this paper to review earlier studies of frontal lobe defects or to present new material on any scale. My aim is simply to draw attention to certain issues raised by earlier workers and to suggest some fresh lines of inquiry. As Teuber (1964) has urged, quite new approaches will be necessary if we are to clear up the many contradictions generated by earlier

inquiries. If we can but find the right questions to ask, I cannot believe that the study of frontal lobe function will prove as unrewarding in the future as it has in the past.

The frontal lobes and cerebral dominance

The first question I would like to ask is concerned with cerebral dominance. Ever since Jefferson¹⁵ claimed to show that intelligence and personality are affected no more adversely by removal of the left than of the right frontal lobe, it has been tacitly assumed that the prefrontal areas are not subject to cerebral dominance.

Jefferson's claim derived considerable support from the careful work of Rylander²⁵, who showed that measurable intellectual defect after operation on the frontal lobes is no more severe after left-sided than after right-sided excisions. While accepting this evidence, I must admit that I have always found inferences drawn from it with regard to the equipotentiality of the prefrontal areas vaguely unsatisfactory. If, as most people believe, cerebral dominance involves a genuine functional asymmetry, it is difficult to accept that it involves only *part* of a cerebral hemisphere and does not extend to the whole of it. Furthermore, even if no inherent superiority can be ascribed to the left frontal lobe, the very fact that it forms part of the dominant hemisphere must surely affect in

some degree its position *vis-a-vis* its fellow.

With these doubts in mind, I have recently reviewed the literature to see whether there is any evidence of a differential effect of unilateral frontal lesions. To my surprise, I soon came upon such evidence, and precisely in the sphere in which one might most reasonably expect to find it, namely that of language and speech. This evidence comes from two main sources: first, the older work on traumatic brain injuries, mainly from World War I; and secondly, more recent studies of leucotomy and lobectomy using various measures of verbal fluency.

Teuber²⁷ has recently reminded us of the merits of Feuchtwanger's study⁸ of 209 cases of penetrating frontal gun-shot wounds. It should be noted that cases with injury involving the central convolution or Broca's area were expressly excluded from his series. None the less, Feuchtwanger drew attention to the incidence of what he called "cerebral language disorders" on 20.9 p.c. of his patients with left-sided but only 2.4 p.c. of his patients with right-sided injuries. This would seem to indicate a significant association with lesions of the dominant hemisphere.

Very similar findings were reported by Kleist¹⁶. In his monumental *Gehirnpathologie*, he describes a group of 13 patients with left-sided frontal injuries well outside the speech areas who showed marked defects in thought and language, and a further 9 patients whose defects were restricted to verbal thought processes alone. In Kleist's view, these defects are not only specific to the left frontal lobe but bear a definite relation to the site of injury within it. Thus he placed particular stress on the posterior portion of the second frontal convolution, area 9 of Brodmann, in relation to defects of verbal thought.

The defects described by Feuchtwanger and Kleist are (1) A certain loss of spontaneity of speech, in the absence of articulatory disorder; (2) Difficulty in evoking appropriate words or phrases, amounting on occasion to frank agrammatism. (3) In some cases, definite impairment of

verbal thought processes. It is pointed out by Kleist that in view of their unilateral character, these disorders cannot be attributed to hypokinetic changes of a general kind, which occur indifferently with lesions of either hemisphere.

These early observations appear to have been largely forgotten, perhaps in reaction against extreme views of cerebral localization. I have also been unable to trace reports of similar speech defects dating from World War II, but it is possible that their relative mildness caused them to be overlooked. There are, however, definite indications that the loss of verbal fluency which has been noted by several workers after bilateral prefrontal leucotomy^{23, 26}, is due to involvement of the left hemisphere. In a recent report, Milner²¹ calls attention to a striking difference between cases with left-sided and right-sided frontal lobe excisions in performance on Thurstone's Word Fluency Test. Although her groups are small, the differences she reports are none the less statistically significant. In this connection, it is noteworthy that relatively greater impairment of verbal as opposed to non-verbal ability has been reported to follow unilateral left-sided leucotomy²³, and that changes in speech rate after such an operation have also been recorded³. All in all, a *prima facie* case can be made for a laterality effect in relation to lesions of the frontal lobes.

Although I have as yet no systematic evidence on this issue, I have had occasion to study a number of patients with anterior left-sided cerebral lesions, some of whom have presented verbal defects extremely reminiscent of those described by Feuchtwanger and Kleist. Indeed I think the condition is best described as a minimal grade of verbal aphasia in the sense of Henry Head¹². Although there is no articulatory defect, spontaneous speech is sparse and there is a noteworthy disinclination to engage on tasks, such as intelligence tests, which call for sustained verbal effort. Although conversational speech may appear normal and there is absolutely no nominal defect, the patients complain of real difficulty in evoking appropriate words and

phrases. As one such patient put it: "Everything is there in my head but I can't bring what I'm saying to my mouth". This lack of fluency is well brought out on tests of the kind used by Milner²¹ and is also shown on certain of the tests of 'divergent thinking' which are described below. Indeed the defect is evidenced in the evocation of ideas no less than of words. But the extent to which there is intellectual defect apart from, or in addition to, the defect of evocation must remain conjectural.

I think it may be concluded that left-sided frontal lesions give rise to high-grade defects of thought and speech which are seldom found with comparable lesions of the right hemisphere. Whether these defects are due directly to localised prefrontal lesions, as argued by Kleist¹⁶, or whether they depend upon remote effects of the lesion on the speech areas, cannot at present be answered. But I think there is a case for regarding the left frontal lobe as closely linked with the machinery of language and as very much a component part of the dominant hemisphere.

"Convergent" and "divergent" thinking

I would like now to turn to the vexed question of intellectual defect after injury to the frontal lobes. As is well known, the evidence is inconclusive and often contradictory. It seems clear, however, that conventional measures of intelligence such as the I.Q. may show little change after extensive frontal lobe operations. For example, Hebb and Penfield's famous patient, K.M., achieved an I.Q. of 98 after extensive bilateral excision of frontal tissue^{1, 7}. At the same time, many clinicians view such findings with scepticism. As they know only too well, patients who acquit themselves adequately on psychometric examination may none the less exhibit gross deficiencies in their everyday behaviour. It is probable, then, that the forms of deterioration to which patients who have sustained frontal lesions are subject are not apparent on the conventional tests of intelligence.

There is another aspect of intelligence tests that has recently given cause for concern and though apparently remote from neurology may not be without relevance to this issue. In educational psychology, it has become abundantly clear that the I.Q. does not provide a reliable indication of potential creative achievement⁹. This shortcoming has led to much research on new tests which it is hoped may provide more satisfactory evidence of latent originality or, as the Americans say, creativity. A number of these tests have been based on the distinction between "convergent" and "divergent" thinking, which we owe to Guilford¹¹. In what he calls "convergent" thinkings, the aim is to discover the one right answer to the problem set. It is highly directed, essentially logical thinking of the kind required in science or mathematics. It is also the kind required for the solution of most intelligence tests. In "divergent" thinking, on the other hand, the aim is to produce a large number of possible answers, none of which is necessarily more correct than the others though some may be more original. Such thinking is marked by its variety and fertility rather than by its logical precision. According to Getzels and Jackson⁹, who have done much of the pioneer work on this field, "divergent" thinking plays a most important part in creative thought.

We have recently embarked on a pilot study of the effects of brain damage on "divergent" thinking, using some of the tests devised by Getzels and Jackson⁹. These are essentially tests of intellectual resourcefulness. One consists in asking the subject to give as many uses, probable or possible, for a given object as he can think of. Another consists in giving the maximum number of meanings which a particular word may possess. Our preliminary findings suggest that tests of this kind give marked difficulty to frontal lobe patients. On the *Uses of Objects test*, for example, they tend to embroider on the main or conventional use of an object, often failing to think up other less probable uses. This is somewhat reminiscent of the inability to

switch from one principle of classification to another that has so often been described on sorting tests²⁰. Here is an example: The patient, a man of 52 who had sustained some left-sided anterior cerebrovascular damage, achieved a WAIS I.Q. of 114. He had no manifest aphasia. When asked to think of as many uses as he could for a *brick*, he replied as follows:

"Other than building houses: (to) make fences, sties, pigsties, — use them as paths. (I've got a little patch of garden edged with bricks). Could be used in rough way in roofing. Fancy bricks could be used in putting up a facade of a building to make it look attractive. It's also used for building pier attractions (?foundations) in the water to build bridges on."

Only when asked to specify possible uses of a *single* brick, other than for building purposes, did the patient add.

"To throw at anybody. As a door stop. No uses after that".

A second patient, admittedly pretty deteriorated, could only say:

"When building a house you have to join bricks together". When pressed, however, he admitted that "you could call a likeable person a 'brick'".

It is my suspicion —at present no more than this— that, thinking is more affected in its "divergent" than in its "convergent" aspects by lesions of the frontal lobes. That is to say, there is a loss of ideational fertility directly comparable to the loss of verbal fluency which has already been described. This defect, I suspect, underlies the loss of imagination so often ascribed to the leucotomised patient, and may indeed account for the banal and stereotyped form so often taken by his attempts at original composition²⁰. If "divergent" thinking genuinely relates to creativity, it may be in this sphere that the frontal lobe patient reveals his most basic handicap.

The regulative function of speech

Lastly, I would like to touch on an approach to the problem of frontal lobe function which we owe to A. R. Luria. In se-

veral recent communications, Luria and his co-workers have proposed that an important outcome of damage to the frontal lobes is failure of what they call the regulative function of speech^{17, 18, 19}. So far as I understand this notion, it means the capacity to initiate, direct and control action in accordance with verbal instructions, whether given by others or self-imposed. As Luria quite rightly points out, such control is acquired relatively gradually in childhood and represents an important evolutionary advance in the regulation of action¹⁷. So far as I am aware, however, he has presented no direct evidence to suggest that the frontal lobes are specifically involved in this developmental process.

In a recent paper Luria, Homskaya and Pribram¹⁹ have described very striking dissociations between action and its verbal control in a patient with an extensive left-sided frontal lobe lesion. This patient, though able to understand and repeat oral directions, was none the less unable to carry them out if they conflicted to any extent with habitual patterns of action. For example, when she was asked to tap *once* when the examiner tapped *twice*, and *vice versa*, she was quite unable to execute the task, in spite of understanding clearly what she was supposed to do. As a rule, she persisted in simple echopractic behaviour. As Luria sees it, the verbal control exercised by the instructions is no longer sufficient to suppress primitive imitative tendencies or to overcome the difficulty in shifting from one mode of response to another so characteristic of frontal lobe patients. In short, the patient knows what she should do, but cannot do as he should; she has lost the regulative function of speech.

I think there is no question that behaviour of this kind is by no means uncommon if it is looked for. The most striking instances of it which I have seen personally have been in cases with diffuse or extensive brain disease, and I am not yet convinced that it should be regarded as a frontal sign rather than as an expression of general brain disorder. At the same time,

we have certainly noted features reminiscent of Luria's description—if a good deal less pronounced—in some patients after frontal lobe excisions. For example, on simple problem-solving tasks the patient may produce the correct solution but apparently fail to formulate the principle upon which it is based. This is often noted on the Sorting Tests devised by Goldstein, and we have seen it too on very simple sequence and alternation problems, of the kind much used in primate behaviour work. We are at present engaged in making some analyses of these forms of disconnection.

I am not clear whether, and if so to what extent, the failures in verbal regulation as described by Luria are related to the minimal grades of expressive dysphasia to which I have drawn attention. It would be necessary to carry out controlled studies of performance on Luria's tests by patients with right-sided and left-sided lesions before any definite conclusion can be drawn. I suspect, however, that this type of disconnection may account, in part at least, for some of the personality changes so characteristic of the frontal lobe syndrome. For instance, the failure in planning to which Penfield and Evans²² long ago drew attention has always struck me not so much as a failure to plan but more as a failure to translate planning into action. Again, the tactlessness so often shown by frontal lobe patients does not seem to depend on any real loss of knowledge of conventional standards of behaviour—indeed purely verbal tests of social judgement may be satisfactorily performed—but on failure to regulate behaviour in accordance with these standards. In other words, there is a dissociation between words and deeds. Although these formulations are admittedly sketchy, they do perhaps embody a conception of frontal lobe function worthy of further exploration.

DISCUSSION

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The more or less marked disintegration of higher functions of the brain with spe-

cial reference to the frontal lobe was described many years ago by *Flechsigs, Meynert, Hitzig, Goltz, Ferrier, Monakow* and others. These authors discussed the psychological ability of establishing synthesis (Bianchi), psychological concentration and even "representations of the faculty of moral-instances".

Lately Psychology developed testing procedures in order to measure the intellectual capacity or at least a testing equivalent to it. Most of these methods describe a number of different single performances using a more verbal or a more non verbal method.

O. L. Zangwill pointed out that most of these methods failed in previous work and he established a difference between the logical and the imaginative thinking and their importance in intelligence. He also described their phaenomenology in frontal lobe lesions.

I think that one should also fix the interest on the more simple non-complex functions of "Antrieb", of the ability to maintain an action (like *Pötzl* called it). The patients with frontal lobe lesions are merely handicapped in testings if they have to keep their initiative and intention towards a task over a longer period of time.

One can therefore, however, use methods of investigation in testing, for instance of motoric actions, with the procedures described by *Oseretzky, Luria, Crawford* and *Stroomberg* and others. One has to take care not so much of the measurement within time-schedules, but in comparing "Antrieb", ability to maintain an action, regardless of the time the patient needs.

These functions (Antrieb) are to be merely differentiated within the frontal lobe region;

It should be pointed out: with test batteries for intelligence measurement like the Wechsler series, etc., one also gets results similar to frontal lesions in *other* cases f.i. in patients with increased intracranial pressure due to tumors in other parts of the brain.

This battery deals with more or less va-

gue dimensions of "intelligence" like general information, general understanding, attention, alertness, memory and concentration, arithmetic-logical thinking, ability to make abstract verbalizations, planning, picking up important details from a situation and motor-sensoric coordination and organisation and so forth.

The higher these complex functions are

in brain pathological cases the less we can use highly differentiated testing instruments.

I think the work with psychological methods to describe simple motor performances and actions and their course in such patients over a longer period of time could add also reduced information to this very interesting discussion.

S U M M A R Y

(1) The need for new approaches to the study of intellectual defect following lesions of the frontal lobe is stressed.

(2) The incidence of minimal expressive dysphasia following left-sided anterior cerebral lesions is described and its relevance to cerebral dominance considered.

(3) The distinction between "convergent" and "divergent" thinking, and its pos-

sible significance for the analysis of frontal lobe defects, is discussed.

(4) Luria's conception of the role of the frontal lobes in the verbal regulation of action is examined. It is suggested that this concept may throw light on certain well-known features of the frontal-lobe syndrome.

R E S U M E N

(1) Es señalada la necesidad de encontrar nuevas formas de estudio de las perturbaciones intelectuales causadas por lesiones del lóbulo frontal.

(2) Se describe la aparición de disfasia expresiva leve como consecuencia de lesiones cerebrales y se considera su relación con la dominancia cerebral.

(3) Se discute la distinción entre el pensamiento "convergente" y el "divergen-

te" y la posibilidad de su importancia para el estudio de las enfermedades del lóbulo frontal.

(4) Se analiza el concepto de Luria acerca del papel que desempeñan los lóbulos frontales en el control verbal de las acciones. El autor sugiere que el mismo puede contribuir a la explicación de algunas características conocidas del síndrome del lóbulo frontal.

R É S U M É

(1) On signale le besoin de trouver de nouvelles approches à l'étude des perturbations intellectuelles causées par des lésions du lobe frontal.

(2) On décrit l'apparition de dysphasie expressive minime comme conséquence des lésions cérébrales et l'on en considère le rapport avec la dominance cérébrale.

(3) On discute la distinction entre la

pensée "convergente" et la pensée "divergente" et la possibilité de son importance dans l'analyse des maladies du lobe frontal.

(4) On examine le concept de Luria concernant le rôle joué par les lobes frontaux dans le contrôle verbal de l'action. On suggère que celui-ci pourrait éclairer certains caractéristiques connues du syndrome du lobe frontal.

ZUSAMMENFASSUNG

(1) Es wird hervorgehoben, dass neue Gesichtspunkte beim Studium intellektueller Defekte nach Laesionen des Frontallappens noetig sind.

(2) Es wird die Haeufigkeit der minimalen expressiven Dysphasie nach linkseitigen zerebralen Verletzungen beschrieben und ihre Wichtigkeit bei der zerebralen Praedominanz eroertert.

(3) Die Unterscheidung zwischen "konvergierendem" und "divergierendem"

Denken und ihre moegliche Bedeutung bei der Analyse der Frontallappen verletzungen wird eroertert.

(4) Lurias Konzept von der Rolle der Frontallappen bei der verbalen Regulierung der Handlungen wird einer Pruefung unterzogen. Es wird die Meinung geaeussert, dass dieses Konzept gewisse wohlbekannte Einzelheiten der Frontallappensyndroms erklaren kann.

REFERENCES

1. Ackerly, S.: A case of Paranatal Bilateral Frontal Lobe Defect observed for Thirty Years. in J. M. Warren and K. Akert: The Frontal Granular Cortex and Behaviour. New York: McGraw Hill. 192-218. (1964).
2. Bianchi, L.: The Mechanism of the Brain and the Function of the Frontal Lobes. Edinburgh, Livingstone. (1922).
3. Bonner, R.; Cobb, S.; Sweet, W. H. & White, J. C.: Frontal Lobe Surgery: its Value in the Treatment of Pain with Consideration of Post-operative Psychological Changes. Res. Publ. Ass. nerv. ment. Dis. 31, 392-421. (1953).
4. Brickner, R. M.: The Intellectual Functions of the Frontal Lobes. New York: Macmillan. (1936).
5. Brickner, R. M.: Brain of Patient A after Bilateral Frontal Lobectomy: Status of Frontal-Lobe Problem. Arch. Neurol. Psychiat., 68, 293-313. (1952).
6. Chapman, L. P.; Thetford, W. N.; Berlin, L.; Guthrie, T. C. & Wolff H. G.: Highest Integrative Functions in Man during Stress. Res. Publ. Ass. Nerv. ment. Dis. 36, 491-534. (1958).
7. Denny-Brown, D.: The Frontal Lobes and their Functions. In Feiling, A.: Modern Trends in Neurology. London: Butterworth. 13-89. (1951).
8. Feuchtwanger, E.: Die Funktionen des Stirnhirns. Monog. aus d. Gesamtgebiete der Neurol. Psychiat. Ed. O. Förster and K. Willmanns, Berlin, Springer. (1923).
9. Getzels, J. W. & Jackson, P. W.: Creativity and Intelligence. New York: Wiley & Sons. (1961).
10. Goldstein, K.: The Significance of the Frontal Lobes for Mental Performance. J. Neurol. Psychopathol. 17, 27-40. (1936).
11. Guilford, J. P. Cited by Getzels, J. W. & Jackson, P. W.: Creativity and Intelligence. New York: Wiley & Sons. (1961).
12. Head, H.: Aphasia and Kindred Disorders of Speech. London. Camb. Univ. Press. (1926).
13. Hebb, D. O.: Man's Frontal Lobes: A Critical Review. Arch. Neurol. Psychiat. 68, 293-313. (1952).
14. Hebb, D. O. & Penfield, W.: Human Behaviour after Extensive Bilateral Removal from the Frontal Lobes. Arch. Neurol. Psychiat. 44, 421-438. (1940).
15. Jefferson, G.: Removal of Right or Left Frontal Lobes in Man. Brit. med. J. 2, 199. (1937).
16. Kleist, K.: Gehirnpathologie. Leipzig: Barth.
17. Luria, A. R.: The Role of Speech in the Regulation of Normal and Abnormal Behaviour. Oxford. Pergamon. (1959).
18. Luria, A. R. & Homskaya, E. D.: Disturbances in the Regulative Role of Speech with Frontal Lobe Lesions. In J. M. Warren and K. Akert: The Frontal Granular Cortex and Behaviour. New York: McGraw-Hill. 353-371. (1964).
19. Luria, A. R.; Pribram, K. H. & Homskaya, E. D.: An Experimental Analysis of the Behavioural Disturbance produced by a Left Frontal Arachnoidal Endothelioma (Meningioma). Neuropsychologia. 2, 257-280. (1964).
20. Milner, B.: Effects of Different Brain Lesions on Card Sorting. The Role of the Frontal Lobes. Arch. Neurol. 9, 90-99 (1963).

21. *Milner, B.*: Some Effects of Frontal Lobectomy in Man. In J. M. Warren & K. Akert: *The Frontal Granular Cortex and Behaviour*. New York: McGraw-Hill. 313-334. (1964).
22. *Penfield, W. & Evans, J.*: Functional Defects Produced by Cerebral Lobectomies. *Res. Publ. Ass. nerv. ment. Dis.* 13, 352, (1934).
23. *Petrie, A.*: *Personality and the Frontal Lobes*. London. Routledge. (1952).
24. *Russell, W. R.*: *Brain, Memory, Learning*. Oxford. Clarendon Press (1959).
25. *Rylander, G.*: *Personality Changes after Operations on the Frontal Lobes*. Copenhagen: Munksgaard.
26. *Rylander, G.*: Personality Analysis before and After Frontal Lobectomy. *Res. Publ. Ass. nerv. ment. Dis.* 27, 691-705. (1948).
27. *Teuber, H. L.*: The Riddle of Frontal Lobe Function in Man. In Warren, J. M. & Akert, K.: *The Frontal Granular Cortex and Behaviour*. New York: McGraw-Hill. 410-444. (1964).
28. *Teuber, H. L. & Rudel, R. G.*: Behaviour after Cerebral Lesions in Children and Adults. *Develop. Med. Child Neurol.* 4, 3-20. (1962).
29. *Tow, P. M.*: *Personality Changes following Frontal Leucotomy*. London: Oxford Univ. Press. (1955).

Some Early and Transient Changes in Psychological Function Following Anterior Cingulectomy in Man

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INTRODUCTION

John Fulton's influence was pervasive in clinical neurology as well as neurophysiology. At a dinner in Oxford with Hugh Cairns and some of his associates Fulton gave a striking account of the profound changes in behaviour observed by workers in his department amongst others following anterior cingulectomy in monkeys. His enthusiasm did much to encourage the project started by Cairns in 1948 to explore the possibilities of limited excision of the anterior cingulate area in the treatment of mental disease in man. The programme included the study of behavioural changes and histological findings in monkeys following cingulectomy; and the trial of anterior cingulectomy in man as an alternative to pre-frontal leucotomy in selected patients with mental disease. The observations on monkeys (Glees et al⁴), confirmed the general pattern of behaviour change noted by others (Smith⁷, Ward¹¹) and provided further information about the fibre connections of this area. The clinical effects of the operation were not dramatic but some worth while improvement occurred in the behaviour of schizophrenics, and the absence of the sometimes gross personality changes noted following standard leucotomy, encouraged its use in patients with well preserved personalities but

severely disabled, especially by obsessional symptoms (Whitty et al¹³, Tow and Whitty⁹). As a therapeutic procedure the operation, which involves a formal craniotomy, has had only a limited application; many of its advantages being obtained from the much more technically simple procedure of orbital under-cutting. However, anterior cingulectomy has now been performed in 22 patients with well preserved intelligence and personality and this has afforded an opportunity to study some of the more subtle psychological changes that occur early after operation. The changes have already been reported in previous communications (Whitty and Lewin^{14, 15}). They have been confirmed and the observations amplified in further cases.

Early mental changes after cingulectomy

In 18 of 22 patients undergoing cingulectomy, subjective and objective changes have been noted during the first one to three days after operation. Sixteen of these patients have been previously reported. Recognition of these changes has largely depended in the patients concerned on clarity of consciousness, well preserved intelligence and cooperation in reporting them. Subjectively patients were aware of a difficulty in distinguishing between external

happenings and their own thoughts and dreams. Objectively this resulted in a type of false reminiscence: but one of which the patient was partially aware of, so that they readily corrected it when challenged and not only admitted its inaccuracy but tried to describe its source.

A patient interviewed two days after operation was asked about his night's sleep. He described it as being interrupted by a visit to some place near his home 12 miles away and gave details of the scene and weather at the time. On further questioning he spontaneously corrected this and described it as a vivid dream. He elaborated on the difficulty of distinguishing it from a real occurrence.

A housewife questioned in the afternoon some 36 hours after operation about her morning's activities at first described the preparation of a lunch for her husband and son. However without any challenging she then stated this was incorrect, and that she had only been thinking of this event, but that it seemed vivid and real to her and that even as she was speaking she had only to close her eyes and think she was doing something and she would have difficulty in being certain that she was not. On questioning she correctly described a visit of the house surgeon that had occurred that morning, and a change of draw-sheets necessitated by her urinary incontinence.

An intelligent high school mistress two days after operation described her symptoms as a difficulty in distinguishing between imagination and reality. She gave an accurate description of events which had occurred in the previous eight hours but interpolated incorrect happenings. These she would always correct if they were challenged and sometimes correct spontaneously. She also emphasised the vividness of her thoughts and their tendency to become indistinguishable from external events if she closed her eyes or "let her attention wander".

A business man when examined two days post-operatively in reply to questioning described a visit from his wife that day. He spontaneously corrected this and said that

he had been looking forward to a visit. He complained of the vividness of his thoughts and described how all their details had an "unnatural clarity". The colour of the objects he thought of and the appropriate accompanying sounds of the imagined events were described as so vivid that "I only have to close my eyes and the thing is happening".

In all these instances patients were not confused in the usual psychiatric sense of the word. They were aware of their personal identity. They knew they were in hospital. They recalled the reason for their being there and the details of their previous mental illness. They were fully aware of the incompatibility of their present circumstances and some of the pseudo-events they recalled. They were fully in touch with current events up to the time of their hospital admission - usually 24 hours before operation. They knew the time of year and the time of day. However they were often unaware of the time since operation and uncertain therefore of the date and day of the week. They were also occasionally hesitant as to whether they had yet had an operation. There was therefore some disorientation in time.

Linked with this change in vividness of thoughts and probably also reflecting the disorientation in time there was a defect of memorising shown as an inability to locate past events correctly in a temporal sequence. In certain cases this resembled a Korsakoff's amnesic confabulatory state, since events of themselves accurately recalled, were misplaced in time and thus at first appeared as confabulation.

A patient interviewed some 36 hours after operation was questioned about his morning's activities. He described an incident in which a power failure had caused him to be stuck in the hospital lift. Details were vivid and convincing but he had in fact not left the ward that morning. On further questioning he doubted the accuracy of his story but did describe correctly the change of dressing to his operation wound. In the lift incident he was in fact

describing entirely accurately an event that had occurred some three days previously.

A student 24 hours after operation described a cricket match as an event of the immediate pre-operative day which he had in fact spent in hospital. A detailed description of the ground and high-lights of the game were given. On pressing him he agreed that the game had not occurred at the time stated. He also described accurately his arrival at the hospital on the day in question, though he was uncertain of its timing. In conversation he spoke of some difficulty in appreciating the passage of time. It was subsequently verified that his description of the cricket ground was accurate in detail and that the particular events he described in the game in which he had distinguished himself were also correct. However this had occurred some weeks before.

A house decorator in the afternoon three days after operation described a visit from his wife that morning. Details were correct but the event had occurred the day before. He was unable to recall whether or not he had had his lunch but recounted accurately what he had in fact had, though unable to say on which day. Tested at this time his digit span was seven figures forward and five backwards. He recalled accurately the name of a flower and a random name and address given him some seven minutes previously. At the end of a three quarter of an hour interview he recounted with fair accuracy the general points of conversation and questioning but could not give their time sequence.

These patients showed a clear inability to orientate events correctly in time and this inability was sometimes marked. However there was no convincing evidence that they had any complete amnesia for events and they did not show any true confabulation, either in the sense of inventing material to cover defects of memorising or by inaccurately elaborating misplaced events, even when encouraged to do so by the examiner. In this respect they differed from a typical Korsakoff state.

Discussion

The site of lesion in 46 cases of cingulotomy has now been verified in seven cases that have come to autopsy. In all but one of these the lesion was accurately placed in the anterior cingulate gyrus on each side. In one it was placed above this gyrus in Brodman's area 32. In two others the lesions were smaller than supposed. In all six there was some involvement of corpus callosal fibres. Detailed histological studies of the hemispheres are not yet available but in no case was there any unintended superficial damage seen in frontal lobes or elsewhere. Of these seven cases two are from the 22 cases discussed in this paper. Both had accurately placed lesions. In one the lesions were unexpectedly small. The evidence is therefore in favour of the psychological changes noted being due to a limited bilateral cingulate lesion. However in four of these cases the syndrome was not found, despite their suitability for examination and a clear understanding of what to look for. In one of these the operative lesion may have been inadequate. In the other three no explanation can be offered for the absence of symptoms: though in one the presence of a pre-existing temporal lobe lesion may be relevant. Allowing that these changes are due to cingulate lesions, a further question of interest is whether they are unique to lesions in this situation.

Bilateral symmetrical lesions of both hemispheres—a necessary feature for valid comparison—are very rarely undertaken as planned operative procedures in regions other than the frontal. However the recent war provided a number of cases of bilateral hemisphere injuries either from through and through wounds or separate bilateral missiles and the evidence from these is that bilateral occipital injuries and biparietal lesions produce characteristic and often long-lasting changes in somatic and psychological function, but they do not contain changes described in this paper. Bilateral temporal lobe injuries when involving the medial aspects of the lobes,

may produce gross defects of memorising (Scoville and Milner, 1957). In such cases symptoms are long-lasting, probably permanent, and the picture is not simply one of difficulty in sequential memory but an almost complete inability to retain new material: and the effect on behaviour is correspondingly profound. Detailed study of these cases has not so far revealed any evidence of the change in subjective vividness of thought and images which is a feature of the early post-cingulectomy state. To elicit this however both clarity of consciousness and adequate powers of introspection are required in the patient.

Following standard leucotomy changes in temporal orientation, in awareness of operation and appreciation of the self have been described (Stengel⁸; Freeman³; Robinson and Freeman⁶). In the first few days after small bilateral frontal brain wounds also a marked defect in time sense may appear. Such patients are not only disorientated in time when questioned but also show a neglect of the passage of time in their behaviour. They may also appear unaware of the fact of their recent wound or operation and at times deny it. These cases usually show some general clouding of consciousness especially in the relevant early post-operative period which precludes accurate observation. However in one case of removal of a small anterior falx meningioma in an intelligent woman of 36 her mental state allowed the elicitation of a syndrome containing both the complaint of vivid thoughts and dreams and difficulty in temporal location of remembered experiences. The picture was that of a post-cingulectomy state and was present for some 4 hours. The recent development of electrolytic lesions placed in selected areas of cortex and sub-cortex as a therapeutic procedure for some forms of mental disease, using a leash of hair-fine implanted electrodes (Walter and Crow¹⁰) has provided a further source of evidence of localised function. Such a procedure has been applied to the cingulate regions in cases of severe obsessional or anxiety states. Changes in time sense have been observed

and a transient confusional state with the features here described has been recently seen in one case where the electrolytic lesions were large (Crow²). In all these instances bilateral damage to the frontal lobes is a common factor. It is possible that in each instance lesions include specific injury to the cingulate area or its connections. It is a reasonable working hypothesis that the effects noted following precise and limited cingulate cortex lesions are also produced by damage to this mechanism in the other and possibly more widespread lesions.

The changes observed are essentially transient. They are rarely found for more than three days after operation. They can be recalled as abnormalities of thought and memorising by patients for some months afterwards and can sometimes be accurately described. After this the memory of them fades, and those cases examined a year or more after operation can give no clear subjective account of what they experienced, though they will still recall in very general terms that they did have some anomaly of mentation. This time scale must raise the possibility that the changes are due to the effect of injury potentials from the operative site: a form of von Monakow's diaschisis. Such discharges occur and can be seen both in electrocorticograms taken from the exposed frontal poles immediately after excision, and within 72 hours of operation in scalp electrode electro-encephalograms. It is also possible however that the changes are due primarily to the removal of the normal function of the anterior cingulate cortex, and that this is rapidly taken over by other areas. Of the two the former seems more probable.

In monkeys following cingulectomy there is for a time —the transience of the phenomenon here too should be noted— a very profound change in behaviour: a change which would be incompatible with their survival in their natural habitat. This has been repeatedly confirmed (Smith⁷, Ward¹¹, Glees et al⁴). This change was so dramatic that it led Ward¹² to suggest that the major effects

of frontal leucotomy and similar operations in man were due primarily to functional disconnection of this area. On present evidence this seems unlikely. Frontal leucotomy usually produces more widespread effects on behaviour and personality, which are more persistent and may occasionally appear to increase with the passage of time. However even though short-lived, the changes described here following anterior cingulate excision also involved for a time a profound alteration in normal mental processes. Difficulty in distinguishing imagery and external events—something akin to hallucinosis—would have marked effects on behaviour: inability to locate past events in time would also be disabling in its own right and would seriously interfere with the rational use of past experience.

One point of special interest is that these changes should occur from lesions in so limited an area of cortex. Since the cingulate cortex is generally regarded as a part of the limbic system it is worth considering whether these two features of the post-cingulectomy syndrome could be formulated in terms of one change basically emotional in character. The detailed fibre connections of the cingulate area in man are not fully known. However if one extrapolates from the known connections in subhuman primates (Glees et al⁴), it would appear to have widespread intracortical connections. It would thus constitute one main gateway for the limbic system to debouch into the neocortex. If we accept Papez's⁵ suggestion of the limbic system as the neurological substrate of emotion, we can envisage the cingulate cortex as providing a pathway for the emotional accompaniment of much cortical activity. The quantitative direction of attention (basically an "emotional" factor) in perception, and in part the consequent vividness of remembered experience would be mediated by

this. Its destruction would alter this function qualitatively and quantitatively. Disorganised injury potentials pouring out into surrounding cortex might well produce the alteration of vividness in normal imagery which these patients notice.

The neurological basis for orientation in time is complex and has been little studied. The mechanism is one which is very easily disturbed, and transient disorientation in time is readily produced by head injuries or toxic encephalopathies when other evidence of confusion is absent.

One factor which plays a part in establishing the time sequence of memories is the vividness or emotional accompaniment of experiences. Any alteration in this quality which restricted the associated environment of remembered experience would reduce the temporal sign of remembered events. It is possible therefore to see a change—a disorder perhaps rather than a simple reduction—in the emotional accompaniment of perception as a basic factor in the early post-cingulectomy state.

The persistent effects of anterior cingulectomy are a slight disinhibition of general behaviour and relative neglect of the emotional impact of external events. These form the basis for the persistent improvement that may be seen in obsessional and anxiety symptoms. Such effects are certainly consistent with the role postulated for the cingulate area, but they are trivial compared with the early effects and the hypothesis would require the existence of alternative connections between the limbic system and the neocortex.

Whether or not such speculation is justified, it is of interest that the anterior cingulate cortex would appear to be involved in memorising and thus take its place with the other components of the limbic system in this respect (Barbizet¹).

S U M M A R Y

The early changes following limited bilateral extirpations of the anterior cingula-

te cortex in man are described. Increased vividness of thoughts and images occurs so

that a subjective difficulty is experienced in distinguishing between thoughts and external happenings. There is also difficulty in locating remembered events in their correct time sequence. These changes are only present for two to three days after operation. A basic change in the emotional accompaniment of perception is postulated as their cause. The role of the cin-

gulate cortex as an intermediary between the limbic system and the neocortex is discussed in terms of these symptoms. It is noted that the memory difficulty may resemble part of the Korsakoff syndrome, and that injury to the cingulate cortex must be considered as a further example of limbic system dysfunction producing defects of memorising.

R E S U M E N

Se describen los cambios que sobrevienen tempranamente a continuación de la extirpación bilateral limitada de la corteza cingulada anterior en el hombre. Las imágenes y los pensamientos se hacen más vívidos de tal manera que se produce la dificultad subjetiva de distinguir los pensamientos de los hechos exteriores. También hay dificultad para ubicar correctamente hechos recordados en el tiempo. Estos cambios sólo están presentes dos o tres días después de la operación. Se postula como causa la existencia de modificaciones bási-

cas en los factores emocionales que acompañan la percepción. Se discute basándose en estos síntomas el papel de intermediario de la corteza cingulada entre el sistema límbico y el neocortex.

Se señala que la dificultad para la memorización se parecería a una parte del síndrome de Korsakoff, y que la lesión de la corteza cingulada debe ser considerada como otro ejemplo de alteración del sistema límbico responsable de los defectos de la memorización.

R É S U M É

Les effets premiers de l'extirpation bilatérale de l'écorce cingulaire antérieure chez l'homme sont exposés. L'augmentation de l'éclat des pensées et des images produit une difficulté subjective de distinguer entre les images et les événements extérieurs. Ces changements restent seulement pendant 2 ou 3 jours après l'extirpation. Le rôle de l'écorce cingulaire comme un in-

termédiaire entre le lobe limbique et le neopallium est discuté. On envisage la difficulté de mémorisation comme une partie du syndrome Korsakoffien, et ainsi la lésion d'écorce cingulaire comme un autre exemple de dysfonctionnement du système limbique produisant un défaut de mémorisation.

Z U S A M M E N F A S S U N G

Die frühen Störungen, die beim Menschen einem umschriebenen zweiseitigen Ausschneiden des vorderen gyrus cinguli nachfolgen, sind hier beschrieben. Ideen und Vorstellungen werden lebhafter wahrgenommen, sodass es schwierig sein kann, zwischen inneren und äusseren Ereignis-

sen zu unterscheiden. Schwierig ist auch die zeitliche Anordnung der Erinnerungen. Diese Störungen sind nur 2 bis 3 Tagen nach der Operation vorhanden. Eine Rolle des g. cinguli als Vermittler zwischen dem limbischen System und dem Neocortex wird vermutet. Es wird betont, dass dieser

Erinnerungszerfall mit einem Korsakowschen Syndrom vergleichbar ist, und ein weiteres Beispiel der Beziehung zwischen

Verletzungen des limbischen Systems und mangelhaftem Erinnerungsvermögen darbietet.

REFERENCES

1. Barbizet, J. (1963): J. Neurol. Neurosurg. Psychiat. 26, 127.
2. Crow, H. J. (1965): Personal Communication.
3. Freeman, W. and Watts, J. W. (1950): "Psychosurgery". 2nd. ed. Springfield, Ill.
4. Glees, P.; Cole, J.; Whitty, C. W. M. and Cairns, H. (1950): J. Neurol. Neurosurg. Psychiat. 13, 178.
5. Papez, J. W. (1937): Arch. Neurol. Psychiat. (Chicago) 38, 725.
6. Robinson, M. F. and Freeman, W. (1954): "Psychosurgery and the Self". New York.
7. Smith, W. K. (1944): Fed. Proc. 3, 42.
8. Stengel, E. (1952): J. ment. Sci. 98, 382.
9. Tow, P. M. and Whitty, C. W. M. (1953): J. Neurol. Neurosurg. Psychiat. 16, 186.
10. Walter, W. G. and Crow, H. J. (1964): Electroencephal. Clin. Neurophysiol. 16, 68.
11. Ward, A. A. (1948a): J. Neurophysiol. 11, 13.
12. Ward, A. A. (1948b): Res. Publ. Ass. nerv. ment. Dis. 27, 438.
13. Whitty, C. W. M.; Duffield, J. E.; Tow, P. M. and Cairns, H. (1952): Lancet 1, 475.
14. Whitty, C. W. M. and Lewin, W. (1957): Brain, 80, 72.
15. Whitty, C. W. M. and Lewin, W. (1960): Brain, 83, 648.

Different Psychological Consequences Due to Superior Frontal and Orbito-Basal Lesions

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Lesions of the brain may be followed by personality alterations of different degrees. The extension and localization of the injury plays a role in this process. Whereas an injury on the border of the longitudinal fissure scarcely affects the structure of personality, the frontal lobe injuries usually produce alterations of character and of the core of personality.

The frontal lobe syndrome occupies as much a central position in the history of clinical pathology of the brain and neuropsychology as do aphasias in the sphere of cortical symptomatology.

In this respect it must be emphasized that which is defined as frontal lobe syndrome cannot be analyzed or defined as clearly as for instance, the clinical picture of an aphasia. Eva Hoch stresses in her excellent psychological study on lobotomy patients that diagnosis is easier "with the naked eye" than with the aid of special tests. However, so far the anatomical basis of the above mentioned psychic alterations are still fragmentary in many respects. As to the psychic alterations of the so-called frontal lobe syndrome one cannot only hold responsible the local cortical injuries of isolated areas of the frontal brain, but also some undamaged centres in other areas deprived of regulation and control.

Karl Kleist delayed for years the conclusion of his pathology of the brain due

to the fact that he "could not have it concluded without the consideration of the brain stem pathology". As a matter of fact, he had to find out, in the course of his work, that frontal symptoms are often connected with the brain stem symptomatology leading to psychic alterations of different kind or degree.

Thus alterations of the character and personality occurred after injuries of the orbital area, but they are often associated with thalamic and hypothalamic lesions.

In the following pages I should like to discuss at first the different psychic phenomena of known or recorded brain injuries, and then try to classify them according to their localization.

The contributions presented to you on this occasion are based on cases of frontal lobe injuries from both the two world wars and on clinical cases in peacetimes.

The brain injured patients with lesions of the frontal lobe are to be found in corresponding percentual rate among the total number of 3000 registered patients of South-Baden. I recognize that this number of patients reveals various deficiencies as to the answer of questions of psychopathology and brain localization. However, it may offer advantages in the way that it was possible to establish a longitudinal section observation of the social evolution and other environmental relations. Through

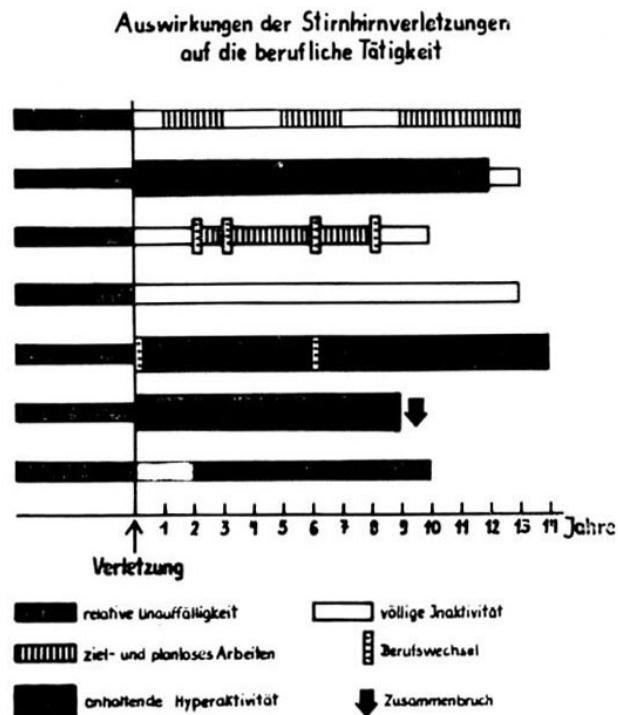


Fig. 1. — This scheme shows that, substantially, 5 groups of social development can be distinguished.

visits to the familiar circles and places of work, and very conscientious inquiries made by an experienced social worker, who was specially trained by us, it was possible to define the picture. The behavior in the clinical environment and in the out-patient consultations hides, as it is well known, a lot of facts which in normal conditions of life play an important role just in these brain injured patients.

With Heuver we examined in frontal lobe patients the professional and social development in connexion to the trauma and have established that very different pictures occur.

To our great surprise, we found among them some brain injured patients who, following the trauma, took up work immediately and were distinguished by increase of capacity in opposition to the time before the trauma. A state of hyperactivity could be noted. They were insensitive to the factory noises and other excitations, for instance, in individual cases, there was a quarrel with the landlord, unfriendly remarks towards a superior or dif-

ferences of opinion in the family as to the education of the children.

In another group a sudden change of occupation followed an episode of hyperactivity. Then there was again an activity under high tension for years, which was released by a change of occupation. It was not possible to recognize the reasons for this modification of mental attitude. In opposition to other brain-injured patients the dates of change of professional activity fall upon a phase of sequelae of the injuries, in which one cannot expect any modification of the condition.

A third group is characterized by an extraordinary irregularity of professional activity and type of occupation. Entirely independent of the previous training, and according to inclination or mood and depending on external influences the hardest unskilled work (e.g. unloading coal at the railway station, harvesting, etc) was carried out. After months of industrious professional activities, equally long periods of absolute inactivity followed. Sometimes kinds of work were executed, pertaining to a classification far below the previous occupation and the anterior professional rank. Among these cases many patients were found, who underwent repeated retraining and therefore had during their lives professional training up to 4 times. One group, since the day of the injury was not able to execute any useful activity. This was especially the case with patients who were injured during their youth, thus struck by an accident before maturity, and who could not find the connexion to their previous professional career. One smaller group was relatively inconspicuous. After a long period of inactivity, they returned to their professional career and from this time on, were able to maintain the occupation with a slight diminution of the total capacity of work. This group differed from the patients with injuries in other localizations in an interruption of approximately two years from the brain injury until the continuation of an activity. As a rule, brain injured patients usually return to their occupation after 3 to 6 months.

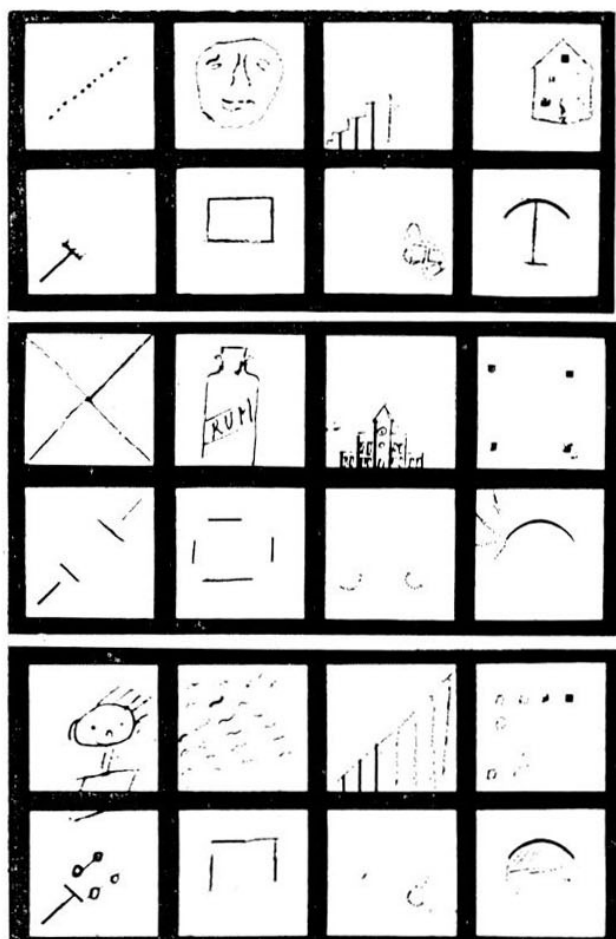


Fig. 2

Considering this behavior at the place of work in both last mentioned groups of high-frontal and orbital basal focal lesions, patients with injuries of the orbital lobe either did not do anything or worked excessively.

In one case one of these patients— after a long latent period— returned to his profession as a mason, and through his hyperthymic, eloquent and at times aggressive behavior, was able to attain the position of a bricklayer's foreman in construction-work. Obstinate towards his superiors and severe to his subordinates, he spoiled the atmosphere of the construction-works quite disastrously. He called the workers: "Dull, lazy peasants". He changed the construction plan for the draining canal and made it less deep so that later the basement was permanently under water. Before the end of the construction works, he sent back

a cement mixer, which had been sent from Constance Lake to the Black Forest and thereby caused a loss of several thousand marks to the construction enterprise. He then turned to welfare institutions and aggressively insulted them by writing letters of the following contents: "It is an unlucky feature in my fate to get so much unproductive help. Formerly one had to have an arian grandmother, today a grandmother from Baden. The boards for the prolongation of the war take jobs away from us. I hope that the atom bomb comes soon. I am already hoping for it like a Jew for his Messias".

Peculiarly patients with high frontal and orbital basal injuries hardly differed at all during systematic tests. The total capacity of high frontal lobe injured patients was perhaps slightly smaller. The time needed for the solution of the tests was longer. What was striking in both groups was the tendency to words perseveration and the almost compulsive willingness to repeat the given optical figure of the various designs of the Wartegg test. The orbital basal injured made efforts to display wittiness, for instance one test-person of the 2nd group drew a rum-bottle. The tendency to repetition, e.g., of points, squares and even of geometric figures is generally recognizable. The lack of imagination is above the average, even in tested patients with fairly good education and background, as for instance, the patient of fig. 4 (former officer) and patient 2, fig. 3 (judge with completed university studies).

These tests might, in any case, be the most appropriate among the usual methods to show, in positive or negative way, the free, constructive capacity, which is related to the functions of the frontal lobe. Occasionally it happens that especially spontaneously frontal lobe injured patients do not finish the test — as shown in fig. 4 — and content themselves with sorting out 3 designs, which they find easier.

The fractionality and incompleteness of many achievements of patients with high frontal injuries, who formerly had an in-

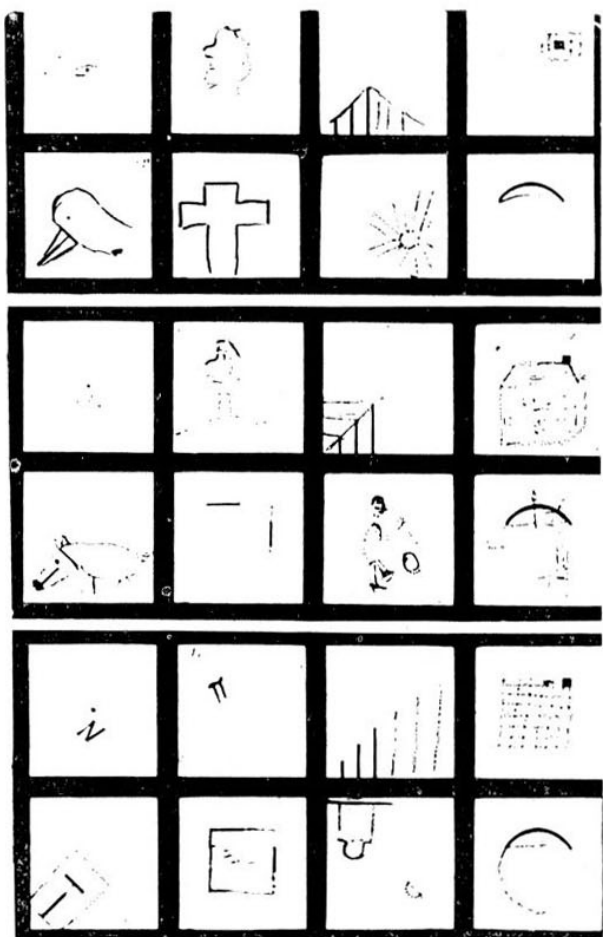


Fig. 3

dependent position, is noticeable. Among the patients in my care there is a stove maker who, occasionally delivers stoves without feet, and a carpenter who omitted some pieces in his chairs.

The group of high frontal lobe injured patients, which are particularly characterized by lack of energy and personal initiative, come less often into the sphere of care institutions, because certain incapacities are compensated by members of the family. Besides, they do not possess enough initiative to apply for their rightful claims at the competent authorities. When the family does not look after them on account of the changes in their personality or the decrease of interests, and quite often because of problems in their marriages (impotence), this may lead to extreme situations, as for instance in the case of an administration employee who suffered from

a high frontal injury. Because of his impotence and almost unmanly weakness after his return from the war, he was put out of the house by his wife and mother-in-law and forced to live in a front building, the only communication between them being reduced to letters. As a result of a bourgeois prestige mindedness discussions about family difficulties were avoided as far as possible. The patient himself went to his office as usual and returned after office-hours. Only at times, he suddenly made indecent exposures from the German side of the Rhine in the direction of Switzerland, where he was observed by custom-officers through binoculars.

Such regressive infantile sexual delicts did not occur in cases of orbital lobe injuries. With these patients completely different instinctive, brutal-egoistic disturbances were quite common. They have periods of hypersexuality, which otherwise, were not observed in patients with brain injuries. Indiscriminate in drinking and in obtaining advantages for themselves, they are also indiscriminate in the choice of their sexual partners, and they often speak quite plainly about this subject. "Who is going to pay the brothel for me?", one patient of this group wrote to the provincial court after his divorce. As an answer to my question what plans he had for the future, he said: "I would like to be a lawyer, boxer or journalist". Noticing my surprise he completed the answer: "to be able to distribute low blows". Prompt reaction, aggressiveness and a blunt manner of expression characterize such patients, most of them with bilateral orbital basal injuries. One may presume of course, that the structure of personality before the injury had a determining influence as well and, on account of this, psychopathologic variations occur in patients with injuries of the same localization.

Among the patients with injuries of the orbital lobe, who at first showed hyperactivity and unstableness, there was a number that suddenly, after decades, committed suicide. Similar observations have already been made by Peters, most suicide candi-

dates being found among the patients with basal injuries of the brain. Considering suicide as a special form of aggression, this expression of self-aggression is in accordance with the previous general behavior of the patients.

Judging by the syndrome only an injury of the orbital basal could have been possible in the following case. This could not be proved in the lifetime of the patient, however, the manifest occipital injury was more noticeable.

The patient K. W. born 1895, a baker, came from a highly industrious and quite ordinary family. Neither psychosis nor

psychic peculiarities were known among immediate relatives. His behavior after a brain injury in May 1915 (in his 20th year) was all the more peculiar. He was called the "scoundrel of K" and was known under this name in the whole neighborhood. He had suffered an occipital injury, from which an initial cortical blindness resulted. The occipital wound suppurated and several operations were necessary to eliminate the pus and remove the bone sequestra. When a limited vision returned later on, W. behaved very conspicuously and peculiarly during medical examinations so that one did not believe the extent

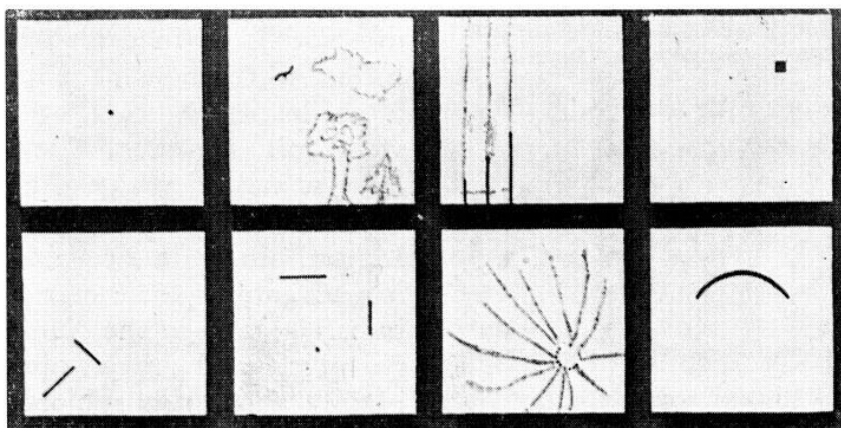


Fig. 4

of his poor vision. The so called simulation tests of the ophthalmologist seemed to confirm the simulation of poor vision. When occasional fits occurred later on, the existence of a brain injury was finally certified. The pension was gradually increased but additional cares were refused. To point out his injury, the patient had a black ribbon made, which he tied around his head to "protect" the wound on the back of his skull. Shortly before the lesion he had married. 14 children were born during the marriage, who nearly all died from tuberculosis and undernutrition (rickets). The patient had numerous affairs with other women, lived together with a gypsy woman for some time at the outskirts of the town, often slept in the fields or in garden-huts and did not care for his family in any way. For years he used to wear dirty an

torn clothes. He used to drink more and more alcohol as sedatives and obtained prescriptions of alcoholic tinctures in litre quantities. By and by he became known in all respective institutions and clinics. He increasingly displayed hysterical fits with disturbance of gait and deafness and at times simulated a total blindness. This however did not prevent him from looking at the show windows of the town which he visited and to take down the prices to buy preferably spirits. In 1946, he was examined at Freiburg clinics. An EEG taken at the time showed temporal right focal disturbances. Later he was increasingly reported for neglect, loitering and begging. He eventually died in 1956 of a bronchopneumonia, which was complicated by delirium. The autopsy evidenced an extensive lesion of both occipital lobes at the

level of the calcarine area, and also a cystic defect of the size of a chicken egg under the right basal frontal lobe. As there was no connection to the liquor space, the defect could not be detected through the pneumoencephalogram (see fig. 5).

Temporally isolated, focal high frontal and orbital basal symptoms are appearing, one after the other in the following case: A 56 year old university professor attracted attention because, in the course of some 6 months, he lost his energy and interests, and became taciturn and affectively unbalanced. He was thought to have possi-

bly overworked himself and was sent to a health-resort. His illness progressed, however. Yet he still felt strong enough to hold a lecture, which he had been planning for a long time. Appearing before a large audience he lost himself in details and could not find an end. At times, he stopped and searched for words, was incapable to find his way through his notes, and left out important links. When invited he used to sit quietly in a corner, greeted everybody in the same stereotyped way and sometimes fell asleep. Shortly afterwards he invited people whom he had met in

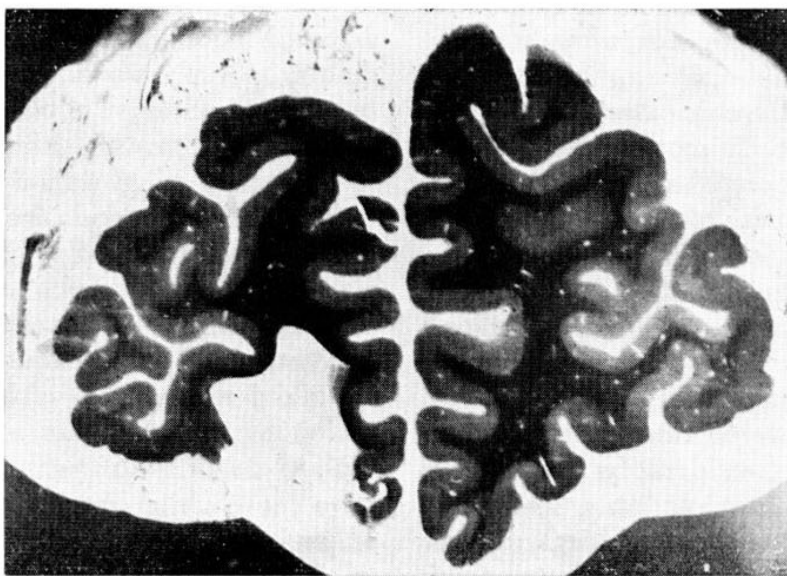


Fig. 5

a street car or somewhere else for dinner. He only came to the clinic after having had several fits with falls and involuntary urination. A glioma was removed from the left upper frontal lobe; according to the operation report the high frontal areas of the convexity and of the pole were removed, the basal area being spared. Subsequently, his condition improved. He was able to hold his lectures i. e. with the help of a text which had been worked out years ago. He only had to be led to the door of the lecture-room by his wife and be given a "push" to be able to walk to the lecturing desk by himself and to speak. His wife had also marked the respective length of the lectures, so that he finished precisely at the

stroke of the clock. Three months later a tumor recidive occurred, which increasingly destroyed the left frontal orbital lobe. At the same time, it was noticed that his facial expression became lively, that he talked a lot, spoke in a carefree manner, cracked jokes and practiced highly improper jokes on a nurse (he presented her an egg-cup filled with milk, into which he put a cyclamen. Around the egg-cup, he placed breadcrumbs as decoration). He found everybody "nice and charming"; he was satisfied with everything, neglected his personal hygiene, and used to go to bed with his necktie and fur-cap.

In this temporally split pathological progression the different symptomatologies

of the dorsal and basal frontal lobe are reflected. Whereas the high frontal injuries produce loss of energy, affective dullness, loss of interest and complete mental incapacity for prospective plans, the basal injuries causes "euphoric absence of critical loss of inhibitions, symptoms of moria and indifference to social habits".

Both groups of brain-injured patients therefore have in common disturbances of behaviour, which to the unsuspecting observer may appear to be psychopathic personalities. The fact that the psychic alteration is temporally connected with a brain injury will not be remembered later on. This is all the more so, as the patients themselves do not point out these connections at all. In my opinion, the organic characteristic of psychic alterations may also be psychologically recognized by more or less marked associated symptoms, as for instance the propensity to perseveration and the inadequacy of affective reactivity.

The different symptoms of the 2 groups of isolated high frontal and orbital basal injuries is less manifest in psychological tests than in everyday life. Following longitudinally the lives of these patients, the prognosis appears considerably less favorable for the orbital basal patients. They call attention in society, they are regarded as trouble-makers and give offence because of their lack of inhibition and aloofness.

They often come in conflict with the law and also many of themselves into extremely difficult situations in their private lives. They scarcely establish firm relations, or only superficially and change their profession and place of work more frequently than anyone else.

High-frontal brain injured are conspicuous for the lack of initiative and their difficult start in any activity. Their results often show shortcomings. They are, on the other hand, often more indolent toward excitations (noises) of the environment than other brain-injured patients. Through their high suggestibility and tendency to be lead by other people they can also be directed in a positive way. If their spontaneity is only weakened and if there are remains of selfdrive they are less noticeable.

For both groups, the time of injury seems to be of great importance. Injuries before maturity and the conclusion of a professional training increase the number of those patients, who cannot find their way in society. Perhaps also in this case patients with basal injuries are more endangered than those with high frontal injuries.

Even in times of peace, traffic accidents have meanwhile contributed a great quota of patients with frontal basal accentuation, so that the total number of frontal injured patients did not decrease in peacetimes.

S U M M A R Y

Loss of drive (Antrieb), bluntness of affectivity, paucity of interest and loss of prospective thinking are the leading symptoms in injuries of dorsal frontal lobe. The injuries of the basal frontal lobe (lesions of basal cortex of the orbital lobe) leave an euphoric loss of the critic, signs of uninhibition and bluntness of feelings, as well as insensibility to social habits. A longitudinal section biographic observation of pertinent cases (with the utilization of clinical data and results of home- and place of work visits) pointed out that frontal brain-injured differ from patients

with brain injuries of other localizations. However, in the group of frontal brain-injured 2 different forms of disturbances of behavior could be differentiated. The different professional and social difficulties of adaptation of frontal lobe-injured are illustrated in a schematic survey. Patients with high-frontal injuries have the tendency to force up their capacity of work during years due to failure of self-awareness. Trivial occurrences bring about an abrupt break-down with permanent incapacity.

Orbital basal-injured patients, in part,

did not find any access to professional life or showed themselves unsteady, changed often jobs and profession and came permanently into conflicts with the environment. The same patients were much more often complicated in forensic proceedings. The disturbances of behavior of these basal frontal-injured patients, which resemble psychopathies, were repeatedly cause of error of medical judgement, the more so

since the patients did not contribute to the anamnesis. The Wartegg-test among the other methods in use seems to give the best evidence for the diagnosis. Positive results of intelligence tests (high IQ) contrast with the failures in practical life. The different clinical picture of high-frontal and basal-frontal injuries is reflected more clearly in the life story than in psychologic tests.

R E S U M E N

La falta de empuje, indiferencia afectiva, disminución de intereses y la pérdida de la capacidad mental prospectiva son los síntomas fundamentales que aparecen en las lesiones dorsales del lóbulo frontal. Los daños frontales basales (lesiones de la corteza basal de la parte orbital) dan lugar a una falta de rigor crítico acompañada de euforia, signos de liberación de inhibiciones, alteraciones emotivas e indiferencia frente a las costumbres de la vida social. La consideración de la línea de vida de varios casos (mediante la valorización de datos clínicos y de los resultados de visitas realizadas en el medio doméstico y en el lugar de trabajo) demostró que los pacientes con lesiones frontales se diferencian de los lesionados de todas las otras localizaciones. Dentro de un grupo de pacientes con lesiones frontales fue posible diferenciar dos diferentes formas de perturbación del comportamiento. En una visión esquemática se consideran las diversas dificultades de adaptación profesional y social de los pacientes estudiados. Aquellos en que la lesión había afectado la parte superior del lóbulo frontal demostraron una tendencia a recargar su trabajo en una forma

exagerada debido a una falsa estimación de sus posibilidades. Hechos nimios dieron lugar a una interrupción brusca de este trabajo con posterior imposibilidad irreversible de trabajo.

Los afectados en la parte basal del lóbulo frontal en parte no pudieron reintegrarse a la vida profesional o bien se mostraron inconstantes, cambiando repetidamente de empleo y profesión, siempre dando lugar a conflictos con quienes los rodeaban. Estos pacientes fueron los que más frecuentemente se vieron envueltos en procedimientos forenses. Las alteraciones de su comportamiento, similares a las psicopáticas, fueron en estos casos muy a menudo la causa de falsos juicios médicos, ya que los pacientes mismos no contribuyeron a aclarar la situación. El test de Wartegg demostró ser el más útil de los instrumentos utilizados. Muchas veces resultados positivos en cuanto a la inteligencia provenientes de tests (cocientes de inteligencia altos) se oponen a fracasos en la vida práctica. El cuadro diferencial de los daños frontales superiores y basales se reflejaron con más precisión en la vida de los pacientes que en los resultados de tests psicológicos.

R É S U M É

Le manque d'élan, l'indifférence affective, la réduction des intérêts et la perte de la capacité mentale prospective constituent les symptômes fondamentaux qui apparaissent

sent dans les lésions dorsales du lobe frontal. Les dommages frontaux basaux (lésions de l'écorce basale de la partie orbitale) provoquent un manque de rigueur critique

accompagné d'euphorie, des signes indiquant la perte des inhibitions, des troubles animiques et de l'indifférence envers les coutumes sociales conventionnelles. La considération de la biographie dans plusieurs cas (mettant en valeur des données cliniques et les résultats des visites faites aux milieux domestique et de travail) démontra que les patients ayant des lésions frontales se distinguent des affectés de toute autre localisation. Dans un groupe de patients ayant des lésions frontales il a été possible de distinguer deux formes différentes de troubles du comportement. On considère schématiquement les différentes difficultés d'adaptation professionnelle et sociale des patients étudiés. Ceux où la lésion avait atteint la partie supérieure du lobe frontal démontrèrent une tendance à surcharger leur travail d'une façon exagérée comme conséquence d'une fausse estimation de leurs propres possibilités. Des faits sans importance provoquèrent une brusque interruption de ce travail, laissant une incapacité irréversible pour travailler.

Les patients atteints à la base du lobe frontal n'ont pas pu se réintégrer en partie à la vie professionnelle ou bien se sont montrés inconstants, changeant plusieurs fois d'emploi et de profession, toujours provoquant des conflits avec les personnes qui les entouraient. Ces patients furent très souvent impliqués dans des affaires phoréniques. Les troubles de leur comportement, similaires aux psychopathiques, furent dans ces cas très souvent la cause de faux jugements médicaux, étant donné que les patients eux-mêmes n'avaient pas contribué à éclaircir la situation. Le test de Wartegg a démontré être le plus utile des instruments employés. Souvent les résultats positifs concernant l'intelligence résultant de tests (hauts coefficients d'intelligence) s'opposent à des échecs dans la vie pratique. Le cadre différentiel des dommages frontaux supérieurs et de la base se sont reflétés avec plus de précision dans la vie des patients que dans le résultats des tests psychologiques.

ZUSAMMENFASSUNG

Antriebsverlust, affektive Stumpfheit, Interessenverarmung und Einbusse prospektiver Denkfähigkeit sind die führenden Symptome bei Schädigung des dorsalen Stirnhirns. Die basalen Frontalhirnschäden (Läsionen der basalen Rinde des Orbitalhirns) hinterlassen eine euphorische Kritiklosigkeit, Zeichen von Enthemmung und Gemütsabstumpfung, sowie von Unempfindlichkeit gesellschaftlichen Gepflogenheiten gegenüber. Eine biographische Laengsschnittbetrachtung einschlägiger Fälle (unter Verwertung klinischer Daten und der Ergebnisse von Besuchen im häuslichen Milieu und am Arbeitsplatz) zeigte, dass Stirnhirnverletzte sich von allen Hirnverletzten anderer Lokalisation unterscheiden. Innerhalb der Gruppe von Stirnhirnverletzten liessen sich aber auch noch 2 verschiedene Formen von Verhaltensstörungen trennen. In einer schematischen Übersicht werden die unterschiedlichen

beruflich-sozialen Anpassungsschwierigkeiten Stirnhirnverletzter veranschaulicht. Hochfrontalverletzte neigten dazu, aus fehlerhafter Selbsteinschätzung sich durch jahrelange "Roboterarbeit" übersteigert zu belasten. Bagatellevorgänge brachten danach einen unvermittelten Zusammenbruch mit bleibender Untätigkeit.

Orbitobasalgeschädigte fanden teilweise keinen Zugang zum Berufsleben mehr oder sie zeigten sich unstet, wechselten wiederholt Stelle und Beruf und kamen ständig in Umweltkonflikte. Die gleichen Verletzten wurden weitaus am häufigsten in forensische Verfahren verwickelt. Die psychopathie-ähnlichen Verhaltensstörungen dieser Basalverletzten waren wiederholt Anlass medizinischer Fehlbeurteilung, zumal die Patienten selbst nichts zur Aufklärung beitrugen. Wartegg-Test erschien von den angewandten Verfahren

noch die meiste Aussagekraft zu besitzen. Positive Intelligenztestergebnisse (hoher IQ) kontrastieren vielfach zu dem Versagen im praktischen Leben. Das unterschiedliche

Störungsbild hochfrontaler und basaler Schäden spiegelte sich in der Lebensgeschichte deutlicher wider als in psychologischen Testergebnissen.

REFERENCES

1. Anton, G.: Symptome der Stirnhirnerkrankung. Münch. med. Wschr. 53, 1289-91 (1906).
2. Anton, G. u. Zingerle, H.: Bau, Leistung und Erkrankung des menschlichen Stirnhirns (1902).
3. Auersperg, A. v.: Zur Frage der Bedeutung des Lokalisationsprinzips im Nervensystem. Med. Welt 8, 14 (1934).
4. Baeyer, W. v.: Zur Pathocharakterologie der organischen Persönlichkeitsveränderungen. Nervenarzt 18, 21 (1947).
5. Berger, H.: Klinische Beiträge zur Pathologie des Grosshirns: Herderkrankungen in der Präfrontalregion. Arch. Psychiat. Nervenkr. 69, 1 (1923).
6. Beringer, K.: Über Störungen des Antriebs bei einem von der unteren Falxkante ausgehenden doppelseitigen Meningeom. Z. ges. Neurol. Psychiat. 171, 451-474 (1941).
7. Beringer, K.: Antriebschwund mit erhaltener Fremdanregbarkeit bei beiderseitiger frontaler Marklagerschädigung. Z. ges. Neurol. Psychiat. 176, 10-30 (1943).
8. Betzendahl, W.: Das Bild des Hirnverletzten nach der ersten Auseinandersetzung mit dem Schaden. Leipzig: J. A. Barth (1949).
9. Bostroem, A. u. Spatz, H.: Über die von der Olfaktorierinne ausgehenden Meningeome und über die Meningeome im allgemeinen. Nervenarzt 2, 505 (1929).
10. Brickner, R. M.: Bilateral frontal lobectomy. Follow-up report. Arch. Neurol. Psychiat. (Chicago) 41, 580 (1931).
11. Brickner, R. M.: The intellectual functions of the frontal lobes. New York: Macmillan & Co. (1936).
12. Duus, P.: Über psychische Störungen bei Tumoren des Orbitalhirns. Arch. Psychiat. Nervenkr. 109, 596-648 (1939).
13. Faust, Cl.: Zur Symptomatik frischer und alter Stirnhirnverletzungen. (Zugleich ein Beitrag zur posttraumatischen, organischen Wesensveränderung). Arch. Psychiat. Nervenkr. 193, 78-97 (1955).
14. Faust, Cl.: Hirnpathologische Gesichtspunkte zur Berufs- und Sonderfürsorge Hirnverletzter. In: Rewald, E., Das Hirntrauma. Stuttgart: Georg Thieme (1956).
15. Feuchtwanger, W.: Die Funktionen des Stirnhirns. (Ihre Pathologie und Psychologie). Berlin: J. Springer (1923).
16. Freeman, W.: Transorbital lobotomy. Amer. J. Psychiat. 105, 734-740 (1949).
17. Freeman, W. u. Watts, S. W.: Psychochirurgie. Hrsg. v. Braunmühl. Stuttgart: Georg Thieme (1949).
18. Goldstein, K.: Die Funktionen des Stirnhirns und ihre Bedeutung für die Diagnosestellung der Stirnhirnerkrankungen. Med. K'i. 19 (1923).
19. Grewel, F.: Psychopathological Analysis of a Case of Pick's Disease. Amsterdam: F. van Rossen (1955).
20. Grünthal, E.: Über die anatomischen, physiologischen und pathologischen Grundlagen der frontalen Leukotomie. Mschr. Psychiat. Neurol. 119, 361-377 (1950).
21. Gruhle, H. W.: Die Hirnlokalisation seelischer Vorgänge (Zentrenlehre). Psychol. Forsch. 24, 1-10 (1952).
22. Guttman, E.: Zur Symptomatologie der Hirncontusion. Die mangelnde Ernstwerdung der eigenen Krankheitserscheinungen. Nervenarzt 4, 207 (1931).
23. Hebb, D. O.: Frontal lobes. A critical review. Arch. Neurol. Psychiat. (Chicago) 54, 10 (1945).
24. Hécaen, H. et Ajuriaguerra, J. de: Troubles mentaux au cours des tumeurs intracrâniennes. Paris: Masson & Cie. (1956).
25. Heuver, E.: Posttraumatische Entwicklung Stirnhirnverletzter auf Grund katamnestischer Untersuchungen. Diss. Freiburg (1955).
26. Heygster, Hans.: Die psychische Symptomatologie bei Stirnhirnläsionen. Leipzig: S. Hirzel (1948).
27. Heygster, H.: Über doppelseitige Stirnhirnverletzungen. Psychiat. Neurol. u. med. Psychol. 1, 114 (1949).
28. Hoch, E.: Die Persönlichkeitsveränderungen nach präfrontaler Leukotomie. Schw. Arch. Neurol. Psychiat. 64, 119-174 (1949).

29. Hutton, E. L.: What is meant by personality? *J. ment. Sci.* 91, 153 (1945).
30. Hutton, E. L.: Personality changes after leucotomy. *J. ment. Sci.* 93, 31 (1947).
31. Hutton, E. L. and Basset, P.: The effect of leucotomy on creative personality. *J. ment. Sci.* 94, 332 (1948).
32. Klages, W.: Frontale und diencephale Antriebsstörung. *Arch. Psychiat. Nervenkr.* 191, 365-387 (1954).
33. Klages, W.: Orbitale und hebephrene Verhaltensweisen. *Arch. Psychiat. Nervenkr.* 194, 62-66 (1955).
34. Klein, R.: Immediate Effects of leucotomy on cerebral functions and their significance. *J. ment. Sci.* 98, 60 (1952).
35. Kleist, K.: *Gehirnpathologie. Handbuch der ärztlichen Erfahrungen im Weltkrieg* Band IV. Hrsg.: O. v. Schjerning. Leipzig: J. A. Barth (1934).
36. Környey, St.: Über ein akutes Ausschaltungssyndrom beider Stirnlappen in Höhe der prämotorischen Rindenfelder und frontalen Augenbewegungszentren. *Arch. Psychiat. Nervenkr.* 114, 649-660 (1942).
37. Kolb, A. u. Lawrence, C.: Klinische Bewertung der präfrontalen Leukotomie. *Ref. Klin. Wschr.* 32 (1954).
38. Kramer, F.: Akinetisches Symptom bei Schussverletzung des Stirnhirns. *Zbl. ges. Neurol. Psychiat.* 34, 78 (1915).
39. Kretschmer, E.: Die Orbita'hirn- und Zwischenhirnsyndrome nach Schädelbasisfrakturen. *Allg. Z. Psychiat.* 124, 358 (1949).
40. Kretschmer, E.: Verletzungen der Schädelhirnbasis und ihre psychiatrisch-neurologischen Folgen. *Dtsch. med. Wschr.* 79, 1709 (1954).
41. Krüger, D.-W.: Die Behandlung der Verletzungen im Bereich der vorderen Schädelbasis und ihre Folgezustände. *Dtsch. Z. Nervenheilk.* 160, 337-372 (1949).
42. Krüger, D.-W.: Über Zeitpunkt und Art der Versorgung frontobasaler Verletzungen. *Klin. Medizin (im Druck)*, Wien.
43. Lange u. Cosack, H.: Kriminogene Persönlichkeitsveränderung durch Stirnhirnschaden. *Arch. Psychiat. Nervenkr.* 105, 291 (1936).
44. Lemke, R.: Über doppelseitige Stirnhirntumoren. *Arch. Psychiat. Nervenkr.* 106, 54-70 (1937).
45. Lindenberg, W.: Hirnverletzung und Kriminalität. *Juristische Rdsch.* 13 (1950).
46. Lindenberg, W.: Hirnverletzung und Pubertät. *Ärztl. Wschr.* 11, 1013-1018 (1956).
47. Müller, E.: Über psychische Störungen bei Geschwülsten und Verletzungen des Stirnhirns. *Dtsch. Z. Nervenheilk.* 21, 178-208 (1902).
48. Pittrich, H.: Stirnhirngeschwülste. *Arch. f. Psychiatr. u. Nervenkrankh.*, Bd. 113, 1 (1941).
49. Quensel, F.: Stirnhirnverletzung mit Charakterveränderung. *Münch. med. Wschr.* 61, 1761 (1914).
50. Richter, H.: Eine besondere Art von Stirnhirnschwund mit Verblödung. *Z. ges. Neurol. Psychiat.* 38, 127-160 (1918).
51. Riechert, T. u. Hemmer, R.: Pseudoneurotische Zustandsbilder bei Gehirntumoren. *Münch. med. Wschr.* 98, 543-547 (1956).
52. Rosenfeld, M.: Über psychische Störungen bei Schussverletzungen beider Frontallappen. *Arch. Psychiat. Nervenkr.* 57, 84 (1917).
53. Rosenhagen, H.: Beitrag zur klinik der Meningeome der Olfactoriusrinne. *Nervenarzt* 7, 39 (1934).
54. Ruffin, H.: Stirnhirnsymptomatologie und Stirnhirnsyndrome. *Fortschr. Neurol. Psychiat.* 11, 34-81 (1939).
55. Rylander, G.: Personality changes after operations on the frontal lobes. Copenhagen: Munksgaard (1939).
56. Schader, H. E. u. Thiel, O.: Über cerebrale Spätschäden nach Verletzung des Auges und der Orbita. *Nervenarzt* 30, 120-124 (1959).
57. Schaltenbrand, G.: *Neurologie, Teil II, (Nervenkrankheiten)*, Bd. 81. Referat: Dietrichsche Verlagsbuchhandlg., Wiesbaden (1948).
58. Scheller, T.: Über Greifautomatismen im Bereich von Mund und Hand sowie über verwandte Phänomene. In: Wartenberg, Die Untersuchung der Reflexe. Stuttgart: Georg Thieme (1952).
59. Schuster, P.: Psychische Störungen bei Hirntumoren. Stuttgart: F. Enke (1902).
60. Spatz, H.: La Maladie de Pick, les Atrophies systématisées progressives et la Sènescence cerebrale prématurée localisée.
61. Spatz, H.: The Proceedings of the First. International Congr. of Neuropathology, Rome, 8. - 13. 9. 1952.
62. Spatz, H.: Über die Bedeutung der basalen Rinde. Auf Grund von Beobachtungen bei Pickscher Krankheit und bei gedeckten Hirnverletzungen. *Z. ges. Neurol. Psychiat.* 158, 208 (1937).
63. Stefan, H.; Kleinschmidt u. Biedermann: Psychische und Charakterveränderungen bei Stirnhirntumoren. Referat: *Z. f. d. ges. Neurol.*, Bd. 104 (1943).

64. *Stengel, E.*: Die Laesionen im Stirnhirn nach praefrontaler Leukotomie. Festschrift O. Pötzl, S. 445-452. Innsbruck: Wagner (1949).
65. *Stier, E.*: Geruchs- und Geschmacksstörungen nach Kopftrauma und ihre Bedeutung für die Unfallbegutachtung. Mschr. Unfallheilk. 50, 282 (1943).
66. *Stertz, G.*: Über den Anteil des Zwischenhirns an der Symptombildung organischer Erkrankungen des Zentralnervensystems: Ein diagnostisch brauchbares Zwischenhirnsyndrom. Dtsch. Z. Nervenheilk. 117-119, 630-665 (1931).
67. *Stockert, F. G. v.*: Hypochondrie und Anosognosie als Störungen der Bewusstheit der eigenen Körperlichkeit. Referat: Med. Mschr. 2, 281-286 (1948).
68. *Vogt, O.*: Zur anatomischen Gliederung des Cortex cerebri. J. Psychol. 2 (1903).
69. *Walch, R.*: Orbitalhirn und Charakter. Rekald, E., Das Hirntrauma. Stuttgart: Georg Thieme (1956).
70. *Welte, E.*: Über die Zusammenhänge zwischen anatomischem Befund und klinischem Bild bei Rindenprellungsherden nach stumpfem Schädeltrauma. Arch. Psychiat. Nervenkr. 179, 243-315 (1948).
71. *Welt, L.*: Über Charakterveränderungen des Menschen infolge Laesionen des Stirnhirns. Dtsch. Arch. klin. Med. 42, 339 (1888).
72. *Woerkom, W. v.*: Psychopathologische Beobachtungen bei Stirnhirngeschädigten und bei Patienten mit Aphasien. Mschr. Psychiat. Neurol. 80, 274 (1931).
73. *Ziehen, Th.*: Über das Bild der sogenannten Moral Insanity nach Hirnerschütterung bei Kindern. Jugendfürsorge 11 (1910).

Pre-Frontal Lobe Epilepsy*

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Although theoretically, seizures originating in the prefrontal cortex should have few initial manifestations, Walker and Jablon¹¹ found that patients with such attacks were aware of a whole gamut of aura — ranging from visual to focal motor. Foerster⁵ considered that adverse movements characterized convulsions due to frontal epileptogenic foci. This conclusion was based upon electrical stimulation of the frontal lobe at operation, a procedure which may induce different seizures than those resulting from lesions. Penfield and Kristiansen⁹ divided prefrontal attacks into conscious and unconscious adverse seizures, but Penfield⁸ stated that, in general, there is no warning or knowledge of an adverse attack unless it originates in the supplementary motor area. Cotte-Rittaud, and Courjon⁴ concluded that patients with conscious adverse attacks were much more likely to have frontal foci than patients who were not aware of the adversion.

In a series of 27 patients with known traumatic prefrontal lesions, the types of attacks are given in table 1.

In this series of 27 patients, 8 had no warning of the attacks and no overt focal manifestations, although the epileptogenic focus was electrographically and presumably anatomically localized to the frontal lobe. In addition 4 patients had no knowledge of the adversion or focal movements at the beginning of their attacks. Such sei-

zures were described as a sudden loss of consciousness; the patient knew he had had an attack only when he came to on the ground or floor with a headache, bitten tongue or wet pants.

Initial adverse movement. The patient may or may not be aware of the turning of the head and eyes. The typical conscious adverse attack is described as a turning or pulling of the eyes to one side which may be associated with other movements of the face, arm or leg, and is usually followed by loss of consciousness, and a generalized seizure which may or may not have lateralizing characteristics. The conscious adverse attack of one patient was described as turning of the head and eyes to the right, flexion of the right arm and leg, followed by loss of consciousness. Some patients claim to be conscious during both

T A B L E I

<i>Aura</i>	<i>Number</i>
None	8
<i>Adverse movement:</i>	
Unconscious	3
Conscious	5
<i>Focal movement:</i>	
Unconscious	1
Conscious	4
<i>Sensory</i>	3
<i>Miscellaneous</i>	3
(dreamy state, gastric, auditory)	
Total	27

* Aided by a grant from the National Institutes of Health, Bethesda, Md.

the adverse and clonic phases of the seizure.

Initial focal movements. These attacks, like the adverse ones, may or may not be consciously appreciated. One patient described his attack as a stiffening of his tongue which prevented him from speaking. He then became dizzy, his head and eyes turned to the right and he had a generalized seizure. The one patient whose attacks were classified as unconscious focal movements claimed he had no memory of his left limbs jerking before he developed a generalized seizure.

Sensory and other initial phenomena. These aura are no different from those associated with parietal and temporal lobe lesions, in fact, the epileptogenic zones may be located in these lobes, in spite of the primary damage being inflicted on the frontal lobe.

Although this series was composed of traumatic encephalopathy the same type of seizures are encountered with vascular, neoplastic and congenital lesions of the prefrontal part of the brain.

Petit mal with spike and wave patterns. Considerable has been written of bilateral spike and wave patterns with concomitant petit mal as manifestations of epileptogenic foci on the medial and inferior surfaces of the frontal lobe. Bancaud et al³ have discussed this problem, and on the basis of depth recording, conclude that the medial and orbital cortices of the frontal lobe play a primary role in the genesis of the bilateral synchronous discharge. They admit that brainstem centers may be secondarily involved. In the majority of cases of 3/sec spike and dome patterns which we have studied by depth electrodes, the electrographic pattern seemed to originate in deeper subcortical structures.

The mechanisms of prefrontal epilepsy

No attempt will be made to describe the maturation of a cortical epileptogenic focus, but some comments on the circuitry of adverse seizures may be in order. Marsan

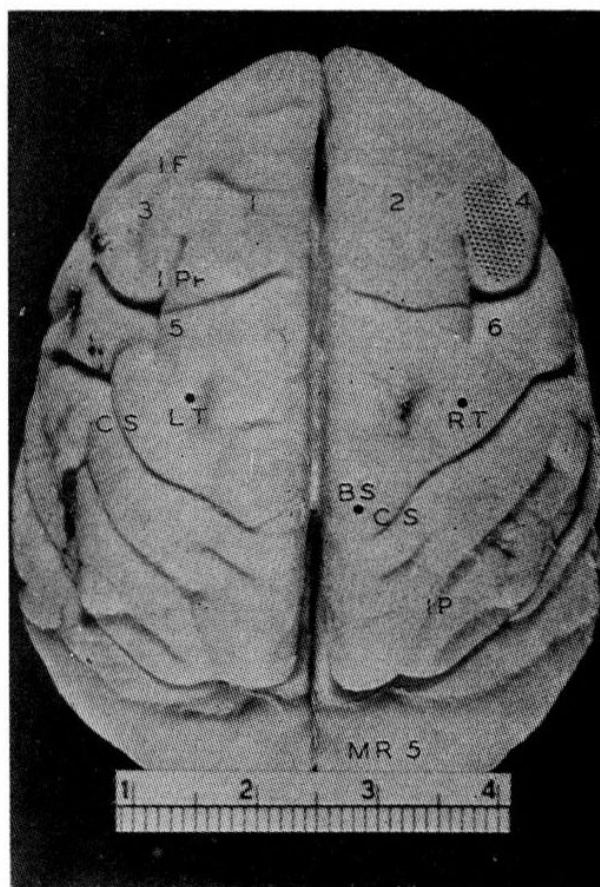


Fig. 1. — Photograph of the convexity of a macaque brain to indicate the site of alum injection (dotted), the location of cortical electrodes (numbers) and the site of stereotaxic insertion of the depth electrodes (R. T., L. T. and B. S.). The abbreviations used in the illustrations are as follows:

AM - amygdala	LI - left insula
BS - brainstem electrode	LT - left temporal electrode
CL - claustrum	MB - mammillary body
CP - cerebral peduncle	NR - nucleus ruber
CS - central sulcus	OC - optic chiasm
FF - Forel's field	Pul - pulvinar
GP - globus pallidus	Put - putamen
H - hippocampus	PRS - pontine reticular electrode
HG - hippocampus gyrus	RT - right temporal electrode
IC - internal capsule	SB - subthalamic body
IF - inferior frontal sulcus	TH - thalamic electrode
IP - intraparietal sulcus	VA - nucleus ventralis anterior
IPr - inferior precentral sulcus	VL - nucleus ventralis lateralis
LG - lateral geniculate body	

and Abraham¹ have found that adverse tonic turning of the head often was closely related to diffuse EEG changes over one hemisphere or more or less restricted areas with only a slight tendency for preferentially extratemporal activation. Because adverse seizures may originate from almost any part of the brain, especially the cerebral cortex, it has been suggested that the

adversion is a cortical phenomenon, and the generalized seizure which follows is of subcortical origin. With the use of chronically implanted electrodes in man and monkey, this hypothesis may be tested.

Although we have made chronic implantations of depth electrodes in more than 20 epileptic monkeys, only one will be discussed here. In this animal, on September

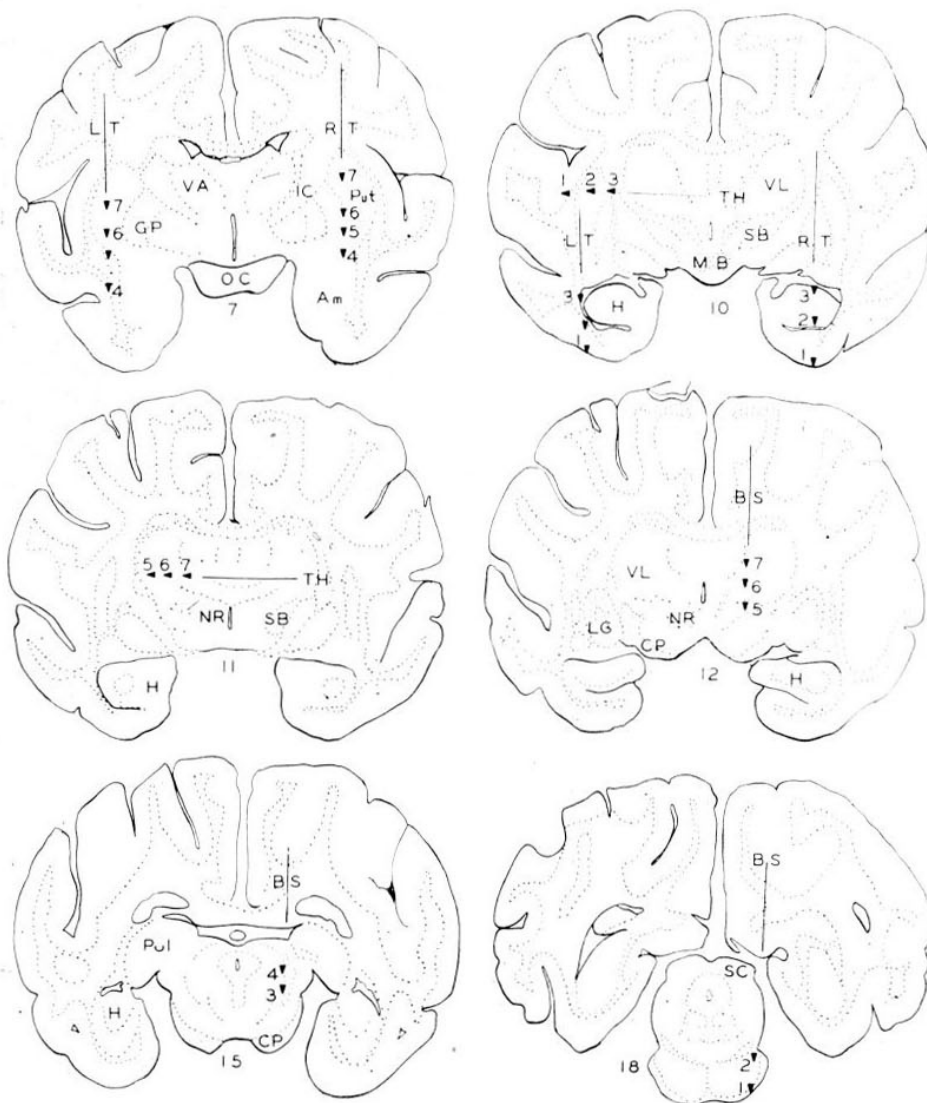


Fig. 2. - Representative serial sections of the brain to show the site of the individual depth electrodes.

27, 1963, an injection of 0.2 cc of alum cream was made into the right prefrontal cortex, and at the same time, 28 depth electrodes on three tresses were implanted as seen in figure 1. Over a period of 7 months, records were made as the animal developed seizures, and as the seizures regressed. The animal was sacrificed on March 28, 1964

and the positions of the cortical and depth electrodes were verified (fig. 2).

Five weeks after the alum injection, the animal was having repeated seizures every two or three minutes. The attacks began with the monkey staring for 12 to 15 seconds, followed by turning of the eyes and jerking of the head to the left. After 15 seconds the

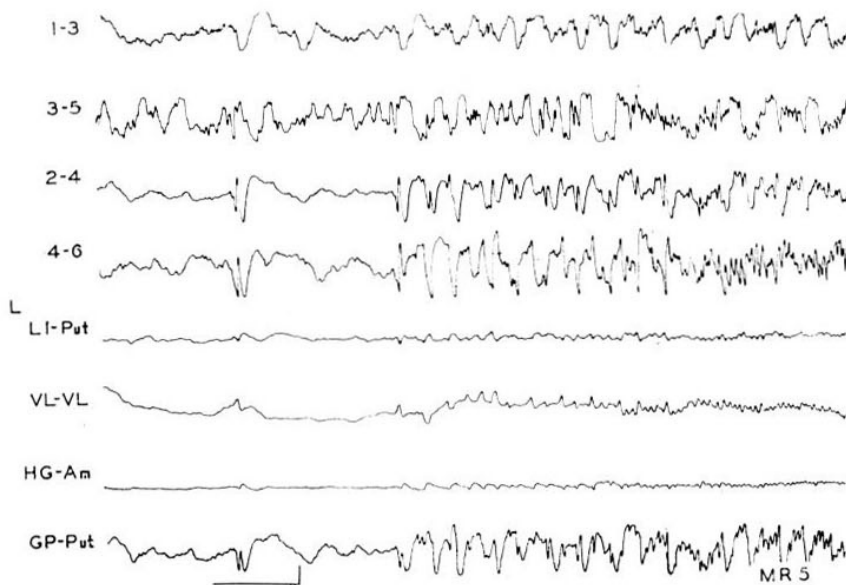


Fig. 3 — Spontaneous attack accompanied by turning of eyes and head to left.

shoulder and upper portion of the trunk began to jerk, followed by the left arm and leg. This progressed rapidly to a generalized attack. The seizure lasted from 1 to 4 minutes. After each attack there seemed to be a transitory weakness of the left arm, face and leg. Electrographically, the attacks were not so stereotyped for the initial attacks of a series began with focal cortical spiking whereas subsequent attacks frequently originated subcortically.

The electrographic progress of the attacks may be followed in the illustrations. Some attacks were initiated by spiky activity at

the site of the alum injection with secondary involvement of subcortical structures particularly the left globus pallidus and putamen. As the series of spikes gradually increased in frequency and somewhat in amplitude, spiky activity appeared in the contralateral cortical leads (fig. 3). Shortly after the onset of the spiking, the animal's head turned to the left. Thirty seconds later, when the head and eyes were jerking to the left, low voltage spikes developed in the nucleus ventralis lateralis of the right thalamus. As the attack progressed to involve the left arm and left

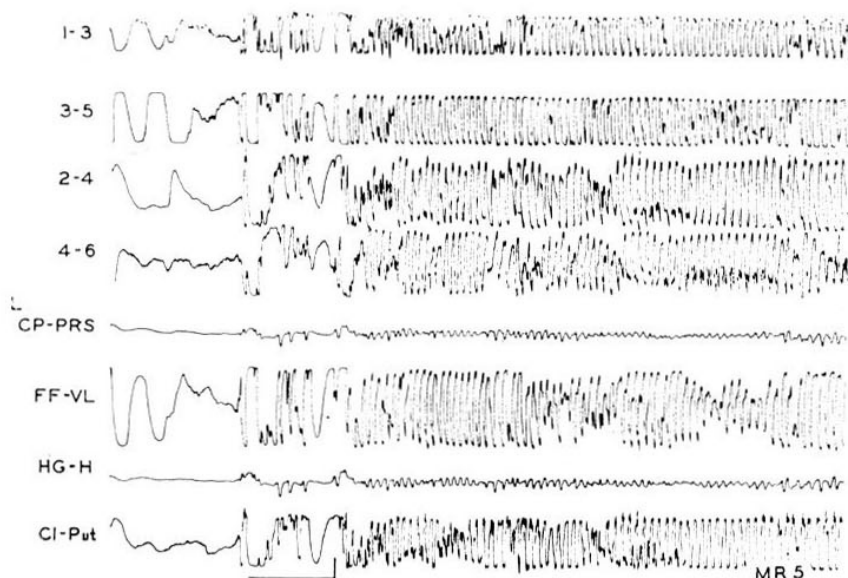


Fig. 4. — Spontaneous attack with turning of eyes and head to left.

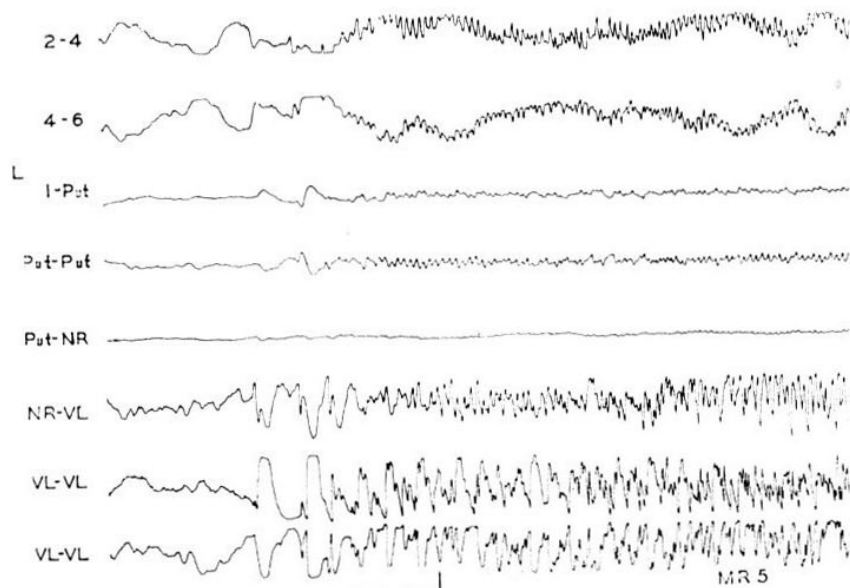


Fig. 5. — Spontaneous attack with turning of eyes and head to left.

face, the frequency of the spiking decreased in all leads. Shortly thereafter it ceased simultaneously.

At times the onset of the attack was more abrupt; as may be seen in fig. 4 rapid high voltage spiking appears almost simultaneously in the cortical leads and in the ipsilateral thalamus and putamen. But this abrupt electrographic onset of the seizure is accompanied by the same turning of the eyes and head to the left, followed by jerking of the head and eyes. The seizure may originate in the thalamus and, gradually, secondarily involve the cortex (fig. 5). However, not only thalamic activity initiated such a seizure but activity within the putamen may bring on a seizure which spreads to involve the cortex without implicating the medial temporal structures nor necessarily the thalamus.

It is thus apparent that the stereotyped clinical seizure may be the result of several different mechanisms, some primarily involving cortical and some subcortical structures. What determines the site of origin of the episode is not known. It should perhaps be noted that generalization of the

seizure seems to occur in this particular case neither through the pontine reticular substance nor through the medial temporal structures. The preferential circuitry of the epileptic discharge from the prefrontal cortex may be even more complicated for the caudate nucleus, the activity of which has not been sampled in this animal, is probably involved.

The natural cause of prefrontal epilepsy

Although the epilepsies originating in the frontal lobe are usually generalized, they are likely to have a benign course. In fact, in the series mentioned, 7 of the patients had had no attacks since the fifth year after injury, and only 6 were having seizures 10 years after the trauma. This remission rate of 77.7 % is considerably higher than the recession of all post-traumatic seizures. Moreover, if the course is not favorable and medication ineffective, the surgical resection of the epileptogenic focus offers about a 50 % chance of elimination of the seizures.

S U M M A R Y

Although on physiological and anatomical grounds, a number of types of epilep-

sy would be expected as the result of prefrontal epileptogenic lesions, in practice,

generalized seizures without a warning, with adersive movements of the head and eyes, and with movements of the contralateral side of the face, arm or leg are encountered.

The circuitry of the epileptic propagation, in spite of consistent clinical seizure pattern, varies from attack to attack. At times the attacks begin in the cortex, at

other times in a subcortical nucleus such as the putamen or thalamus. It may begin abruptly or gradually.

The surgery for prefrontal epilepsy is based upon the demonstration of a constant focus within the prefrontal area. Depth recording may be necessary. The results of both medical and surgical treatment are relatively good for relief of seizures.

RESUMEN

Si bien las bases anatómicas y fisiológicas llevarían a suponer la existencia de una serie de tipos de epilepsia resultantes de lesiones epileptógenas frontales, en la práctica se da la aparición de sacudidas generalizadas sin previa advertencia acompañadas de movimientos adversivos de la cabeza y ojos y movimientos de la mitad contralateral de la cara.

El circuito de propagación epiléptica, a pesar de tener un esquema clínico consistente, varía con cada ataque. A veces éstos

comienzan en la corteza, otras veces en un núcleo subcortical como el putamen o el tálamo. Puede comenzar abrupta o gradualmente.

La cirugía de la epilepsia prefrontal está basada en la demostración de un foco constante dentro del área prefrontal. Puede hacerse necesario un registro de profundidad. Los resultados de los tratamientos ya sean médicos o quirúrgicos son relativamente efectivos para el alivio de las sacudidas.

RÉSUMÉ

Bien que sur des bases physiologiques et anatomiques on s'attendrait à l'apparition de certains types d'épilepsie comme résultat de lésions préfrontales epileptogènes, dans la pratique on trouve des secousses généralisées sans avertissement, accompagnées de mouvements adversifs de la tête et des yeux et de mouvements du côté opposé de la figure, du bras et de la jambe.

Le circuit de propagation, bien qu'ayant un tracé clinique consistant, varie avec

chaque attaque. Parfois elles commencent à l'écorce, d'autres à un noyau souscortical comme le thalamus ou le putamen. Leur survenue peut être subite ou bien graduelle.

La chirurgie pour l'épilepsie frontale est basée sur la démonstration de l'existence d'un foyer constant dans l'aire préfrontale. Un enregistrement en profondeur peut se faire nécessaire. Les résultats des traitements médicaux et chirurgicaux sont relativement effectifs pour atténuer les attaques.

ZUSAMMENFASSUNG

Obwohl aus physiologischen und anatomischen Gründen eine Reihe von Epilepsietypen als das Resultat praefrontaler epileptogener Laesionen angesehen werden sollten, findet man in der Praxis verallgemeinerte Anfaelle ohne vorhergehende

Warnung mit gegenseitigen Bewegungen von Kopf und Augen und mit Bewegungen der entgegengesetzten Seite des Gesichts, des Armes oder des Beines.

Die Kreisfoermigkeit der epileptischen Propagierung, trotz einer bestimmten kli-

nischen Anfallsform, aenderte sich von einem Anfall zum anderen; zuweilen beginnen die Anfaelle im Cortex, dann wieder in subcorticalen Kernen, wie z.B. im Putamen oder Thalamus. Der Anfall kann ploetzlich oder allmaehlich beginnen.

Die Chirurgie der praefrontalen Epilep-

sie fusst auf der Demonstration eines bestehenden Herdes in der praefrontalen Zone. Tiefe Elektroenkephalogramme koennen notwendig sein. Die Ergebnisse sowohl der medizinischen als auch der chirurgischen Behandlung fuer die Erleichterung der Attacken sind verhaeltnismaessig gut.

DISCUSSION

C. Ajmone Marsan (Bethesda, Md., U.S.A.)

As it is customary, Dr. Walker's presentation has been concise, clear and interesting. My comments will bear only on a few specific points but I also wish to make it clear that my experience in this field is rather limited and, in any case, could hardly be compared with that of the speaker, both in the clinical and in the experimental approach to this general aspect of brain pathophysiology.

It is true that the anatomical and physiological differentiations of the frontal cortex are in general lost during epileptic activation of the same structure. Dr. Walker has suggested some of the reasons for this discrepancy. Somewhat akin to one of such reasons is the experimental finding that one can easily obtain in cat and monkey, when, by means of physiological techniques, one attempts to plot the cortico-subcortical connections or, to determine their functional hierarchy. Thus, repetitive electrical stimulation of most areas of the frontal lobe will induce an after-discharge with preferential projections to the non-specific portions of the brain-stem. This fact manifests itself with the appearance of self sustained, epileptiform activity within these diffuse subcortical structures as the most common and the most striking phenomenon, particularly if one compares the results obtained by applying a similar experimental approach to other cortical regions. Thus we have here, at least experimentally, the substrate for a very rapid generalization of a seizure which will then lose most, if not all its characteristically localizing features.

Dr. Walker has mentioned the occurrence (apparently not so exceptional) of a specific somatosensory or even visual aura in cases of traumatic lesions of the frontal lobe. In order not to complicate further an already difficult field, it would be probably worth clarifying this point. If, as Dr. Walker himself has pointed out, we may be dealing here with epileptogenic foci that are located outside the frontal lobe and are actually in these specific sensory (i.e. somatic or visual) regions of the cortex, in spite of the frontal location of the traumatic lesion, these unusual types of aura can be reasonably accounted for and, in any case, their occurrence should be considered as being purely coincidental with the existing (and more obvious) frontal lesion.

Another point which I hope Dr. Walker can clarify for me is that relating to the report of the rather common absence of "warning" in frontal seizures. It would be of interest to know in how many instances were seizures actually *observed*, in which the presence of some "warning" could be reliably ruled out. Since Dr. Walker has also told us that, for instance, a patient would often have no memory of the jerking of his limbs, is it possible that the absence of warning be actually a memory defect; that is, an incapacity on the part of the patient to remember he had some form of warning just before the attack?

The experimental part of Dr. Walker's report was certainly impressing. In this, the discrepancy has been emphasized between an apparently stereotyped clinical

pattern, and a quite variable electrographic pattern of the seizure. This discrepancy is a well known, negative—and discouraging—fact in the clinical field. In the latter, we can, up to a certain point, account for the discrepancy on the basis of the great limitations in our scalp recording technique, whereas, experimentally, such limitations become much less important. I wonder, however how is it possible to be certain of the "stereotypicity" of the clinical features since the description of

these depends, in general, on the simple visual observation whereas the electrical events can be objectively and precisely recorded. In view of the unquestionable importance of the implications of the reported findings I would thus appreciate it if Dr. Walker could elaborate on the method, and especially on the criteria with which the numerous clinical features were assessed in their temporal and motor patterns and in their relation to the electrographic changes.

REFERENCES

1. Ajmone-Marsan, C. and Abraham, K.: A seizure atlas. Suppl N° 15, EEG and Clin. Neurophysiol., 215, pp., 1960.
2. Ajmone-Marsan, C. and Ralston, B. L.: The Epileptic Seizure. Springfield, Ill., Charles C. Thomas, xii + 251 pp., 1957.
3. Bancaud, J.; Talairach, J. and Bonis, A.; Schaub, C.; Szikla, G.; Morel, M.; Bordas-Feren, M.: La Stereo- electroencephalographie dans l'épilepsie. Masson & Cie, Paris, vii + 321 pp., 1965.
4. Cotte-Rittaud, M. R. and Courjon, J.: Semiological value of adverse epilepsy. *Epilepsia*, 3° 151-166, 1962.
5. Foerster, O.: The cerebral cortex in man. *Lancet*, 2: 309-312, 1962.
6. Gastaut, H.: The Epilepsies. Charles C. Thomas, Springfield, Ill., 1954.
7. Gastaut, H.; Roger, J.; Ouahchi, S.; Timsit, M. and Broughton, R.: An electro-clinical study of generalized epileptic seizures of tonic expression, *Epilepsia*, 4: 15-44, 1963.
8. Penfield, W. and Jasper, H.: Epilepsy and the Functional Anatomy of the Human Brain, Boston, Little, Brown and Co., xv + 896 pp., 1954.
9. Penfield, W. and Kristiansen, K.: Epileptic Seizure Patterns, Charles C. Thomas, Springfield, Ill., viii + 104 pp., 1951.
10. Walker, A. E.: Post-Traumatic Epilepsy, in Rowbotham, C. F. "Acute Injuries of the Head. Their Diagnosis, Treatment, Complications and Sequela". Edinburgh and London, E. & S. Livingston Ltd., 4th Ed. 15: 486-509, 1964.
11. Walker, A. E. and Jablon, S.: A Follow-up Study of Head Wounds in World War II. VA Medical Monograph, Washington, D. C. U.S. Gov't. Printing Office, x + 179 pp., 1961.

Bilateral Defect of Frontal and Orbital Lobes

A clinical and psychological study

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Broad bilateral resections of the frontal lobes following cranio-cerebral trauma are generally rare. The clinical observation and psychological findings reported in the present study are also of interest because of the patient's bilateral defect of the orbital lobes.

Clinical case report

The patient, aged 54 (case card N^o 73826) was admitted on April 1, 1965 for fits of loss of consciousness following cranio-cerebral trauma.

On October 6, 1944, he was wounded on the front by a shell splinter which entered the right frontal region and came out through the left frontal region. The patient was unconscious for 6 days; esquilectomy was performed and there remained a certain loss of bone substance.

It should be mentioned that before the accident the patient was a capable and energetic man; both as a lawyer and as an officer he was professionally among the foremost. After the accident, he suffered from memory disturbances, and became irritable and anxious; owing to the behaviour disturbances he was pensioned off in 1949.

In June 1964, the patient had a first generalized convulsive seizure; a second seizure occurred two months later, and since

November 1964 the seizures became more frequent, occurring every night and lasting 2-5 minutes. Most of the seizures took place in the night time.

General examination. Lack of the bone substance in the frontal regions, measuring 10/8 cm. (Fig. 1). Blood pressure 110/60 mm. Hg., pulse rate 78/minute.

Neurological examination. Tendinous reflexes were brisk on both sides, somewhat brisker on the right. Cutaneous abdominal reflexes were comparatively lower on the right; the cutaneous plantar reflex was normal. There were no coordination or sensory disturbances. Bilateral diminution of the smell perception.

The patient had 1-2 psychomotor seizures daily: the onset was sudden, accompanied by obnubilation, carphologic movements, mastication, verbal repetition or other types of movement with an automatic character. The seizures lasted about 3-5 minutes, and the patient could not remember anything that had happened during the seizure.

The electroencephalographic examination disclosed a high voltage background tracing with a rapid irregular alpha rhythm of 11-12 cycles/second; the rhythm was intermingled with frequent theta waves of 5-6 cycles/second and frequent beta waves of 18-22 cycles/second, and some low voltage spikes. In hyperpnea, rare low voltage

spikes appeared without any definite location. Low voltage spikes sometimes appeared on the frontal leads on both sides (Fig. 2).

On April 14, 1965, he was operated on under general anaesthesia. The skin was incised along the former frontal cicatrix and the scalp was turned back. Bilateral semicircular incision of the dura including the paramedial pedicles; the falx was incised after ligating the sagittal sinus. After turning back the dura, the lack of both frontal poles up to the precentral area, and of both orbital lobes up to the chiasma was found; porencephaly was noted and the frontal horns of the lateral ventricles could be seen. There was a marked gliosis of the temporal poles and in the precentral area on both sides. The meningo-cortical adhesions were detached and an electrocorticographic control examination was performed. In the upper third of the middle frontal gyrus, on the right side, an epileptogenic zone was found, and coagulated. The electrocorticographic control examination did not detect other epileptogenic zones. The dura was sutured and an acrylic plaque was applied over the site of the missing frontal bone substance. The post-operative course was normal apart from the fact that during 7 days the patient displayed states of drowsiness alternating with

states of accentuated psychomotor agitation, high blood pressure variations (arterial blood pressure ranged between 190/100 and 80/60 mm. Hg), and temperature variations within the same day (between 40°5 and 36°2 C). No change was noted at the general neurological examination and the EEG control examination.

The general mental examination did not reveal any manifest psychical disturbances except for a hypomaniac behaviour. Orientation in time and space was correct. In general, the patient remembered older events better than more recent ones. For instance, he related, correctly different periods of his life; he knew where he had fought in the wartime and remembered the different places he has passed through, giving precise details. Discalculia was not observed. The reasoning and differentiation between various objects and persons were correct, but rendered more difficult by his hypomaniac behaviour.

Psychological findings

The psychological examination was performed at the end of May 1965 when the general state of the patient was very good; there were no clinical signs of cerebral oedema and the aspect of the EEG tracing was stationary.

General behaviour. The entire behaviour of the patient showed a marked moriatic colouring and a hypomaniac attitude. It is of interest that at first sight, after a brief examination, two of our psychiatrists said: "If we hadn't seen the post-operative cicatrix we would have made a diagnosis of hypomania".

The patient was logorrheic, "wittily" optimistic: according to his own words he "took everything lightly". Thus, he called a cigarette "a coffin nail", explaining that tobacco was a poison which had made him call it so. He was touchy at the slightest allusion and sometimes reacted violently, inadequately to the slightest irony. Each test carried out was freely commented upon, but the comments were frequently

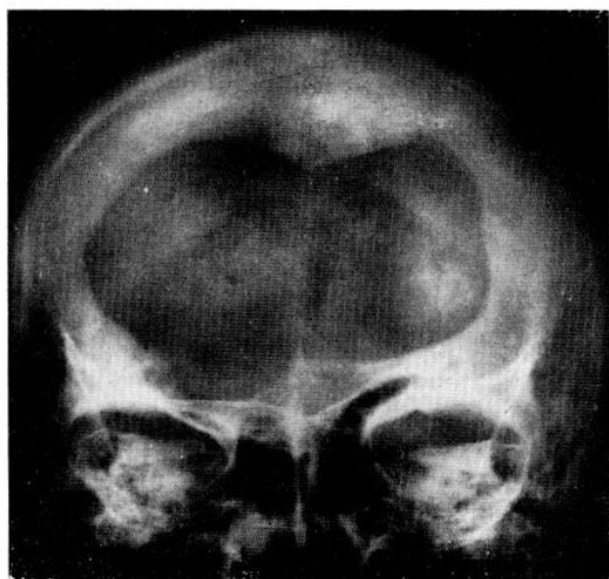


Fig. 1. — Front cranial radiography.

stereotypical. He was very sure of himself and he considered himself "honour bound" to perform every test. There was a flight of ideas and during the examination the

patient frequently alluded to his "conquests" and frequent adulteries.

The *reaction time* was determined with the help of visual and auditory stimuli with

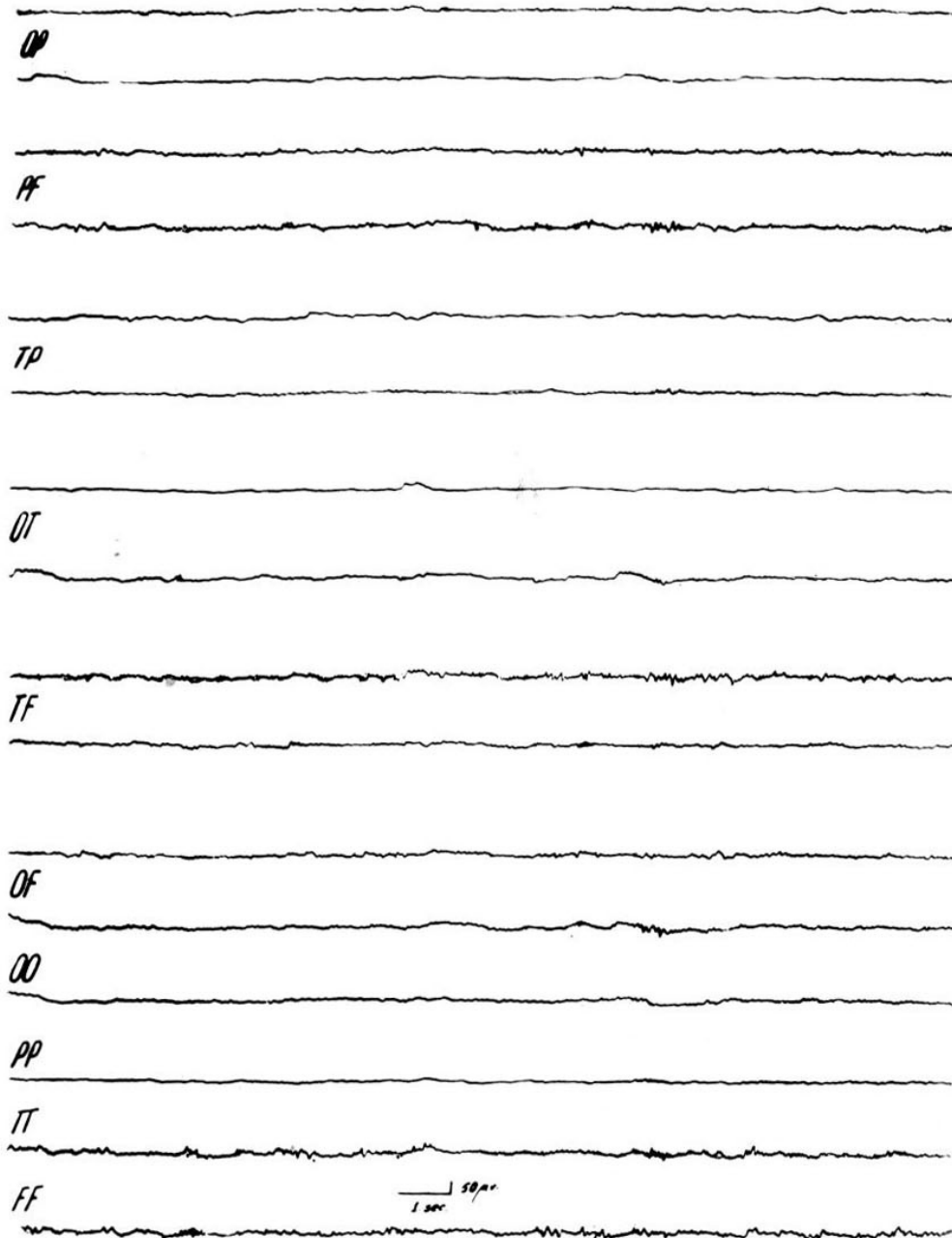


Fig. 2. — The electroencephalographic record (see text).

the reaction time apparatus. The visual reaction time was at the upper normal limit (201 milliseconds) and the auditory reaction time was slightly increased (185 milliseconds as compared to 140-150 milliseconds in the controls).

The *curves plotted* following photic and auditory stimulations (in the course of 20 stimulations with 5 prior exercises at the beginning of each test, for training the patient) showed no significant discontinuity with a plateau aspect (decreased reac-

tivity) of the auditory reaction time, the patient presenting a certain degree of latency (Fig. 3).

Perception. The rapidity, accuracy and plenitude of perception was determined by means of a Diehl mechanical tachistoscope; several perceptive structures composed of coloured geometrical figures of different shape, colour, number and spatial position were presented at an exposure time of 110 milliseconds. The patient was asked

to draw what he had seen; his drawings were correct in a proportion of 35 % as compared to 100 % in the controls therefore, a high deficiency. Errors were found with all the parameters, most of them pointing to incomplete perception (Fig. 4 A and 4 B), particularly of the spatial stimuli.

The perception of sizes was examined by testing the possibility of building up again the sequence of sizes. The patient was

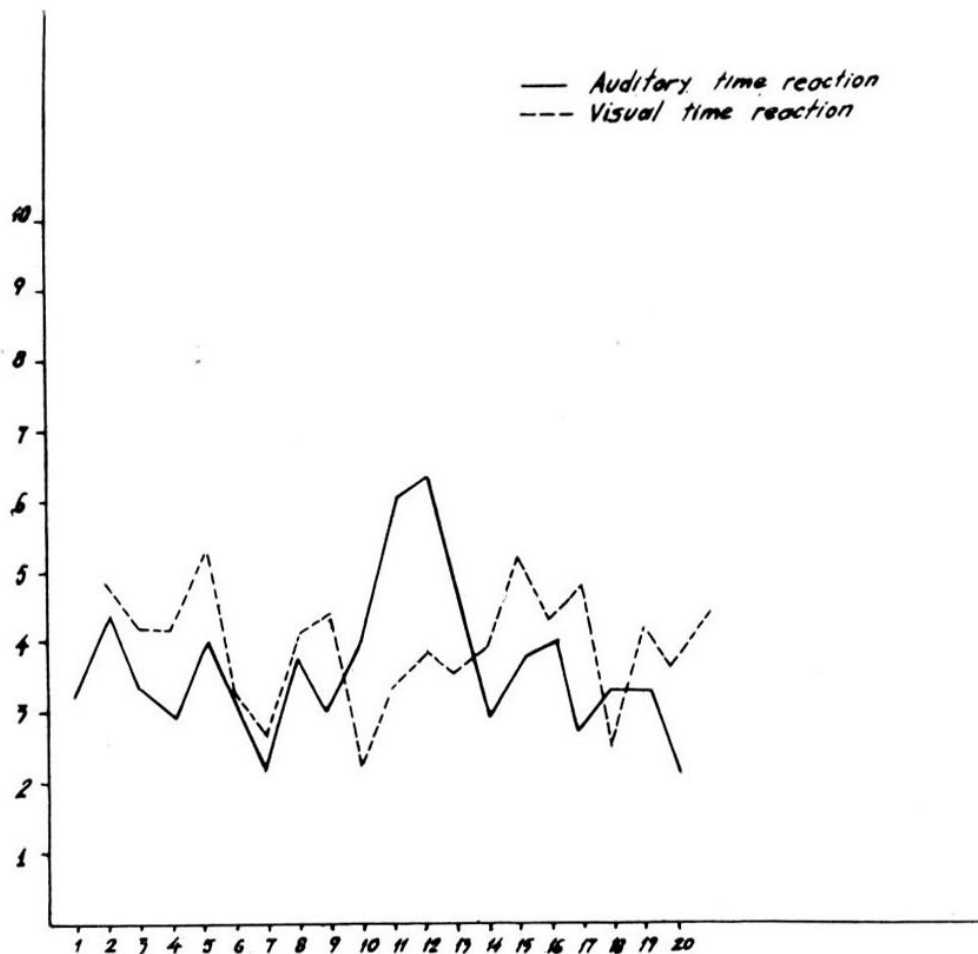


Fig. 3. — The auditory reaction time and the visual reaction time (see text).

given a group of 10 geometrical figures of different sizes and was requested to arrange them according to size, from the smallest to the largest and conversely, from left to right and right to left, from bottom to top and top to bottom. The patient performed the test in 3 seconds, the same as the controls.

A normal performance was likewise obtained on testing the *colour perception*, when the patient had to sort out colours of different shades.

The *kinaesthetic perception* was determined with Michotte's kinaesimeter. The patient reproduced, with elimination of the visual analyzer, the standard distances with

differences of $+5 + 10 + 5$, pointing to an efficiency at the lower limit of the reproduction of movement.

The perception of tactile stimulations was determined by the Galifret-Granjon test. The patient's performances were normal.

The perception of thickness was determined by the Decroly test with wooden objects; performances were normal.

The perception of complex visual structures, implying the perception of spatial relationships between different objects was done by the complex visual structure test, developed and applied in our laboratory by Sen Alexandru and I. Vernea. The patient was shown 20 photographs with 2-3-4-5 objects built one on top of the other in a restricted space: on each photo, every object could be considered both as the background and as the object of perception. The patient was requested to look at and name the objects: The patient performed the test as well as the control subjects.

Simple auditory perception was examined by the location of auditory stimuli. The patient was asked to locate the position of an auditory stimulus source in 10 different places, starting from the vertex, at variable distances. His performance was normal.

The perception of rhythm, implying the perception and reproduction of certain complex auditory structures, was determined by the Mira Stambak rhythm test. The patient obtained 17 points as compared to 21 in the controls. He was not able to perceive the last four rhythms.

Memory. The capacity to memorize and reproduce was examined by the "fifteen word" test (Claparède-Rey). The patient was asked to choose 15 words out of the basic word stock (every-day vocabulary), to memorize them and reproduce them in 5 successive stages on the basis of auditory perceptions; at the 5th stage he was able to memorize 8 words as compared to the 14 words of the control subjects, a fairly poor performance.

The memorization curve presented a characteristic disharmonic aspect, made evident

by the initial leap (I-II) and by the subsequent stationary aspect (III-IV-V) of the performance.

Order of tests	I	II	III	IV	V
Patient	4	7	7	8	8
Controls	8.6	11.8	13.4	13.8	14.0

The ability to recognize was determined by the "20 plus 20 portraits" test. The patient was given 20 photographs representing men and women (each photo was shown for 2 seconds); the photos were then mixed up with 20 more photos of persons not shown before, and the patient was asked to identify the former.

The patient gave 16 correct answers as against 20 (100 per cent) of the controls, and pointed to 19 of the photos not shown at first; therefore in this test, too, he showed a certain degree of visual memory disturbances. During the test he discussed each photo (for instance "I don't know her, but her hair is peroxided" or "here's an athlete", etc.); during one of the tests he recited Eminescu's poem "Luceafarul" (The Evening Star).

The control test. An auditory reproduction test was applied, i.e. the "reconstruction test". The patient was shown 10 simple geometrical figures (outlined in India ink) arranged in a given order; after 2 minutes study, he was requested to arrange them in the same order.

Although the test was repeated twice (Fig. 4), the patient was not able to arrange the geometrical figures in the same order, even when only 7,5 or 4 figures (per cent performance) were used. This was the most severe defect recorded up till then and must be corroborated with defective perception of the position in space of the stimulus at the tachistoscope test, i.e. marked failure in the field of the spatial perception pattern (memorization and reproduction of the perceived spatial structures).

Attention. The capacity of concentrating one's attention was determined by the Bourdion test and showed a marked defect. In

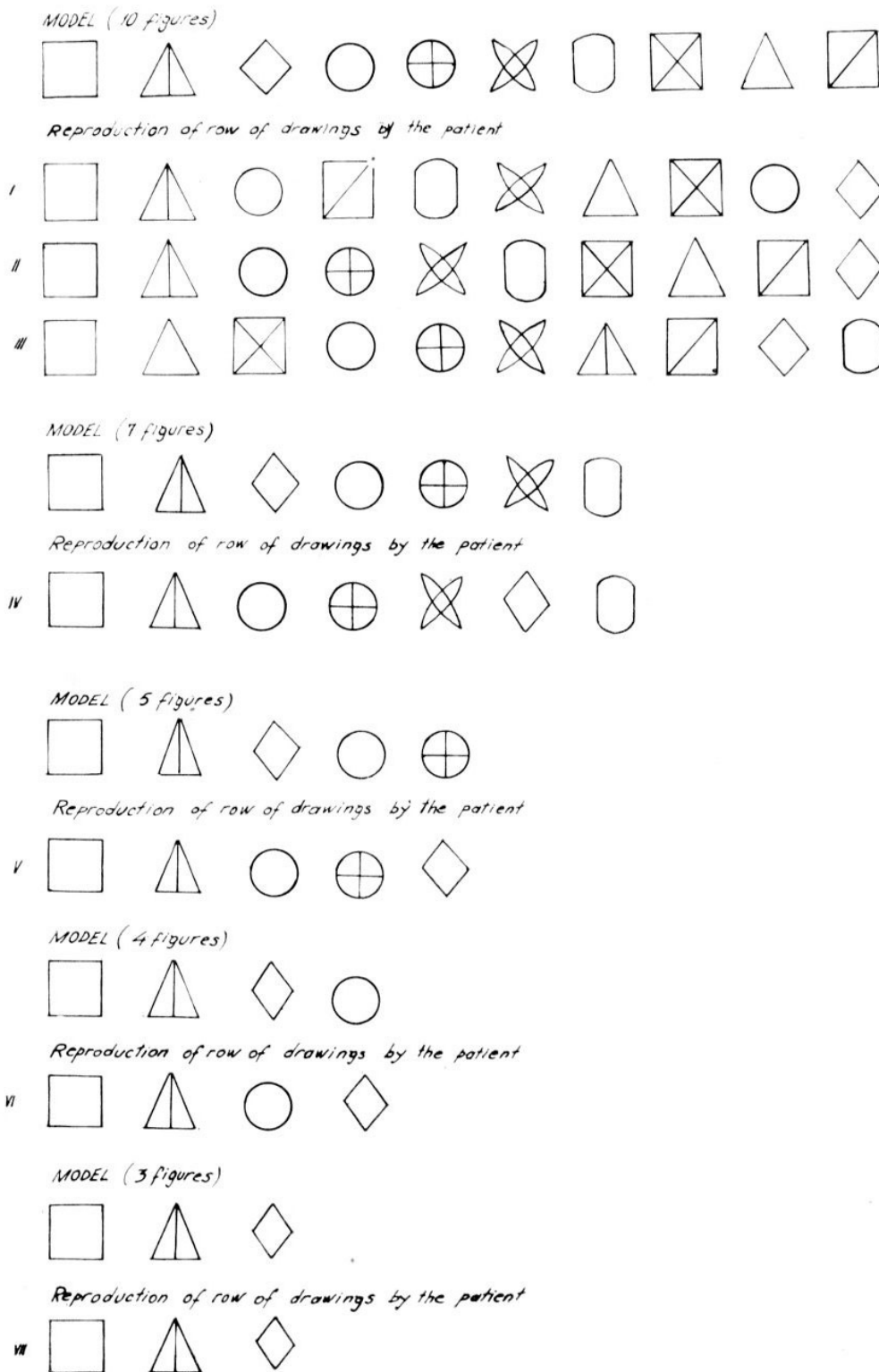


Fig. 4. — The visual memory test with reference to spatial orientation (recognition of a sequence of objects) (Vermeulen's figures were used). In I, II and III the three repetitions that were permitted (see text).

10 minutes (duration of the test) the patient was able to go over 1840 signs as against 2474 of the controls and omitted 23

signs as against 11, with an omission index of 1.25 per cent as compared to 0.46 per cent of the controls (7 in the 5th minute,

11 in the 9th minute, 2 in the 10th minute and 1 in the first three minutes), pointing to a defect following rapid fatigability.

The mobility of attention, determined by the test of looking for numbers, pointed to a severe defect (Fig. 5). The patient had the greatest difficulty in locating the num-

bers on a plane perception space, although the area was small (a 36/36 cm. square). Neither did he identify methodically or analyze the space, making several attempts and many errors, with frequent and increased latencies up to 33.5 seconds. He was able to perform the test in 9 minutes as compared to 3 min. 57 sec. of the controls

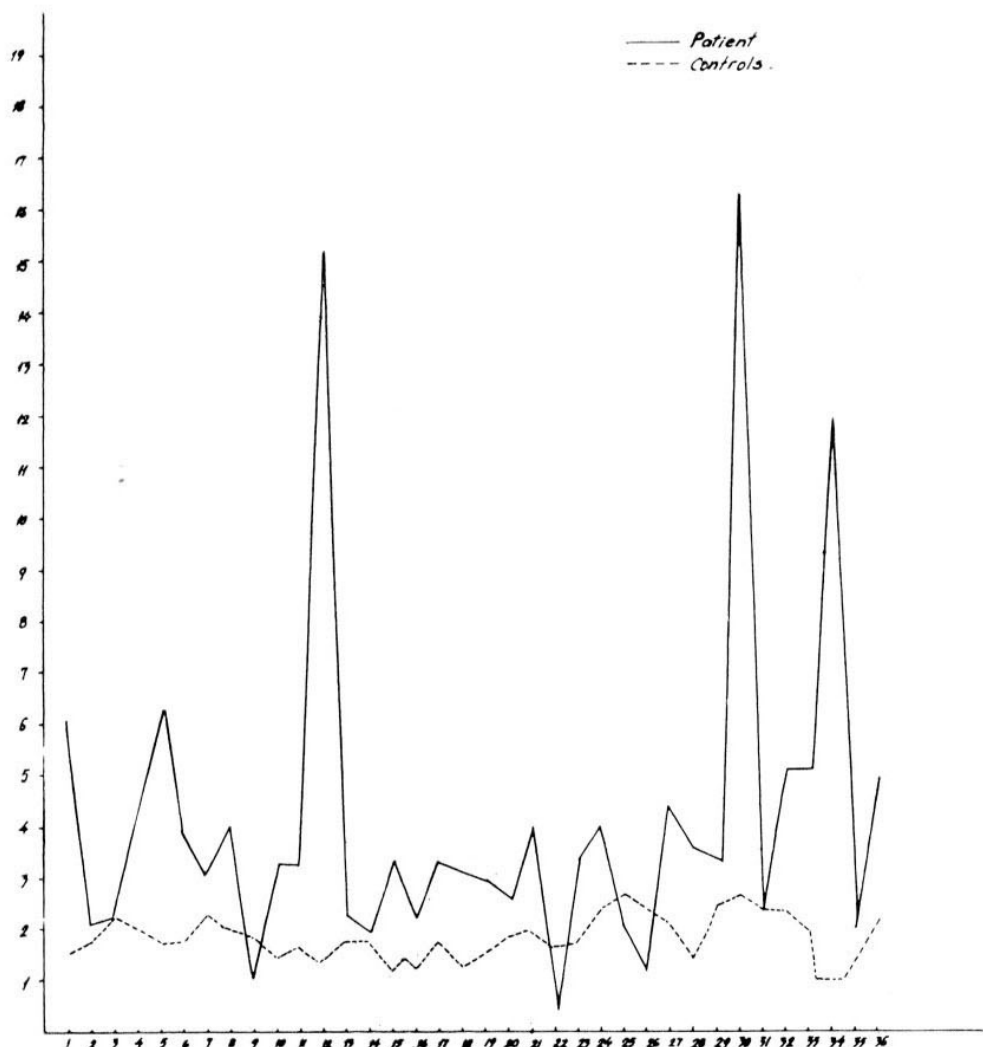


Fig. 5. — Graphical representation of the test in which numbers were looked for. Latency of the time necessary for finding each number was written down. Note the presence of certain moments that appear fairly rhythmically and in which the latencies show a significant increase, whereas the rest of the tracing is in general close to that of the controls.

(in the individual variant, when the patient carried out the test by himself), obtaining an average of the latency periods (36 numbers looked for) of 9 sec. as compared to 3.46 seconds of the controls in the surveyed variant (when each searching for

a number is made under the supervision of the examiner and marked down separately from the viewpoint of latency.)

At the *control identification test* when a geometrical drawing was shown for 2 seconds and then again shown together with

4 bits of paper with similar drawings (Benton type), the patient was able to perform the test in a proportion of 80 per cent as against 100 per cent of the controls.

Thinking. The patient was subjected to different tests, and the following aspects were noted:

The *classification and systematization capacity* was examined by the sorting of pictures and the Weigl test (geometrical figures), the answers were normal. The patient grouped correctly into 5 categories a number of 15 pictures. However, the reasoning was linked to the category of the objects in only two groups (cutlery, clothing), for the other groups the criterion was one of *utility*, a criterion of inferior type from the logical point of view to that of the *category* criterion ("something to eat", "a travelling item", "a toilet object").

The patient performed the Weigl test correctly both as regards shape and colour.

The *coding test* was carried out in a proportion of 100 per cent, using the code correctly and promptly translating the message from the cipher into the letter system showing a satisfactory mobility of thought.

The Koohs cube test was likewise performed 100 per cent (in the 4 cube variant).

The patient performed in 12 minutes, as against the controls' 5 minutes, the *Sequin test*, but qualitatively the execution was correct without repeated trials and errors. The patient worked according to a previously established plan, the resulting performance being in keeping with this plan.

The *exclusion test* was likewise performed in a proportion of 85 per cent. The patient eliminated correctly the notions that did not correspond to the sequence of ideas presented; the reason given was in agreement with the criterion of exclusion ("the apprentice is not qualified", "spectacles cannot be weighed", "the walking stick doesn't cover anything").

The *similitude test* was performed 75 per cent the patient determining correctly the similarity relations. His critical spirit was normally efficient. When the absurd story test was proposed (Weisenburg-Mc

Bride modified by us) the patient carried out a 100 per cent performance, formulating the absurd aspects of the story perfectly, with short latencies.

The *associative capacity* (in the verbal plane) was examined by the associative-verbal experiment and was normal.

The *verbal construction capacity* was tested by means of the T.A.T. plates; characteristic aspects were found. The patient understood the subject, but the story he concocted took on a dramatic aspect, with dialogues, exclamations and interjections, with and adequate mimicry and intonation. The patient gave moralizing advice to the characters on the plates, telling them not to behave wrongly again. In general, the theme used by the patient was that of an innocent girl abused by a man without scruples, and themes linked to family to family morals. Preoccupations of a sexual character were visibly exacerbated. For instance, plate III represented a young girl, sadly leaning her head on her right hand. The patient immediately said: "Ah poor me! I believed him to be an honest man" and "he has found another girlfriend, I shall never talk to him again".

The picture of a little girl with a doll in her arms, talking to her mother, suggested the following: "what's the matter with the child? I don't suppose she's thinking of marrying, is she? Take care, child, you've done wrong, don't do such a thing again!". And the patient had been asked to construe a story about the past, present and future of the two characters in the picture.

Emotional sphere. The affectivity of the patient had a maniacal colouring; he was permanently euphoric, optimistic, logorrheic with a lively mimicry, rapid gestures alternating with inhibitory latencies. He laughed often, was amiable, argumentative, polite, ready to cooperate.

The patient was examined again two months later, the same tests being used. The performances were compared:

The *capacity to memorize and reproduce* (examined in the course of 5 successive examinations) yielded definitely better results:

1st examination

4-7-7-8-8 words remembered.

2nd examination

5-9-11-12-13 words remembered

Better results were also obtained at the *recognition memory test*. The patient recognized 18 of the 20 photographs shown him as compared to 16 at the former test, and there was no mistaken recognition: he also recognized the geometrical figures in a proportion of 100 per cent as against 80 per cent at the first test.

Visual memory with reference to spatial orientation was just as poor as at the previous examination.

Attention. The capacity of concentrating was improved as compared to the first examination. The number of signs he identified increased (from 1840 to 1960), the number of omissions was lower (from 23 to 10).

It should be mentioned that the patient talked incessantly while performing the tests. He uttered aloud every letter that had to be checked. He would say: "Before an hour passes, I'll be ready. Not a letter will remain unchecked. I do know something about sports. They're awfully complicated but I know everything about them, though people say I'm mad".

Thinking. At the Koohs test the same performances were maintained. The *exclusion test* was performed 100 per cent as compared to 85 per cent at the previous examination.

DISCUSSION

Many studies have been published on the effects of lobectomy in animals (Fulton⁵, Messini⁹, German⁶ and in man Bianchi², Schuster¹³, Brickner³, Ackerley and Benton¹, Freeman and Watts⁴, Prick¹¹).

The *psychological findings* after the second intervention can be divided into three groups:

— prevailing symptoms evident at the first contact with the patient;

— visible disturbances on careful examination;

— normal findings.

A. The most important disturbances which dominated the clinical picture were in the emotional sphere, the patient behaving in a hypomaniac manner. Of interest regarding his behaviour are the flight of ideas which took on the following aspects:

a) a tendency to megalomania, originality, the desire to show his superiority in all spheres. Euphoria and a tendency to joking, mostly inadequate, appeared to the foreground of the clinical picture;

b) the patient commented upon each test, was combative and considered every test as a "debt of honour". Of interest was his tendency to concrete thinking, to a childish manner of living in the concrete; this as noted in the way in which he interpreted the T.A.T. plates, the patient talking to the characters on the plates;

c) he was preoccupied by the sexual aspects and often made jokes and gave his opinion in this connection, his sexual potency being considerably diminished after the first operation.

This case agrees with the findings of Brickner³ who observed in his patient ideas of grandeur and a childish arrogance with a strong belief in his own powers. In his case the disturbances were made evident after a careful examination, since at first sight he appeared to be normal. At any rate, it appears that disturbances in the mental sphere which develop after bilateral frontal lobectomy may be divided, according to Brickner³ into symptoms with an emotional colouring and symptoms without an emotional colouring. This was also confirmed by our patient.

The increased reactivity to emotions and distractiveness have been attributed to the lack of control over the subcortical vegetative structures (Messimy⁸).

In our case the disturbances in the emotional sphere were probably more accentuated because of bilateral involvement of the orbital lobes, whose role in emotional mechanisms is well known (Livingstone, Fulton et al.,⁷).

B. Other evident psychological alterations were:

a) Evident disturbances in the field of visual perception of movement and visuo-spatial perception. The position of the stimuli in space was extremely defectively perceived by the patient under rapid tachistoscopic presentation conditions. This observation, which we consider of particular importance, may be correlated to the findings of H. L. Teuber¹⁴ who mentions that in patients with frontal lesions strange disturbances develop in connection with the location of certain visual reference points, when appraising unusual positions. It is worthy of note that the visuo-spatial memory disturbances were still present at the second psychological examination.

b) Evident alteration of the mnemonic function occurs both in the auditory and the visual sphere; in the course of the subsequent evolution the tests showed a slight tendency to improvement. At the reconstruction test, in contrast to certain data in the literature cited, visible difficulty was shown to exist in the ability to learn by visual memory, a defect which may be correlated with the defect in perception of the position of the stimulus in space observed at the tachistoscopic examination.

c) Disturbances in the concentration and fixing of attention, especially severe in our patient, and which are likewise reported in literature, showed a slight tendency to improvement.

d) As regards the process of thought as such, there is a fact of particular importance, i.e. at all the tests at which it was possible to use the patient's former experience (as for instance in the test using concepts of size or concepts of left-right, the

Weigl test, the exclusion test, the similitude test, etc.) his performance was comparatively good. These negative findings are in keeping with those of Nauta and Teuber¹⁰. On the contrary, when the patient was tested in a way that did not permit the use of reference points from his past experience (as for instance to reproduce a sequence of geometrical figures in an order arbitrarily established by the examiner), his performance was very poor and became, with time, still worse.

e) His critical spirit, as concerns the solving of intellectual problems was efficient, whereas as regards social behaviour, it showed a constant tendency to decrease. In this latter connection there was also an evident diminution of self-control.

The defect in planning one's activity, or the defect in the possibility of organizing one's behaviour according to past experience has been reported by Ackerley and Benton¹. The impossibility of learning anything new and the diminution of control are particularly severe defects acquired in bilateral frontal lesions.

C. The performance of the patient was *normal* in all the tests involving the perception of sizes, outlines, thickness and complex auditory and visual structures. A good performance was likewise obtained in one of the thinking tests.

In conclusion, it may be stated therefore that the psycho-pathological findings demonstrates an unequal performance within the framework of various psychic processes. The more accentuated disturbances appeared in the affective and emotional sphere of life, in fixing the attention, and in the field of both visual and auditory reproduction. Of particular interest are the memory and visuo-spatial recognition disturbances.

S U M M A R Y

The clinical history of a patient with bilateral post-traumatic defect of the frontal and orbital lobes is presented.

The general behaviour and the mental functions are studied. Patient's maniacal behaviour, childish baldness, visual percep-

tion of movement as well as visual-spatial perceptions are particularly considered.

The findings obtained by serial psycho-

logical examinations are discussed as compared with the data of the literature.

RESUMEN

Los autores publican la observación clínica de un enfermo que presenta una lesión bilateral de origen traumático de los lóbulos frontales y orbitales. Se analizan tanto el comportamiento general como las diversas funciones intelectuales del enfermo.

Los autores insisten en el comportamien-

to maniaco y en la arrogancia infantil del enfermo así como en los disturbios que el mismo presenta en el campo de la percepción visual del movimiento y del espacio.

Los datos que los autores obtuvieron mediante exámenes psicológicos repetidos se discuten en relación con los datos de la literatura.

RÉSUMÉ

Les auteurs présentent un cas clinique de lésion bilatérale du lobe frontal et orbitaire secondaire à un traumatisme crânien. L'on a étudié le comportement général ainsi que les différentes fonctions intellectuelles.

On insiste sur le comportement maniacal sur l'arrogance puérile sur les troubles de

la perception visuelle du mouvement ainsi que sur la perception visuo-spatiale du malade.

Les données ainsi obtenues par les examens psychologiques successifs effectués sont comparées à celles de la littérature.

ZUSAMMENFASSUNG

Es wird über den klinischen Zustand eines Patienten mit bilateraler traumatischer Verletzung der frontalen und orbitalen Hirnlappen berichtet. Sowohl das allgemeine Verhalten des Patienten als auch die verschiedenen Funktionen des Intellekts werden analysiert.

Auf das maniakalische Verhalten des Pa-

tienten, auf seine kindische Arroganz, auf die Störungen im Bereich der optischen Wahrnehmung der Bewegung und des Raumes wird näher eingegangen. Die an diesen Patienten durch wiederholte psychologische Untersuchungen erfassten Befunde werden den Angaben der Literatur gegenübergestellt.

REFERENCES

1. Ackerley, S. Sp. and Benton, L. A.: Report of a case of bilateral frontal lobe defect. In "The frontal lobes", A.R.N.M.D. Baltimore, The Williams & Wilkins Company, pp. 479-504, 1948.
2. Bianchi, L.: The function of the frontal lobes. *Brain*, 18, 497-522, 1895.
3. Brickner, R. M.: An interpretation of frontal lobe function based upon the study on a case of partial bilateral frontal lobectomy. In "Localization of Function in the cerebral cortex A.R.N.M.D. Baltimore, The Williams and Wilkins Company, pp. 259-351, 1934.

4. *Freeman, W. and Watts, J. W.*: Psychosurgery. Springfield, Ill, Ch. C. Thomas, 1942.
5. *Fulton, J. F.*: Physiology of the nervous system. 2-nd ed. New York, Oxford University Press, 1943.
6. *German, W. C.*: An experimental study of the function of the frontal lobes in dogs. Arch. Neurol. Psychiat., 27, 961-982, 1932.
7. *Livingston, R. B.; Fulton, J. F.; Delgado, J. M. R.; Sachs, E. R.; Brendler, S. J. and Davis, G. D.*: Stimulation and regional ablation of orbital surface of frontal lobe. In "The frontal lobes", A.R.N.M.D., The Williams & Wilkins Company, Baltimore, pp. 405-420, 1948.
8. *Messimy, R.*: Troubles sensitifs et sensoriels au cours des lésions du cerveau préfrontal. Paper presented at the second symposium of the Fulton Society, Vienna, September 4, 1965.
9. *Messini*, — Quoted by Prick (11).
10. *Nauta, W. J. and Teuber, H. L.*: Frontal lobe and basal ganglia: behavioral effects of lesions in rodent, carnivores and primates. Paper presented at the second Symposium of the Fulton Society, Vienna, September, 4, 1965.
11. *Prick, J. L. G.*: The integral structural functional relations of human frontal brains, being the symbolic prefiguration and basis of the existentialia of human existence. Psychiatria, Neurologia, Neurochirurgia (Amst.), 68, 115-150, 1965.
12. *Richter, C. P. and Hines, M.*: Increased spontaneous activity produced in monkeys by brain lesions. Brain, 61, 1-16, 1938.
13. *Schuster, P.*: Psychische Störungen bei Hirntumoren. Berlin - Charlottenburg, Ferdinand Enke, 1902.
14. *Teuber, H. L.*: Space perception and its disturbances after brain injury in man. Neuropsychologia, 1, 47-57, 1963.

Case of Disturbed Music Expression After Severe Brain Injury

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Ever since amusia had been subject of theoretical examination the relationship between music and language and their pathological disturbances were discussed in Neurophysiology and Neuropathology. Nowadays, however, much more attention is paid to the disturbances of speech in frontal lobe lesions than to the so-called amusic disturbances: i. e. impressive and expressive disturbances of music and the disturbances in the relationship of music and language. We want to give a brief description of a case showing the combination of expressive amusia with a comparatively rare pathological modification of speech.

A 45 years old foundry worker was unconscious at his hospital admission after a heavy road accident in October 1956. 2 days later he regained consciousness. X-ray revealed fracture of base of skull. Patient developed symptoms of motoric aphasia and spastic hemiparesis. In the course of rehabilitation of this aphasic disturbance the man slowly regained his faculty to speak, describe objects, colours and pictures. Faculty to read, write and count was undisturbed. Spontaneous speech faultless, understanding normal. But the patient suddenly was unable to speak dialect, none of his relatives could understand him properly. His accent was peculiar, a kind of clumsy, literary German; it sounded, as if this language were not his native tongue.

At second admission in October 1958 he was partly successful in speaking idiom,

but one had the impression to hear a foreigner imitating Austrian dialect. His speech was not at all monotonous, the intonation perfectly right. The situation did not change when he spoke to different persons.

The second important disturbance noticed was the inability to sing or to find melody, or even to recognize tunes, although the patient had loved music and had been member of a choral society before his illness. He furthermore could not remember the text of the songs he had known before. It must be mentioned that the patient's musical talent was average, he had never learned to play an instrument. The man was examined according to *Auguste Jellinek's* scheme.

The result was the following: in October 1958 the patient was able to sing individual sounds, imitate sounds and whistle, but he was not able spontaneously to produce a melody, a harmonic succession of tones. He had also difficulties in finding the right text. He could remember neither text nor melody of the numerous songs known to him before his illness. He was fully aware of this inability.

If a melody was sung to him, he could carry on for a short time, but soon he lost the tune, the rhythm being comparatively correct.

He could easily reproduce individual sounds sung to him, but had difficulties in the imitation of simple, wellknown tunes,

the worst was spontaneous singing or singing with instrumental accompaniment. His understanding of music was undisturbed, the patient recognized melodies and pieces of music, he could also note mistakes.

There were no difficulties in describing the measure of a musical piece, in imitating rhythm and beating time of known melodies. Noises were recognized by him.

Neurological findings: brain nerves except weakness of innervation of right oral facialis normal. In the right upper extremity slight spasticity, minor weakness. KNIPS on the right, reflexes on the right more pronounced. At VA weaker sink and pronation tendency at the right, BDR and CrR without difference.

In the lower extremities tonus normal, strength slightly reduced on the right, Babinski right. PSR and ASR more pronounced right. No frontal signs, no cerebellar signs, gait slightly spastic paretic on the right.

Encephalography: revealed atrophic process with local atrophy on both sides frontal, basal, slight deformity of the frontal part of the ventricular system to the left side.

Cranial Xray: normal, no indication of fissure or fracture lines.

EEG: slightly abnormal with monophasic Alpha and Theta above the lateral parts of the left hemisphere.

Ophthalmological finding: anophthalmus after enucleation 1948 because of trauma on the left side. On the right: normal finding fundi and field of vision normal. Vision was 6/6 Jg I.

Otolaryngological finding: on both sides slight defective hearing of the internal ear, stimulation of vestibularis equal on both sides, sedimentation rate 3/2, RR 140 /70.

WaR. negative in liquor and serum. Li-
quor 30 mg%. 6/3 cells.

Summarizing the findings, there are 2 symptoms, each in itself as well as their combination appear remarkable.

Firstly the patient's inability to reproduce tunes, secondly his altered language, i. e. loss of his idiom after trauma.

Since Falret 1876 first observed a case of

motoric aphasia who was unable to speak but could sing, a series of similar cases have been described.

Less frequent were amusic disturbances after restitution of aphasia. Our case belongs to the latter group. The fact, that recognition and understanding of melodies was undisturbed and merely the production of melodies affected let us assume expressive motoric amusia.

Feuchtwanger distinguishes 2 forms:

1. expressive amusia of the dyspractic (apractic amusia, the proper motoric amusia)

2. constructive amusia (resp. constructive musical agnosy).

Our case completely lacked signs of apraxia, above all kinetic ("gliedkinetische") apraxia of oral, labial and laryngeal musculature. The faculty to sing and whistle a few sounds, was, as already mentioned above, preserved, a motoric - apractic disturbance in the sense of Liepmann therefore could not be proved.

Considering *Kleist's* classification our case cannot be regarded as a thumbness of sound corresponding to dyspractic amusia described by Feuchtwanger but as a thumbness of melody with paramelodic disturbances respectively with pronounced difficulty in finding melody, (melodic amnesia). There is no indication of a disturbance of motional ideation in non-music practises.

Our case, therefore, doubtlessly represents a fairly pure form of constructive amusic disturbance, although Feuchtwanger could not prove such pure forms so far, but has merely seen combinations of constructive and dyspractic disturbances. It strikes us as not very important that the patient could not play an instrument, the difficulty in textfinding without other signs of aphasia are no theoretical problem. As stressed by Hoff, the text words in connection with singing are on a comparatively low level, they therefore may be rather adjoint to melody than to speech. It is well known that for healthy people sometimes melody is necessary to remember the words.

According to existing literature, classification of amusic disturbance in our case seems to be quite easy. It is difficult, however, to classify the disturbance of expressive speech. To explain the patient's inability to speak idiom and his changed, peculiar pronunciation, we may assume two factors.

According to many authors, i. e. Bing, Minkowski, Kleist, Isserlin, etc., the loss of the faculty to speak dialect and the remaining use of literary language indicate the connection with the group of aphasia in polyglots. As result of this assumption we may regard our case as an exception of Pitres rule (1896) according to which in the course of restitution of aphasia the most familiar language is first of all restored. It seems to be a disturbance belonging to the group of Kauders "polyglottic reactions". Doubtlessly psychodynamic factors are of some importance.

Minkowski described a similar exception of Pitres theory. He reports the case of a Swiss - German, speaking typical Swiss idiom who suffered a cranial trauma with motoric aphasia. In the course of rehabilitation of aphasic disturbance, this man suddenly spoke literary German. Even one year after his recovery his language was strange, his familiar accent only slightly traceable. After the accident the patient was also unable to sing. Unfortunately no detailed analysis is given in regard to amusic disturbance. For the explanation of the aphasic disturbance besides the psychic factors Minkowski believes the optic moment in the literary language to be of importance in the course of restitution. Thus acquired languages in some cases would be restituted quicker than the mother tongue that was learned by hearing, while foreign languages are consciously acquired with the support of the acoustic, motoric and optic apparatus.

Comparing Minkowski's case with our observation, the parallel is striking. It must be considered, however, that Swiss dialect greatly differs from the Austrian idiom.

In regard to the aphasic disturbances in our case and considering the psychic fac-

tors we may assume the disturbance to be a polyglottic reaction.

Another interpretation must be mentioned. As already stated above, the literary language that the patient used after the trauma was peculiar in sound. There can be no doubt that the music elements of speech have changed after the injury. As already pointed out by Kroll the music qualities of speech, rhythm and intonation are of great importance.

According to Kroll even the intervals must not be regarded as something passive or negative, but as an active inability process, the disturbance of which may lead to the distortion of whole structure of a sentence. Kroll believes that the music qualities of speech, that often reveal the affective state of a person, are phylo —and onto— genetically older than the articulated speech, which may be considered as the intellectual part of the language.

Monrad - Krohn described the music qualities of the language as "prosodic" qualities and observed their isolated disturbances.

As prosodic qualities he names the stress of syllables and words, rhythm of speech and intervals, change of musical pitch and stress of tone from syllable to syllable and finally the speed of speech.

It is the prosodic qualities that give the expressive force to speech. In the pathological changes of the prosody, *Monrad - Krohn* differentiates between a change of the melody, dysprosody, and a loss —hypo— i. e. aprosodia, as it is often the case in the lesion of the basal ganglia, specially in *Paralysis agitans*. Dysprosody, according to *Monrad - Krohn*, is a disturbance of the higher functions. In this respect it may be compared with *Feuchtwanger's* constructive amusia. It must be stressed, however, that *Monrad - Krohn* objects to a connection between melody and speech and the specific musical expression; in his cases of dysprosody he specially refers to the absence of amusic disturbance: "Prosody is a linguistic means of expression and may be disturbed independent of the musical faculties; disturbances of prosody have nothing to do with amusia." It must be

stated, as it is also stressed by Monrad - Krohn, that this kind of music ability of expression must be a phylo —and onto— genetic earlier development. According to Jackson's theory it will be of greater resistance towards brain lesions than no later acquired qualities. Isserlin, for instance, emphasizes, how surprising it always is to realize that patients with severe paragrammatic disturbances speak with pronounced natural sentence melody. Both statements possibly explain the scarce observation of dysprosody and the naturally rarer combination with motoric amusia. According to Monrad - Krohn's definition our case may be regarded as a dysprosodic disturbance of speech.

To the question, whether it is a polyglottic reaction or a dysprosody in the sense of Monrad Krohn, no definite answer can be given.

To the definition of both conceptions and the possibly existing connection little attention has been paid so far.

Concerning localization opinions on motoric amusia differ. Kleist localized lesions causing motoric expressive amusia in the third frontal gyrus; Henschen in the pars triangularis of the 3rd frontal gyrus. Some authors have pointed out, that amusia in general is not merely, as speech, represented by lesions in the left hemisphere. Kroll stresses that singing, as a primitive, phylogenetically older function, seems to be more attached to the right hemisphere.

Feuchtwanger states, that music, a very complex function, cannot be strictly loca-

lized, Kleis pleads for a bilateral representation. As to our case it is remarkable that besides a massive atrophy in the left frontal lobe an atrophy of smaller degree could be proved by EEG in the right frontal lobe.

Monrad - Krohn believes that dysprosody is not caused by a local lesion, he assumes prosody of speech to be the result of the general activity of the brain. This may also be applied to the disturbances in polyglots, whereby Pötzl, however, assigns a special distributing function to the gyrus supra-marginalis.

We are therefore inclined to believe that lesions of the frontal lobe on both sides may be responsible for a disturbance of the faculty of music expression.

Summarizing the existing theoretical considerations, we are bound to stress the problem concerning the connection between the guiding symptoms, namely the motoric amusia and aphasia in polyglots, respectively dysprosody. In both instances faculties of music expression are affected.

Returning to the question about the connection of music and speech in neurophysio and neuropathology we want to quote Feuchtwanger: "In my opinion there is not enough empirical material of significant cases that would prove a purely acoustic (constructive) disturbance of expressive speech including amusic expressive disturbance. Therefore examinations concerning expressive aphasia in connection with music expression must be carried on in the future."

S U M M A R Y

A case of motoric aphasia with right-sided hemiparesis occurring after a severe cerebral concussion is briefly demonstrated. After restitution of aphasia the faculty to speak dialect was lost and merely literary German with a peculiar, strange accent was spoken. At the same time disturbances of singing and finding melodies with well-preserved understanding of music appeared. Difficulties in the classification of the aphasic disturbance in this special case

are discussed. It could be interpreted as aphasia in polyglots as well as dysprosody in the sense of Monrad - Krohn. The connection between expressive amusia and the mentioned aphasia with isolated disturbances of music elements of speech is also pointed out.

Considering similar cases in the literature and the encephalographic findings in the presented case, localisation of the described lesions is discussed.

RESUMEN

Se expone brevemente un caso de afasia motora con hemiparesia del lado derecho, aparecida luego de un grave traumatismo cerebral.

Luego de la recuperación de la afasia el paciente había perdido la facultad de hablar en dialecto y hablaba solamente alemán literario con un acento extraño y muy particular. Al mismo tiempo aparecieron alteraciones en el canto y la evocación de melodías aunque se mantenía bien conservada la comprensión de la música.

Se discuten las dificultades en la clasificación de la perturbación afásica en este caso especial. Pudo ser interpretada como afasia en políglotas así como también como disprosodia en el sentido de Monrad-Krohn. Se señala también la relación entre amusia expresiva y la mencionada afasia con alteraciones aisladas de los elementos musicales del lenguaje.

Se discute la consideración de casos similares en la literatura, los hallazgos encefalográficos en el caso presentado y la localización de las lesiones descritas.

R É S U M É

On expose brièvement un cas d'aphasie motrice accompagnée d'une hémiparésie du côté droit, survenue après un grave traumatisme cérébral.

Après la disparition de son aphasie le patient avait perdu la faculté de parler en dialecte et parlait seulement un allemand littéraire avec un accent étrange et très particulier. En même temps apparurent des altérations dans le chant et l'évocation de mélodies, tandis que la compréhension de la musique était encore bien conservée.

On discute les difficultés qui existent

pour la classification du dérèglement aphasique dans ce cas particulier. Il a pu être interprété comme une aphasie de polyglottes et aussi comme une disprosodie dans le sens de Monrad-Krohn. On signale aussi la relation entre l'amusie expressive et l'aphasie avec des altérations isolées des éléments musicaux du langage ci-dessus mentionnée.

On discute la considération de cas similaires dans la littérature, les données encéphalographiques dans le cas présenté et la localisation des lésions décrites.

ZUSAMMENFASSUNG

Es wird ein Fall von motorischer Aphasie und rechtzeitiger Hemiparesie infolge einer schweren zerebralen Konkussion kurz besprochen. Nach der Heilung der Aphasie ist die Fähigkeit im Dialekt zu sprechen verloren gegangen und es wurde nur ein literarisches Hochdeutsch mit eigenartigen, seltsamen Akzent gesprochen. Zur selben Zeit stellten sich Störungen beim Singen und Einfallen von Melodien ein, während das Musikverständnis gut erhalten blieb. Es wurden die Schwierigkeiten bei der Klassifizierung der aphasischen Störung in diesem speziellen Falle besprochen.

Sie könnte als eine Aphasie bei Polyglotten aber auch als Dysprosodie im Sinne von Monrad-Krohn interpretiert werden. Die Verbindung zwischen der expressiven Amusie und der erwähnten Aphasie mit isolierter Störung von Musikelementen der Sprache wird hier hervorgehoben. Indem man ähnliche Fälle der Literatur und die EEG-Aufzeichnungen in dem präsentierten Falle in Betracht zieht, wird die Lokalisierung der beschriebenen Läsionen diskutiert.

• Book Reviews

Higher Cortical Functions in Man by Aleksandr Romanovich Luria, (English translation by Basil Haigh). Prefaces by Hans Lukas Teuber and Karl H. Pribram. Basic Books, Inc., Publishers. Consultants Bureau, New York 1966.

Cerebral cortex has always been a thrilling subject; at present its study wins great interest as the most varied techniques incorporated to medical research as a result of scientific progress are applied to it.

Electron microscopy, Biochemistry, Electrophysiology and Pharmacology are some of the basic disciplines introduced with the purpose of attaining the intimacy of cerebral cortex.

The examination of psychic activity pointing to the definition of cortical disturbances of the brain has become an indispensable part of clinical investigation in Neurology, which is directed towards the localization diagnosis of a lesion as well as towards the appreciating of the restoration of formerly disturbed brain functions.

The book follows the Pavlovian trend both concerning the applied methodology and the concepts for the interpretation of cortical function of the human brain in psychic activity.

The author states that the main purpose of his research is to study the action of a specific analyzer in the structure of each functional system and also what kind of disturbance of higher cortical function results as a consequence of the lesion of one of the responsible cortical divisions.

The book is divided into three parts, the first dealing on higher mental functions and their organization in the brain, the second, on disturbances of the higher cortical functions in the presence of local brain lesions, and the third, on methods of investigating the higher cortical functions in local brain lesions (syndrome analysis).

The author rejects the notions of centers in the form of large and small groups of cells directly responsible of specific mental processes.

He sustains the concept that localization of higher mental functions is wide and dynamic over the cortex and that it is based on constellations of groups of cells topographically disseminated but working synchronically and exciting themselves mutually.

In the chapter dealing with the structural organization of the cerebral cortex, the author presents the concept of primary, secondary and tertiary fields, which—in a normally functioning brain—act together with their systems of relay and connection, among themselves and between them and the subcortical divisions of the analyzers working like an elaborately differentiated whole.

The author states that the disorder produced as a consequence of a pathological alteration in the state of a precise area of the brain, seldom leads to the loss of function but favors the appearance of depression symptoms or of stimulation of the activity of that area.

Among the perturbations arising after lesions of the occipital and occipito-parietal regions, different kinds of perception disturbances are treated as well as agnosias, spatial disorientation, disturbed logical-grammatical and arithmetical operations and altered intellectual processes.

The disorders of intellectual operations observed in lesions of the premotor region are probably associated to disintegration of the dynamic pattern of speech acts. In these cases capacity to perform spatial synthesis and logical-grammatical operations is preserved, which differentiates these patients from those with parieto-occipital lesions. Defects of dynamic in intellectual processes are a part of a general disturbance syndrome of the kinetic organization of different motor acts.

Lesions of the frontal lobes lead to considerable changes appreciable in the state of the cortical divisions of the motor analyzer, and also cause major alterations of the regulation of motor and autonomic processes by means of the system of verbal connections. In this kind of patients the systems of preliminar synthesis formed with an influence of speech connections and determinants of the subsequent course of mental and nervous processes seem to be the most affected ones.

This book constitutes a contribution of the highest quality to psychoneurologic literature. It is written by an outstanding authority on that field, well known all over the world, who exhibits a nice example of clinical scientific investigation following the Pavlovian trend. It will be of great interest for neurologists, psychiatrists and psychologists.

V. Soriano