

Cerebral Localization

Editors

K.J.Zülch O.Creutzfeldt
G.C.Galbraith



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Cerebral Localization

An Otfrid Foerster Symposium

Editors

K. J. Zülch O. Creutzfeldt G. C. Galbraith

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With 95 Figures

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Welcome

Ladies and Gentleman,

May I welcome you to this department of the Max-Planck-Institut für Hirnforschung and to the IIInd "Kölner Symposium" which is devoted to the localization of function. This Max-Planck-Institut in Frankfurt and Cologne succeeds the old Kaiser-Wilhelm-Institut für Hirnforschung, Berlin-Buch, of OSKAR VOGT. However, our department feels particularly obliged to maintain the traditions of the Neurologisches Forschungsinstitut Breslau of OTFRID FOERSTER which was lost by the last war. In the past both institutions were particularly successful in the field of our discussion, namely in the "Lokalisationslehre, or cerebral localization". Cologne, situated on a cross-way from north to south and east to west, is a town which has always been host to guests from all over the world, from its Roman time to the medieval holy Roman Empire of German Nation, as it was called, from then it has been one of the Centers of the European Hansa League, and has remained one of the cross roads of Europe ever since. It gives us a particular pleasure to welcome guests from all over the world for this hopefully successful discussion, which is dedicated to one of the great localizers, OTFRID FOERSTER. This year is the centenary of his birth.

I would also like to commemorate one of OTFRID FOERSTER's eldest coworkers and friends, PERCIVAL BAILEY. I had invited him but unfortunately he had to decline the invitation. He said he would be happy to receive all the details of the forthcoming discussion. But just a few days ago I heard from HEINRICH KLÜVER, whom I also had hoped to have here as our Senior member, that PERCIVAL BAILEY had died on the 11th of August. Our thoughts are full of commemoration for this great neurosurgeon and neurological scientist.

I am happy to express my thanks to Drs. O. CREUTZFELDT, G.C. GALBRAITH and K.-A. HOSSMANN for their help in organizing this discussion which we hope will be successful.

Cologne, August 1975

K. J. ZÜLCH

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I. Motor Functions

Critical Remarks on „Lokalisationslehre“

K. J. Zülch¹

"Localization is an artificial observer-made attribute of the brain"
(W. GOODDY and W. MCKISSOCK, 1951)

The discussion of "Lokalisationslehre im Hirn", i.e. cerebral localization, raises a number of preliminary questions. By general acceptance it has come to mean localization of functions in the nervous tissue. And since our subject is "cerebral localization" the cortical/subcortical structures will prevail. What is localization? What kind of function can be localized, a primary or elementary or a complex pattern consisting of many elementary functions, i.e. the performance of an act, a "Leistung" in the sense of V. WEIZSÄCKER? These are some of the first problems to be clarified.

Is localization meant in the pragmatic clinical sense, which helps us to localize focal disease? Or is it defined in the strict sense of neurophysiology, where a function is tightly correlated to a morphological unit? And what does this mean in a logical process? Is it a localized function (a subtraction symptom) which manifests itself? Is it the "discharging" after "stimulation" of a topographical structure which defines "the" function or a "destroying" (JACKSON, see PHILLIPS 1973) lesion? Or must both run logically parallel? Can one then deduce the "positive" of a "normal" function from the "negative" of a "deficiency" syndrome?

We could continue with this catalogue of definitions indefinitely but without producing any satisfactory answers. Our general discussion later will bring out the difficulties of this type of debate. Perhaps the answer will be easier to elicit if we first turn to the history of localization and then critically point to the errors made in this process from the present standpoint.

Before the Christian era there certainly was some knowledge of the "localization" of certain functions in the brain. It seems that the Egyptians knew that a traumatic subdural hematoma could lead to a contralateral paralysis of the body for which they would then attempt surgical relief (COTTRELL, 1957). Similar knowledge is ascribed to HIPPOCRATES. One would then name GALEN - as well as other medieval physicians - who must already have had the concept that the muscles of face, tongue, jaw, eyelids, and eyes could be paralyzed separately and must therefore have a separate

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cerebral representation (ena topon archen: one point of origin!). But there is no point in giving a complete history and we may pass on to GALL without losing too much of the course of development.

Although he blurred the picture with his phrenology he was basically right with regard to the principle of localization of various functions (see SOURY 1899 according to BERGER 1927). This system of GALL was one of the first great errors in localization because it was based on a doctrine and not on exact observations. Sir GEOFFREY JEFFERSON's Godlee Lecture (1952) referred to the physiological research of LONGET and TODD, and the anatomists TÜRCK, BETZ and VICQ D'AZYR, and ROLANDO and LUYS, which finally led to the classical experiments of FRITSCH and HITZIG (1870) and FERRIER (1878, 1880).

WILDER PENFIELD (1972) in his Fritsch and Hitzig Centennial Lecture in Munich rightfully marked the beginning of sound basic work on the localization of function with their experimental stimulation of the cortex because it actually introduced a new era. This work was immediately followed by FERRIER, who first used the faradic current.

In 1876 FERRIER anticipated the charting of the human cerebral cortex, before systematic electrical stimulation studies had been made in man, by transferring the map of his stimulation of the monkey cortex to an outline of the human brain (see CLARKE and DEWHURST, 1973, Fig. 138 A and B).

Such a proceeding was a real danger, of which O. VOGT and O. FOERSTER were quite aware when they agreed to mail their results of cortical stimulation, both in monkey and in man, to each other only on Friday nights. By doing this they were sure that they personally received the post over the weekend and remained uninfluenced.

We have already mentioned the beginning of the era of human cortical stimulation starting with HARVEY CUSHING (1908), VICTOR HORSLEY (1909) and FEDOR KRAUSE (1911), which gave parallel results to the stimulation experiments of GRÜNBAUM and SHERRINGTON (1903) on the monkey cortex.

We shall stop here at the end of this first phase of experimental work on localization but must return to it when we present the criticism of the main antagonists to such a topistic classification in the brain.

The second parallel route of observations on localization was developed at the bedside by clinicians such as BROCA² (1861), who had already been preceded by BOUILLAUD (1825) although he did not receive appropriate recognition.

² When one considers the enormous extent of the infarct of BROCA's case, one is surprised that he dared to correlate "aphasia" with this cortical lesion (see L. van BOGAERT, in: "Traité de Médecine", Fig. 2, p. 342, Paris: Masson et cie. 1949), but he had the luck to be correct in his concept.

Only when the observations of FRITSCH and HITZIG later became known in the scientific world did the clinical reports of BROCA (1861) and WERNICKE (1881) arouse the necessary attention that the concept of the localization of speech was accepted.

But a more precise topistic differentiation was necessary to enable recognition of localization of function in the cortex. This already stemmed from the work of MAGENDIE, SYLVIUS and REIL, SOEMERING, ROLANDO and GRATIOLET, VICQ D'AZYR and ELLIOT SMITH, and finally from TÜRK and BETZ.

The next generation of anatomists gave more precise information about brain structure and function. Of these REMAK, BAILLARGER, v. KOELLIKER and MEYNERT were actually the first who tried to correlate functions to circumscribed brain areas.

The last stage of finer structural investigations, which designated the cytoarchitectural areas of the cortex, was started by the Australian, A. W. CAMPBELL (1905), who was followed by BRODMANN (1909), C. and O. VOGT (1919, 1937), and finally by C. von ECONOMO (1925, 1929), not overlooking the studies on the architecture of myelination by FLECHSIG (1920) and on the vasculature by PFEIFFER (1930, 1940). The gross differences in observations and interpretations of these patterns will be discussed later. - All this research rapidly converged by many different approaches toward the same goal, i.e. localization of function.

But where were the great antagonists, the "holists", the "universalizers", the adherents of the theory of equipotentiality of the neural structures? This concept started with the experimentalist FLOURENS (1824), who, on the basis of his studies with the pigeon, concluded that the loss of function was not due to the loss of a specialized part of the brain but rather to a quantitative loss of brain substance.

Another great experimental scientist, FRIEDRICH LEOPOLD GOLTZ (1881) joined FLOURENS in his fight against FERRIER at the 17th International Medical Congress in London in 1913, which must have been an historical event. FLOURENS has had many partisans during the last century and a half including LASHLEY (1929, 1946) (with his observations on the rat) and, in Germany, GOLDSTEIN (1925, 1930) and V. WEIZSÄCKER (1931, 1943). But, before starting to discuss their criticisms we must describe JACKSON's views more fully. He felt that he was neither a "geographical localizer" nor a "universalizer", but rather as standing somewhere in between. JACKSON (1835-1911) anticipated the difference in size of the cortical motor and sensory representation of various parts of the body when he stated that the grey matter must be much more extensive for the thumb and index finger, "the most specialized parts of the body", than for the upper arm. He seems to have been very critical and reluctant in supporting "localization" although he added much to our knowledge of the localized "destroying" and "discharging" lesions. Although he described for instance a patient (1868, see PHILLIPS 1973) whose fits always began in his left thumb and who was found after death to have a tubercle the size of a hazelnut in the posterior part of his right third frontal convolution, he was reluctant to consider too strict a local-

ization. In 1890 he³ stated: "I am content with the supposition that the non-disability of a muscular region when some movements of it are lost by destruction of a part of a centre is accounted for by that muscular region being "represented" by other movements in other parts of the centre or in other centres".

However, his fellow clinicians all over the world were less cautious and the time came, when, not only were elementary body functions such as "movement" localized, but later the "philosophers" of localization allowed their imagination to go so far as to assign a precise localization in the brain for special mental or emotional, as well as neuropsychological and behavior patterns, and even for insufficiently defined general states of our mind as consciousness or wakefulness. This trend certainly reached its climax in the work of KARL KLEIST (1934, 1937) with his famous "brain chart", which was severely criticized in the Frankfurt Congress of Neuropsychiatry in 1936. Some parts of his map almost seemed to outdo GALL.

Ironically, Sir HENRY HEAD had long since rejected the work of such "diagram makers", but a systematic criticism was expressed only in the neuropsychiatric meeting mentioned above.

Let us briefly review some of the critical objections. The first concerned the methodological approach: what did the "localization" of "function" actually mean? When a function such as elevation of the foot occurred on stimulation of a certain cortical area, or when the relevant muscles were paralyzed after excision of that area, was it correct to conclude that the "function" of elevating the foot could be "localized" in this area? The conclusion was considered justified particularly when a pathological process, such as a tumor, caused an epileptic seizure of the foot elevators by stimulation or their paralysis by destruction.

While for practical purposes it still seemed logical to "localize" a certain "motor function" under such circumstances, these methodological prerequisites were later no longer exactly applied. Not only were "clinical entities" such as chorea localized but even "obesity", an endocrine symptom, and also a "sound image", or a "concept" (V. WEIZSÄCKER 1931, 1943) in the field of cerebral neuropsychology. Investigators thus localized "functional disturbances" and "normal functions" (e.g. wakefulness and consciousness) as colleagues such as LANGE (1937, 1938) critically complained. He objected justifiably that psychopathological syndromes could not be correlated with normal psychology.

"These errors had already led to the fact that the brain chart was now fully occupied and no empty spaces were left." A harsh light was thus thrown on the "localization theory" of the CNS. VON WEIZSÄCKER (1931, 1943) described this situation as approaching "intellectual barbarism" (for details see ZÜLCH, 1964, 1967).

Apart from this methodological criticism, additional pointed remarks concerned the methods of investigation used in "localizing".

³ JACKSON, J. H. (1890) Lumleian Lectures on Convulsive Seizures.

1. Let us consider the neurophysiological experiments. I do not need to enumerate all the pitfalls of an inadequate methodology or of a poor interpretation of the results.

I remember a discussion with the late VON WEIZSÄCKER, who was trying to convince me with some diagrams of PENFIELD's stimulations of the anterior central convolution, where the points were scattered around a center like a swarm of bees ("Punkt-wolke", SCHALTENBRAND, 1950), that localization was not possible even in the motor area. This happened although he knew from other neurological observations that the "Schwellener-müdung" can be the cause of these results.

In the meantime more sophisticated methods, micro-leads, averaging etc., give more precise results as regards methodology, but the errors of interpretation still exist despite the most modern electrophysiological techniques. It is often exceedingly difficult to determine whether a stimulus has caused "excitation" or "inhibition" of the morphological substratum in the CNS or one in the center and the other in the surroundings. This was recently emphasized by Sir FRANCIS WALSHE (1964).

2. In the brain of BROCA's famous case, one wonders how he could have reached any conclusion from this extensive lesion with regard to the localization of aphasia.

An analysis of the extent of a pathological process in the cerebral tissue is extremely difficult. What is the range of the effect of a gunshot wound of the cortex? Is it confined to necrosis, to circulatory disturbances (see ZÜLCH, 1964, Figs. 1, 2, 3b; SCHOLZ, 1937), or oedema? Can one define a traumatic lesion only from the extent of the opening in the skull? SCHOLZ emphasized correctly the need for caution. He demonstrated polytraumatization in a brain with an apparently circumscribed superficial lesion.

On the other hand, how far does a tumor affect brain tissue? What are the remote effects caused by mass displacement and herniation at the mesencephalon and medulla oblongata? What strangulation can occur, with or without circulatory disturbances, at the edge of the tentorium causing, at a distance, an infarct of the occipital lobe and also at the falx and at the wings of the sphenoid bone? What EEG changes can these produce (see discussion at the European EEG Colloque de Marseille à Cologne, 1964; ZÜLCH, 1963, 1964)? What other parts of the nervous system are affected by a tumor from a distance such as secondary lesions of the third nerve? We have published extensively on this subject (RIESSNER and ZÜLCH, 1939; ZÜLCH, 1959, 1963, 1975; ZÜLCH et al. 1974).

But even if the morphologist is able to examine the brain in detail, in the gross and histologically, and even if functional disturbances have been determined in advance by exact clinical tests, it is difficult to correlate morphology with function because it is still impossible to establish by anatomical investigation whether the ganglion cells of a given region were capable of function. Sometimes we can establish with certainty that they were necrotic, but there are many changes in which we cannot define whether or not the ganglion cells are still functioning, for instance in

NISSL's "chronic" or "ischemic" cellular changes. It is often impossible with conventional methods, even supplemented by histochemistry, to establish the degree of damage in a tissue. Moreover, human postmortem material is usually some 24 hours old when fixed, and therefore no longer suitable for more subtle enzyme studies, nor is electron-microscopic examination possible.

And finally, in the case of circulatory disturbances, function may be impaired while the structure still shows no histological change. Investigations by OPITZ and SCHNEIDER (1950) have shown that a 50% reduction of the blood flow through the human brain can cause gross functional disturbances both in the EEG and in the neurological findings (e.g. paresis or aphasia), although at this time the ganglion cells of the region responsible show no change demonstrable by any method so far available (see ZÜLCH, 1967). Only when the blood flow falls to below 15% of normal and oxygenation below 20%, does structural damage occur, and even this requires a certain time before it becomes demonstrable histologically.

In summary, it is often impossible to evaluate the functional state of ganglion cells on the basis of microscopic appearances. We have known this for a long time from our findings in brain tumor investigations as demonstrated by completely normal ganglion cells in the presence of an oligodendrogloma in a patient with a verifiable history of seizures of some decades.

Let us not go too far into the field of neuropathology but rather consider clinical observations. I may cite here a long paper by the late Vienna neurologist PÖTZL on the sensory systems in man with the most complicated schematic drawings of the integration of the sensory pathways via the commissures of both hemispheres. The object of this discussion was a patient with a frontal abscess who had transient bilateral paresthesias all over the body, which ceased after the evacuation of the abscess. Every neurologist or neurosurgeon today would have immediately remarked that these paresthesias followed pressure of a tonsillar hernia on the nuclei of GOLL and BURDACH. Yet at the time such concepts were not yet generally known.

The best results in the localization of functions from pathological and neurophysiological observations have always been attained when stimulation, and afterwards destruction of an area have been followed by positive and negative symptoms of the same type. Yet, one may still ask whether the "deficit" symptom after a lesion regarded as "negative" gave the right to assume that the opposite "positive" was the "normal" function of that area. Could it not be that deficit symptoms were the remaining effects of the surviving neighboring areas which took over in a vicarious way? Or that the symptom was the effect of a deep substratum "suppressed" up to that time in the hierarchic system, which then took over according to the concept of JACKSON's levels? Or, finally, was it a corresponding point of the contralateral hemisphere which was able to reestablish the function ascribed to the area destroyed? How much should the action of "diaschisis" or "plasticity" in this process of reorganization of function be considered?

What was the nature of the organization of the cortex? Did the areas "represent" a function in the sense of JACKSON, a very neutral term, which did not clarify anything. Or did the cortex "coordinate" or "organize" function? What was the *primum movens* in the many known feedback systems of a function? What regulates what? What did it mean to define an area as a "center" for a function? All these problems have been the subject of long discussions.

We have mentioned the finer organization of cortex and nuclei and must now return to define these units, the architectural areas, which are such important landmarks for stimulation work in neurophysiology and for localization by the clinicians. A. W. CAMPBELL (1905) introduced this method to subdivide the surface of the brain according to histological patterns. The most precise and thorough work, however, is that of K. BRODMANN (1909), who, stimulated by O. VOGT (1903), distinguished 52 cortical areas, which are still the basis of most experimental work. C. and O. VOGT, working in the Berlin-Buch-Institute, later outlined a maximal subdivision of more than 150 different areas of the cortex and innumerable nuclei in the depths. A similar work of C. V. ECONOMO (1929) tried to bring the existing knowledge into a more orderly pattern, without, however, attaining general acceptance. Yet this subdivision of V. ECONOMO and KOSKINAS (1925) was the only one to be acknowledged later by PERCIVAL BAILEY and V. BONIN (1951) who particularly criticized the BRODMANN and VOGT areas while they maintained that they were hardly able to distinguish more than 19 areas.

A. HOPF, in the last "symposium on localization" in 1964, rejected the criticism of the current attempts of cytoarchitectural subdivision by stressing the point that in fact all cytoarchitectonics had already been proven by the myeloarchitectonics and had stood the tests of strychnine neuronography.

Actually this cytoarchitectural work had not only been paralleled by FLECHSIG's excellent myelo- but also by R. A. PFEIFFER's angio-architectonical areas. At present we note the first highly interesting attempts to build up parallel patterns of a chemo- and an enzymoarchitecture of the brain (FLEISCHHAUER, 1959; FRIEDE 1966).

In the range of this architectural work and in other attempts to attain a precise morphological description of the surface, many new errors have been brought into the theory of localization. As an example, RUDOLF WAGNER (see NEUHOFF, 1974) attempted to take quantitative measurements of the surface of the convolutions of "Elite Gehirne" in the last century, as in the case of the brain of GAUSS (see V. NEUHOFF, 1974). Even before this, anatomists had already tried to explain particular capacities, such as mathematics, by the size of particular convolutions. And even VOGT himself held the opinion for a long time that in a right-handed person the convolutions of the left side are larger. And finally OSCAR VOGT himself made similar attempts to explain genius based on the particularities of the architecture by pointing to the number, size and position of cells, which should explain the particular capacity of "association".

We have now finally to consider the criticism of the "holists" against any finer localization. We remember that FLOURENS started this line, GOLTZ (1881) and MUNK (1881) took over, PIERRE MARIE (1906) and VON MONAKOW (1914) continued, and that it found its climax with LASHLEY as an experimentalist and GOLDSTEIN and VON WEIZSÄCKER as late neurological philosophers. Although as a clinician GOLDSTEIN (1932, 1946) was a pragmatic "localizer" (see GOLDSTEIN and COHN, 1932), as a methodologist and psychologist he rejected this doctrine. It did not seem possible to him to correlate a circumscribed function with a known circumscribed lesion because the whole brain was active even if parts were destroyed. In any case the symptoms were to be looked at before the concept of the "Vordergrund-Hintergrund-Model". And v. WEIZSÄCKER rejected the possibility of localizing a "Leistung" which could not by any means be represented in the cortex. The same "Leistung" in the human body could be achieved by various and changing patterns of muscle or sensory organ functions integrated into this pattern as, with all his authority, VON MONAKOW had already more or less entirely rejected the possibility of explaining "Leistungen" by the cooperation of localized functions.

This reminds us of the old discussion of HUGHING JACKSON on a lower level, emphasizing the point that the central nervous system knows nothing of muscles, but knows only "movements". Similarly WALSHE (1943) spoke of "performances" versus "performing parts".

To WALSHE we owe other very valuable critical contributions in the field of localization. He started the destruction of FULTON's (1949) concept of the "strip" area 4 versus 6 a β which was ultimately abandoned. It is interesting to read his criticism of PENFIELD's concept of a "centrencephalic" system responsible for certain generalized forms of epilepsy.

This may show that methodological problems and technical trials run through the discussions of 19th and 20th century's criticism like a red thread. While the localization of primary "elementary functions" such as movements or sensations was easy and generally accepted, and helped in "clinical localization" and thus diagnosis, it seemed impossible to come to more than a vague concept about the structural dependence of the complex or secondary functions, i.e. the higher "Leistungen" and particularly the psychological "Werkzeugleistungen". This ends our very condensed historical introduction to the criticism of "Lokalisationslehre", which can be summarized in the following points.

1. The uncertainty about the boundaries and subdivisions of the normal morphological substrata, the areas and nuclei.
2. Failures or the inability to define, neuropathologically, the boundaries of "destroying" lesions and, neurophysiologically, the "function" of an area.
3. Prohibited deduction from the "negative" of a defect symptom to the "positive" of a function.

So the discussion goes from basic morphology to philosophy and logic. Yet, the evaluation of all the criticism seemed more than

ever necessary in order to clarify the failures made in this process of localization during the last century and to warn us to avoid these in our present work, since they are still commonly made in our very sophisticated work with single neurons as well as in correlation of defects to morphological areas.

Let us end with a little story which may explain the origin of this symposium. It concerns the three levels of education which a neurologist must have. Two elder neurologists meet at the Annual Congress and one asks the other's advice as to where he should send his son for neurological training. The answer is: "at the lower level he must study with NONNE; he is an excellent clinician and neurological practitioner. At the middle level he ought to be sent to Breslau to work with OTFRID FOERSTER, where all the ambiguities in his mind will be cleared up and neurology will seem to be a systematic science consisting of clear and crisp data and patterns. But finally he must finish his training with VON WEIZSÄCKER, where he will be informed that nothing he has learned before about the structure and function of the nervous system is to be believed". Perhaps it is because I started neurology with OTFRID FOERSTER and later did a year with VON WEIZSÄCKER that I was so keen to hold this discussion on localization.

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Cortical Motor Map of Macaca Mulatta after Chronic Section of the Medullary Pyramid¹

C. N. Woolsey^{2,3}

It is an honor and a privilege to be invited to participate in this symposium celebrating the one hundredth anniversary of the birth of OTFRID FOERSTER. I recall vividly Professor FOERSTER's lecture on the dermatomes of man (4), which he delivered at the Johns Hopkins University School of Medicine when I was a medical student. I am happy to acknowledge that his work on cortical localization (3, 5) has had an important influence on my own studies and teaching in this field.

FOERSTER was born not long after FRITSCH and HITZIG (6) in 1870 had first shown that movements of skeletal musculature can be produced by galvanic stimulation of the rostral cortex of the dog's brain. He was a *foetus in utero* during that four months of intense activity, from March through June 1873, when FERRIER (2), inspired by J. HUGHLINGS JACKSON, extended FRITSCH and HITZIG's observations to the brains of several mammals, including the monkey, which faradic stimulation.

FOERSTER grew up and received his medical education in a period of great activity centered on the motor areas. HORSLEY and SCHÄFER's (7) map of the motor areas of the monkey, published in 1888, could have been known to him as a medical student. Slightly later, in 1889, MILLS (10, 17) projected the monkey map to the human brain, providing what was one of the first maps of the motor areas of man.

It is interesting to note the gross similarities between these early maps of monkey and man, the maps of the VOGTS (15) for the monkey and of FOERSTER (4, 5) for man, and those of today. They differ primarily in detail and in interpretation.

HORSLEY and SCHÄFER considered their map to illustrate a single motor area, extending across the parietal lobe, through the pre-central region, onto the medial wall of the hemisphere. Later LEYTON and SHERRINGTON (9) demonstrated in anthropoid apes that

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² The author is greatly indebted to his collaborators in the larger study, still to be published, from which data used in this paper were taken. See reference 19 for the names of these individuals.

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the precentral gyrus has a low threshold to electrical excitation and the "motor cortex" came to be defined as the Betz cell area.

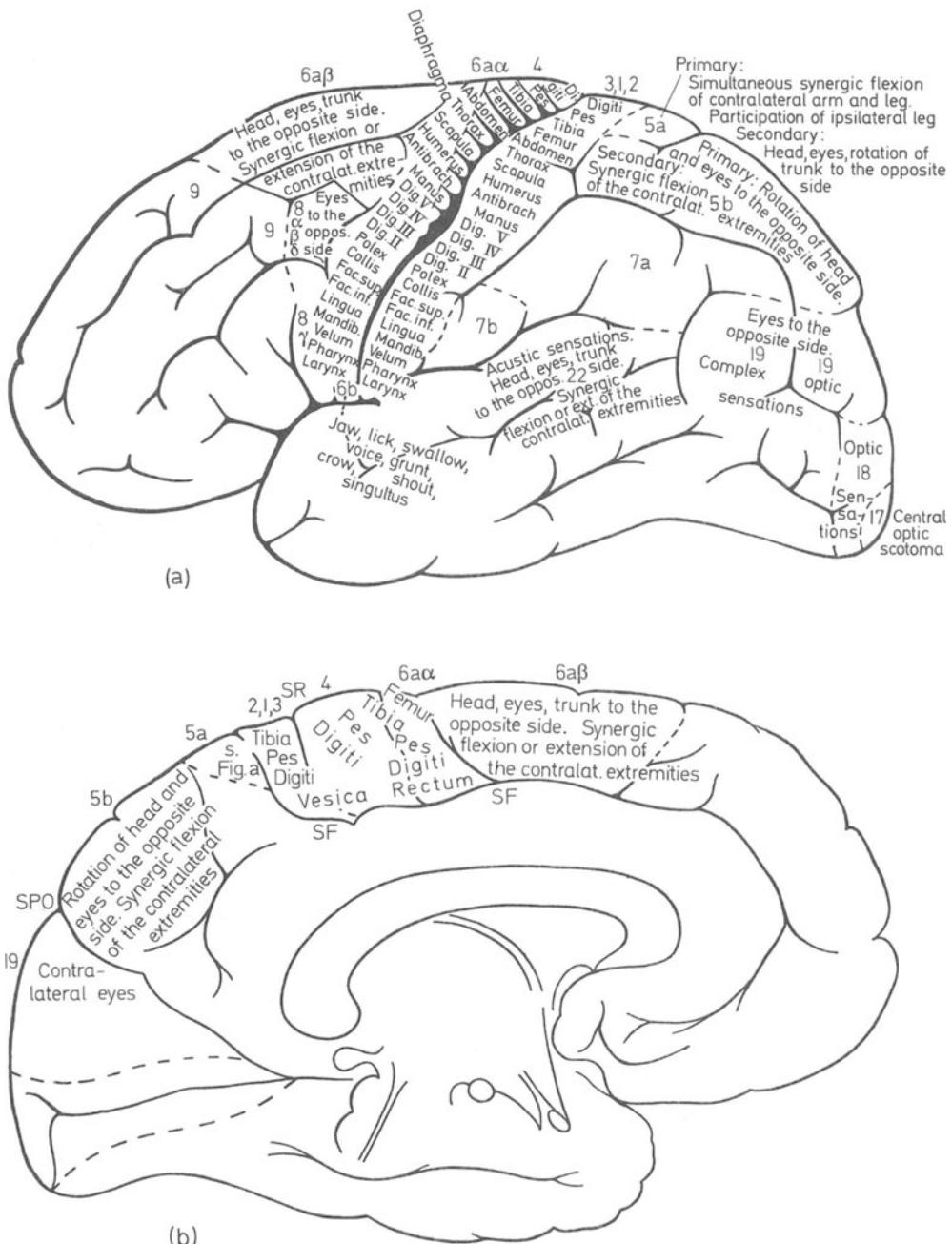


Fig. 1. FOERSTER's map of the motor areas of man. From FOERSTER (5, 21)

The VOGTS and FOERSTER analyzed the cortical motor fields into pyramidal and extrapyramidal systems (Fig.1). The more detailed movements of all areas were thought to be mediated by the pyramidal tract, whose origin was considered to be the Betz cells of the precentral gyrus. The extrapyramidal areas, covering broader reaches of frontal, parietal, and other areas of cortex, mediated adversive movements of head and trunk and flexor-extensor synergies of the limbs.

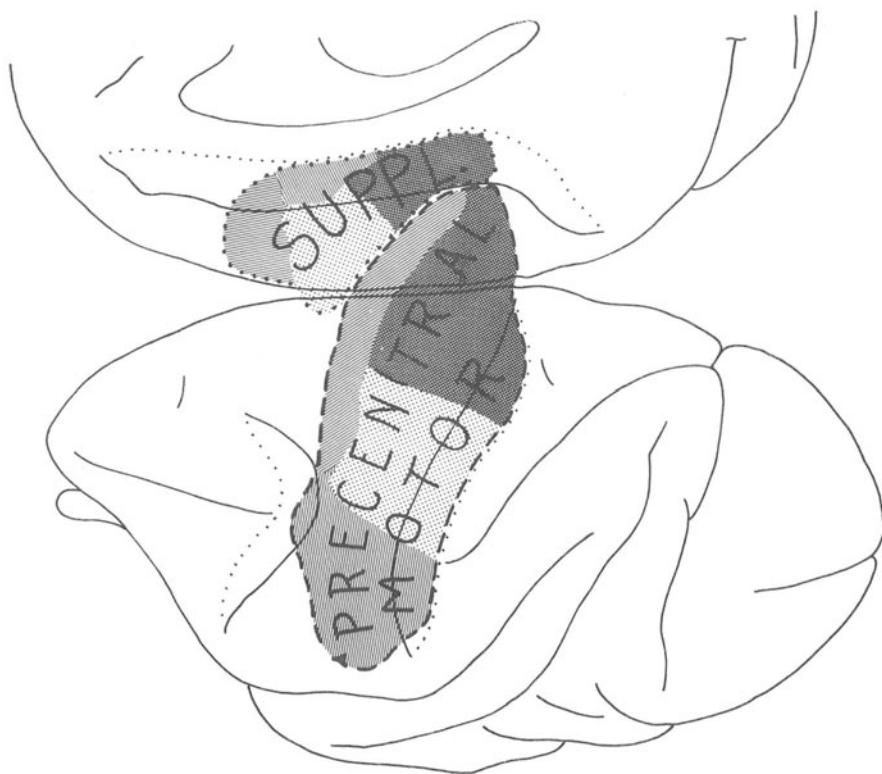


Fig. 2. Location and general arrangement of supplementary and precentral motor areas of Macaca mulatta based on the stimulation experiments of WOOLSEY et al. (20). For significance of markings, compare with simiusculi of Fig. 4

Present views are in some respects similar but in others considerably different. In 1949 and 1951, PENFIELD and WELCH (12, 13) described the "supplementary" motor area in man and monkey on the mesial aspect of the hemisphere in that region of the cortex to which HORSLEY and SCHÄFER had extended the dorsolateral motor field and from which the VOGTS and FOERSTER had elicited adverse movements and flexor and extensor synergies of the limbs. In 1950 WOOLSEY et al. reported and in 1952 described in detail (20)

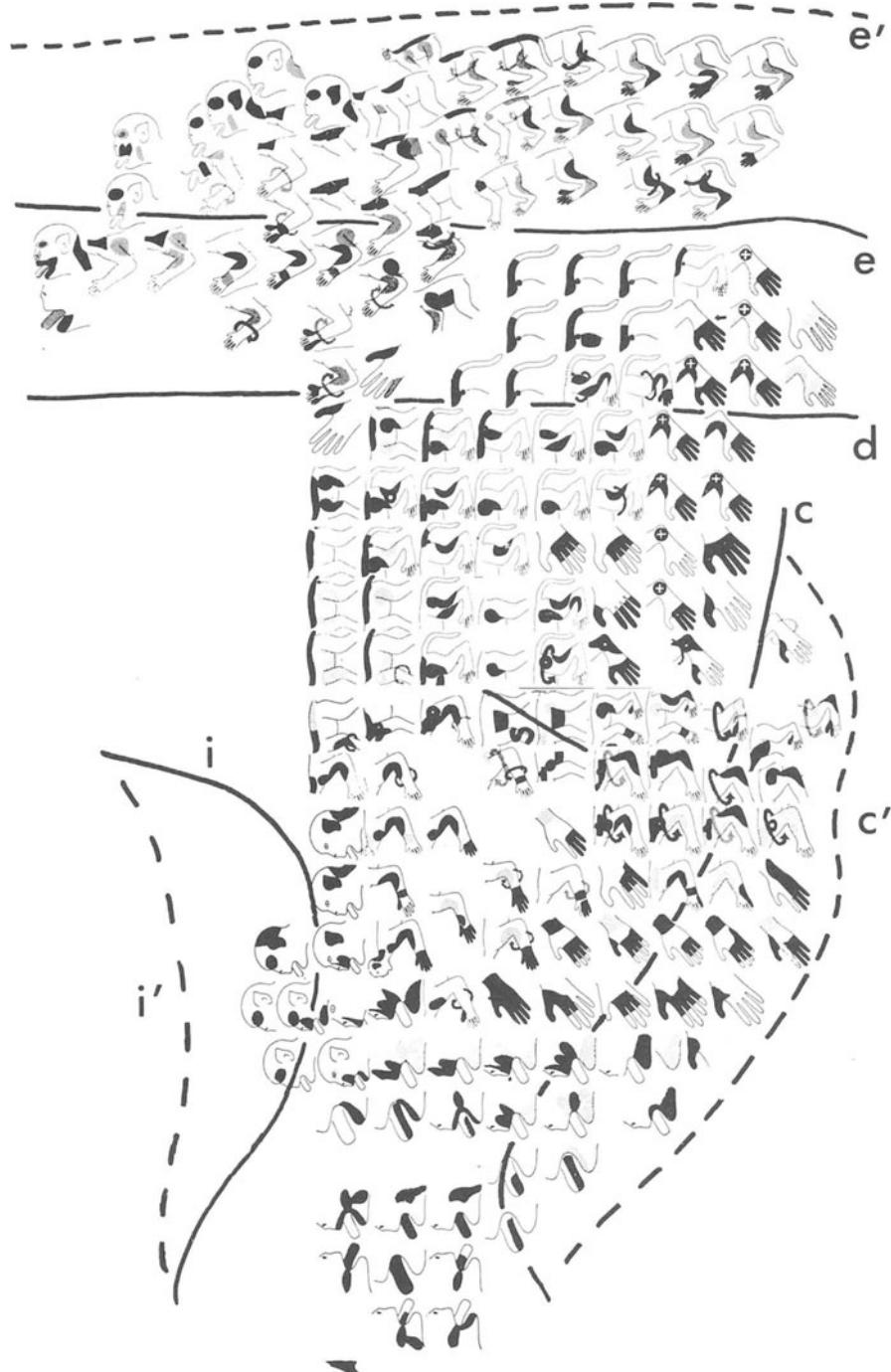


Fig. 3. Figurine map of precentral and supplementary motor areas of *Macaca mulatta*, from WOOLSEY et al. (20). Labels: c, central sulcus; c', bottom of central sulcus; d, dorsomedial margin of the hemisphere; e, dorsal lip of callosomarginal sulcus; i, caudal lip of inferior precentral sulcus; i', bottom of inferior precentral sulcus; s, superior precentral sulcus

the precentral and supplementary motor areas of *Macaca mulatta*. Figure 2 shows the general arrangement and Fig. 3 is a figurine map of these two areas. Note the orientations of the limbs and the representations of the epaxial musculature in the two areas. Stimulation of these epaxial representations, precentral and supplementary, probably accounts for the adverse movements elicited by the VOGTS and FOERSTER from these regions of cortex. The basic plan, in terms of "simiusculi", is given in Fig. 4, which also illustrates the arrangements of body representations in the postcentral gyrus and in the "second" somatic area of the parietal operculum. The labeling (16) is intended to indicate that each of these "periorolandic" areas is both motor and sensory in function, though in differing degrees.

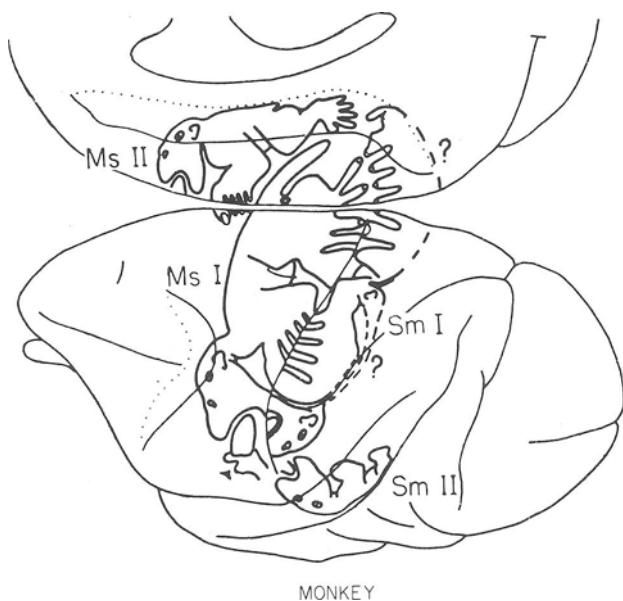


Fig. 4. Simiusculi of precentral (Ms I), supplementary (Ms II), postcentral (Sm I), and second somatic (Sm II) areas. From WOOLSEY (17)

Even after chronic removal of the precentral and supplementary motor areas, the postcentral gyrus on stimulation yields focal movements which topologically are closely related to the pattern of sensory representation in the gyrus. This is demonstrated by Fig. 5 (16), which compares the postcentral tactile localization pattern of a normal monkey with the postcentral motor pattern defined in an animal from which the precentral and supplementary motor areas had been removed some months before.

Similarly, we have found that the detailed movements elicitable from the normal supplementary motor area are still obtainable after careful and complete aspiration of the precentral motor area.

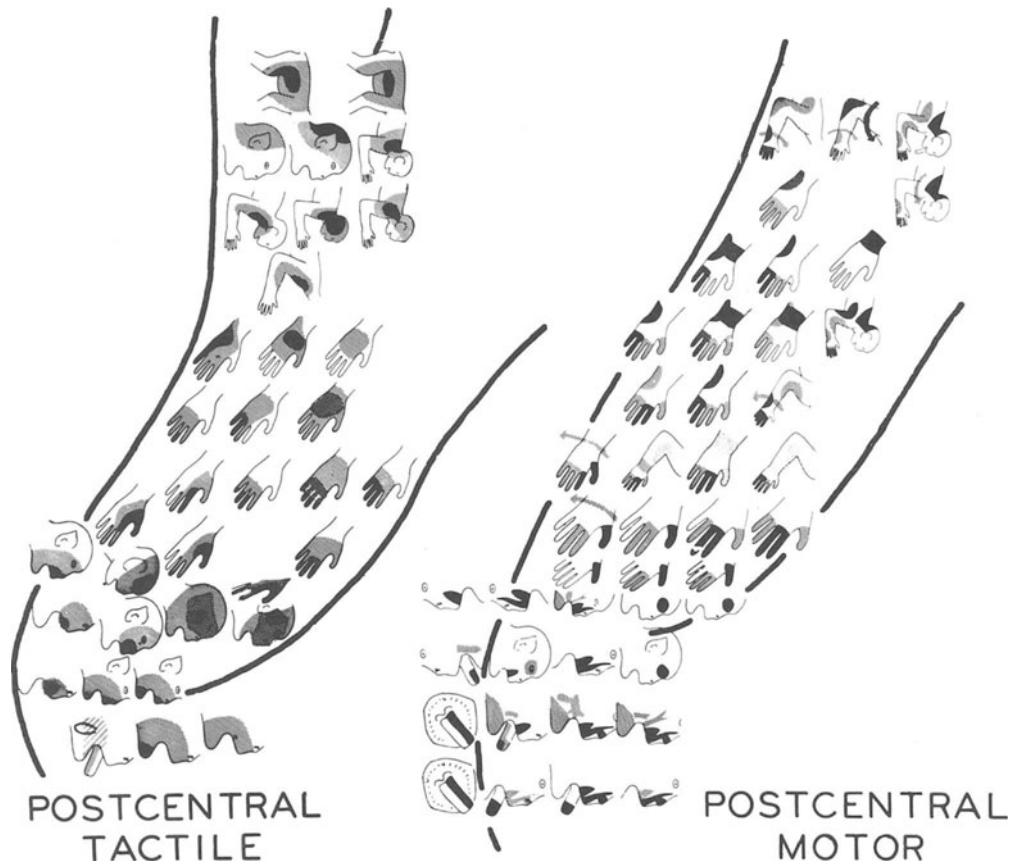


Fig. 5. Comparison of postcentral motor localization pattern, defined by electrical stimulation several months after removal of the precentral and supplementary motor areas of the same hemisphere, with the postcentral tactile localization pattern of a normal monkey. From WOOLSEY (16)

We thus conclude that the detailed movements produced by electrical stimulation of the postcentral gyrus and of the supplementary motor area are not dependent upon the precentral Betz cell area. They are, however, dependent upon fibers descending in the pyramidal tract, which, as we now know, has a more extensive origin than the Betz cell area.

BERTRAND's (1) electrophysiological experiments indicated a contribution from the supplementary motor area to the pyramidal tract. LEVIN and BRADFORD (8) found that 20% of cells undergoing retrograde degeneration after transection of the corticospinal tract were in the parietal lobe. PEELE (11) demonstrated Marchi degenerations in the pyramidal tract after parietal lesions and we have made similar observations (unpublished) after removal of the second somatic area. The area of cortex activated antidromically by electrical stimulation of the medullary pyramid (WOOLSEY and CHANG, 18) includes the whole parietal lobe and the precentral and supplementary motor areas.

Let us now look at the effects of chronic section of the pyramidal tract at the level of the trapezoid body in *Macaca mulatta*. The pyramid is sectioned by a parapharyngeal approach, after drilling an opening through the basiocciput bone with a dental burr. Following tract section under full vision, the dura is either closed with interrupted sutures or the bony defect is filled with gel foam and the muscles inserting on the base of the skull, and still attached laterally, are sutured over the gel foam. These procedures prevent herniation of the brain stem and development of symptoms dependent thereon.

The functional status of a monkey 465 days after unilateral tract section was found (19) not to "differ in any significant respect from the description of the effects of pyramidal lesion in the monkey given by TOWER (14) in 1940." This statement holds for the two animals to be reported on here.

Figure 6 is a Heidenhain stained cross section of the medulla at the level of the inferior olives of an animal (67-287), whose left pyramid was sectioned 142 days previously. It shows a completely degenerated left pyramid and an intact right one.

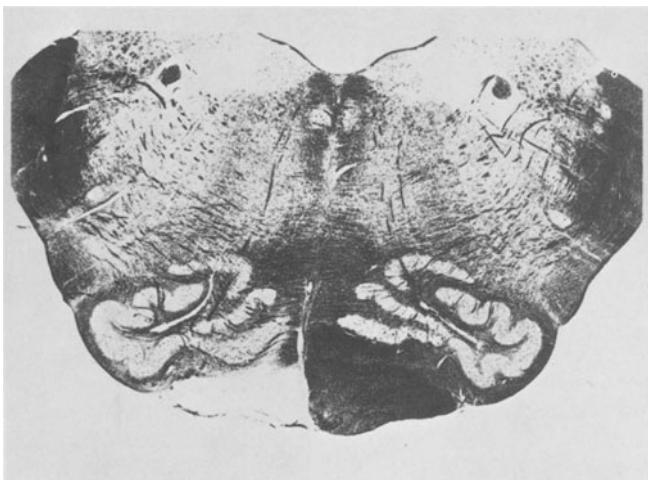


Fig. 6. Heidenhain stained cross section of medulla of animal 67-287, whose left pyramid was cut at the level of the trapezoid body 142 days previous to motor mapping experiment

Figure 7 is a photograph of the exposed rolandic regions of both hemispheres on which the sites of electrical stimulation were marked during the experiment. The numbers indicate the order in which the cortical sites were stimulated. Symmetrical loci were chosen, first on the right and then on the left, to permit as close a comparison of stimulus values as possible between the two hemispheres. Sixty-cycle A-C stimulus trains of two sec duration, at two min intervals, ranging in strengths from 0.1 to 5.0 mA (root mean square values), were used. Movements were elicited by stimuli of just above threshold value. Generally exploration began precentrally near the central sulcus, where thresholds

are lowest, and proceeded forward with rising thresholds. The postcentral gyrus was next explored and finally the supplementary motor area was approached either after removal of a part of the other hemisphere or by retraction with a special retractor.

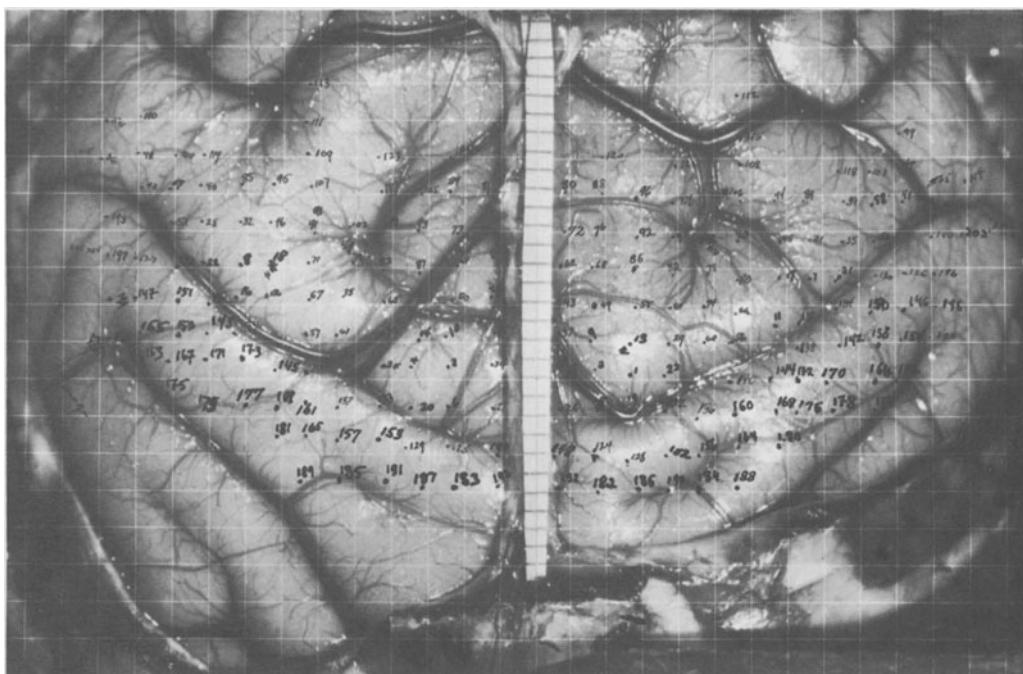


Fig. 7. Photograph of the pre- and postcentral regions of monkey 67-287, showing sequence in which cortical points were stimulated, as recorded during the experiment. Rostral brain up

Stimulus values were controlled by keeping a chart of the points on which thresholds were recorded. Three or more individuals observed the movements and a description of the observations made was tape recorded. Later the data were converted into figurine charts.

The upper half of Fig. 8 is a figurine map for the right hemisphere, whose pyramid was intact. The map illustrates movements obtained from the dorsolateral surface both precentrally and postcentrally. Note that detailed movements of fingers and toes were obtained both precentrally and postcentrally. The markings on the figurines indicate the regions of the opposite side of the body in which movements occurred. Arrows indicate directions of movement. Strength of movement is indicated arbitrarily by two grades of shading. The lower half of Fig. 8 illustrates the movements obtained from the left hemisphere, whose pyramid was cut. The responses are now limited mainly to flexions and extensions of knee and elbow, protractions of thigh and retraction of shoulder, pronation of forearm and extension of the wrist. Nearly all movements of the digits have been lost, although it is of

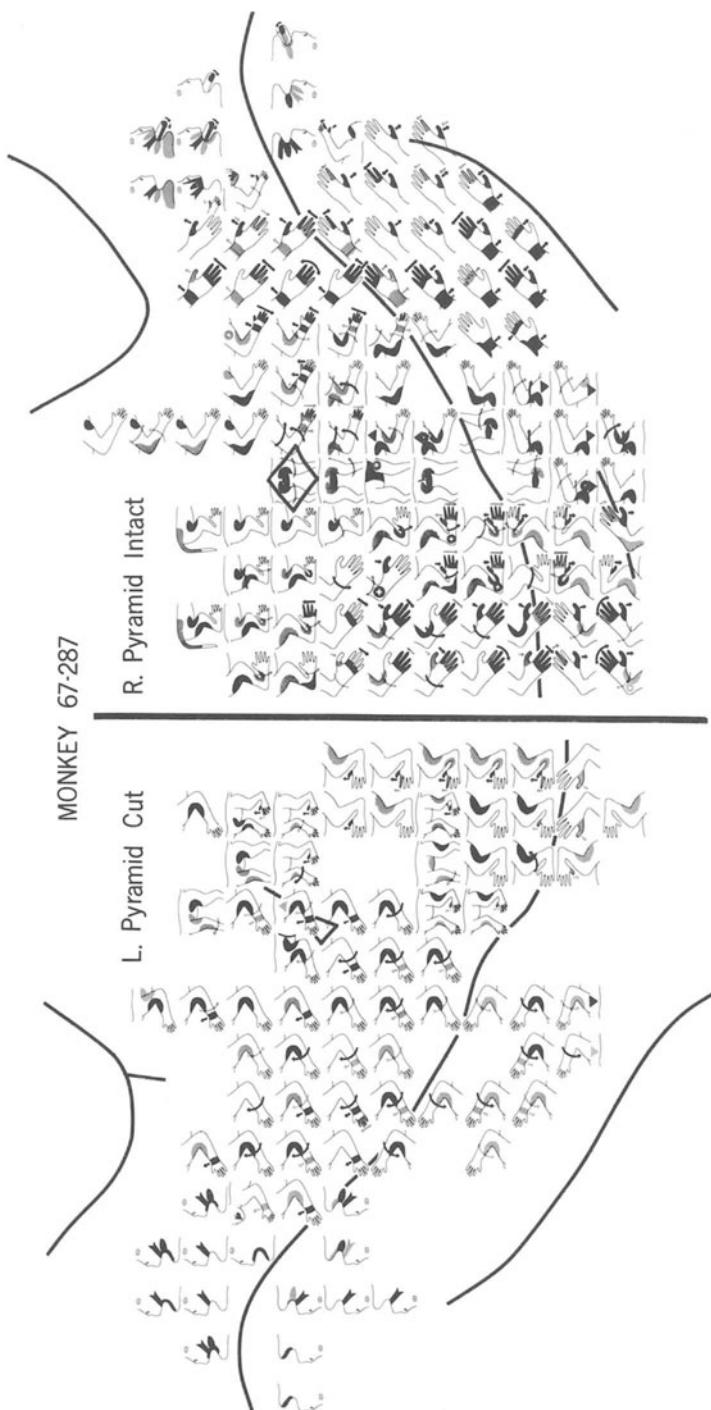


Fig. 8. Figurine map of the pre- and postcentral region of right (upper) and left (lower) hemispheres of monkey 67-287. Note detailed movement pattern elicited from the normal right hemisphere and the paucity of movements obtained from the left hemisphere

interest that the hallux still extends. The boundary between arm and leg subdivisions is preserved. Postcentrally many points failed to respond to strong stimulation, but the movements obtained were similar to those obtained precentrally.

The striking differences in stimulus values between the two hemispheres and the differences on the right side in various parts of the precentral area and the higher thresholds postcentrally may be noted in Fig. 9.

A second animal (68-73) was stimulated 471 days after section of the left pyramid. The medulla at the level of the inferior olives is shown in Fig. 10.

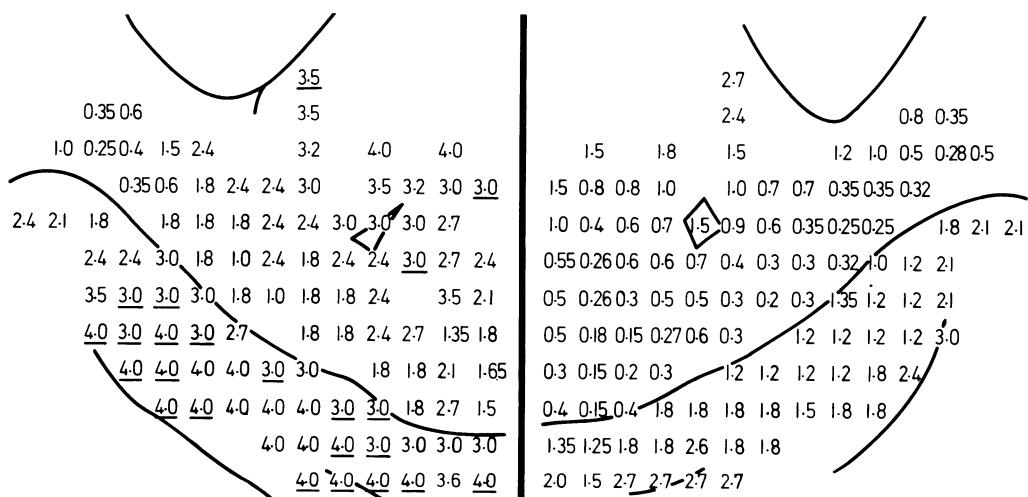


Fig. 9. Stimulation thresholds for monkey 67-287

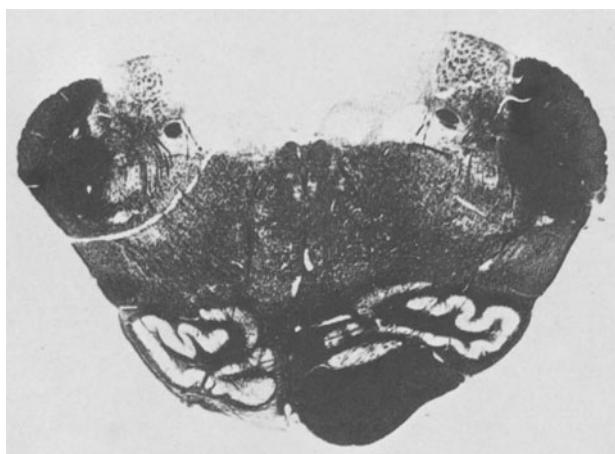


Fig. 10. Heidenhain section of medulla of monkey 68-73, whose left pyramid was cut 471 days before the motor mapping experiment

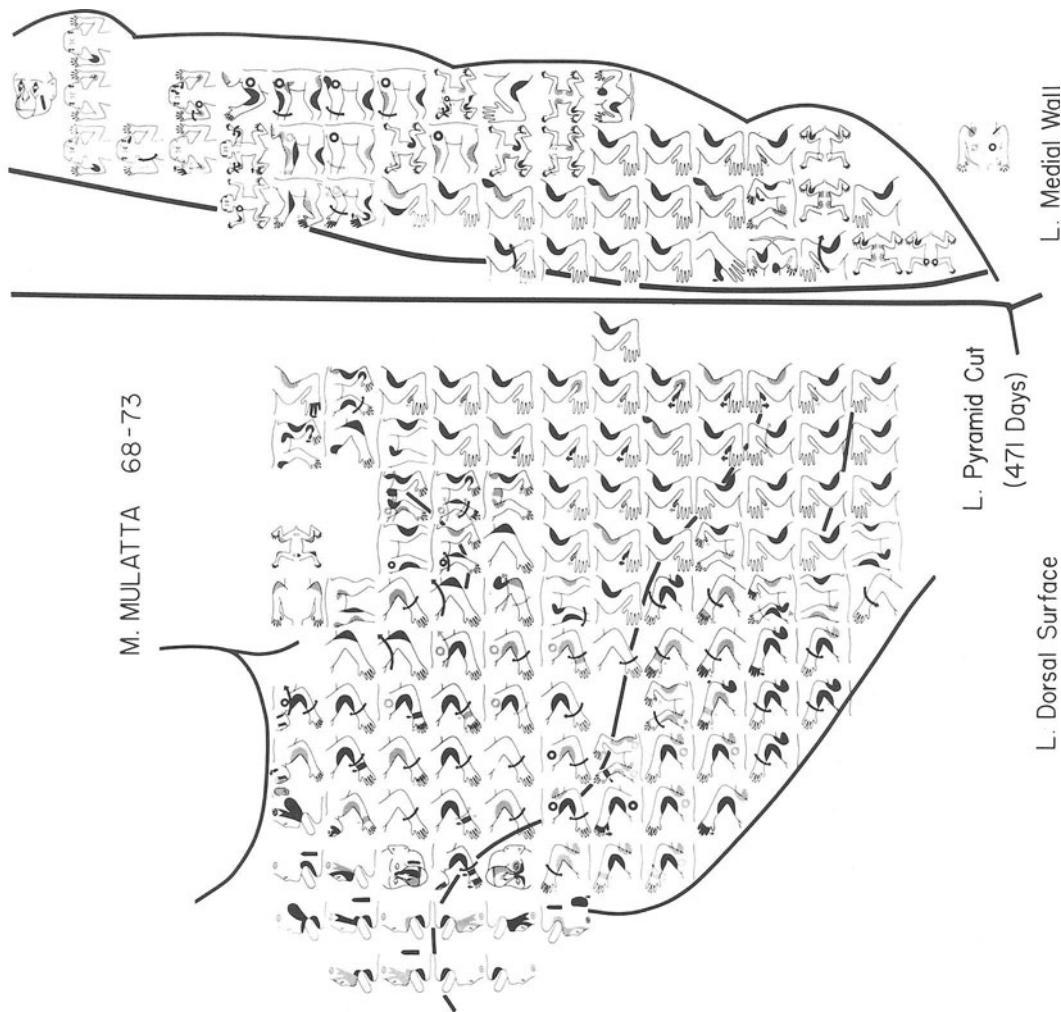


Fig. 11. Figurine map of left precentral, supplementary and postcentral areas of monkey 68-73

Figure 11 is a figurine map, illustrating the results of stimulating the precentral and supplementary motor areas and the postcentral gyrus on the left. The face areas in this experiment, as well as in the preceding one, were not affected by pyramid section. All three regions of cortex were similarly altered. Nearly all digital movements were eliminated. Again the hallux extended as the only digital movement of the foot. There were a few dorsiflexor movements of the ankle and in the hand some flexor and extensor movements of the digits together. The main movements were flexion of the knee and elbow, but shoulder, forearm and wrist movements also occurred as flexor or extensor synergies. Comparison of this map with that of animal 67-287 indicates that the cortex of 68-73 was somewhat more responsive at similar stimulus values than was 67-287. This may correlate with this animal's

longer period of survival after pyramid section. Figure 12 records the stimulus threshold values for this animal. Only a few points were stimulated in the right hemisphere. These all gave rise to movements at low threshold values ranging from 0.2 to 0.9 mA, depending on the site stimulated.

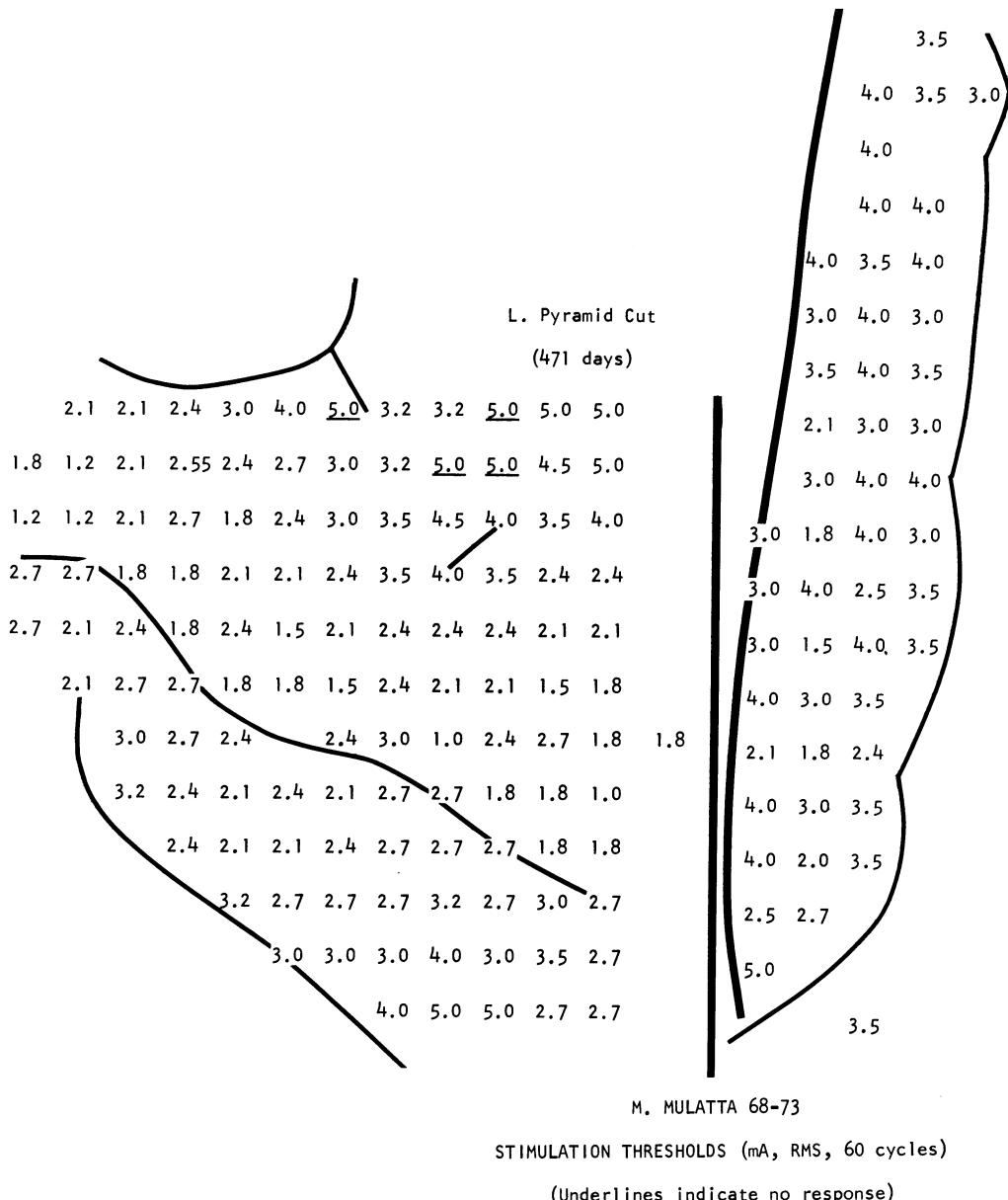


Fig. 12. Stimulation thresholds for monkey 68-73

In conclusion, section of one pyramid markedly raises the thresholds of excitation in precentral, postcentral, and supplementary

motor areas and greatly simplifies the movements which are obtainable, virtually eliminating the finer movements at all joints but particularly affecting the movements of fingers and toes. The movements which remain resemble in their character the flexor and extensor synergies described by FOERSTER as do, to a degree, the less versatile movements which the behaving animal makes with the extremities affected by the pyramidal section.

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Discussion

Dr. GLEES: Do you believe that this motor function might be conferred from the cortex via the corpus callosum or to the ponto-medullary level where there might be a transmission to other descending tracts?

Dr. WOOLSEY: My view is the latter. We did cut the corpus callosum in earlier experiments and we couldn't see any difference.

Dr. HASSSLER: We are very interested in this stimulation of the postcentral gyrus, the sensory area, after interruption of the pyramidal tract. I should like to know whether these maps after the section of the pyramidal tracts are identical or whether differences arise?

Dr. WOOLSEY: After section, the postcentral map becomes very much simplified. The arm areas and leg areas still retain their specific functions. Boundaries are respected but instead of very detailed movements one mainly produces flexions of the arms and legs. However, the postcentral map is not altered by removal of precentral cortex weeks in advance (see Fig. 25 in HARLOW and WOOLSEY, Eds., Biological and Biochemical Bases of Behavior. Madison, Wis.: Univ. Wisconsin Press 1958).

Dr. OBRADOR: How do the animals behave after sectioning uni- or bilaterally pyramidal tracts?

Dr. WOOLSEY: We have studied the animals' behavior afterwards, particularly the ability to pick up objects using the thumb and index finger. Some of these movements are lost and remain lost, particularly the ability to pick up small candies about $1\frac{1}{2}$ mm in diameter from a flat surface. After section of the pyramid they can never do this. The best they can do is to use all fingers simultaneously to pick up a grape or, later on as improvement occurs, they may be able to pick up a stationary piece of apple about $\frac{1}{4}$ in thick by coming down over it with all fingers. We have never seen them using the thumb and the index finger alone.

Dr. KUYPERS: I have forgotten the thresholds to pre- and post-central gyrus stimulation after pyramidotomy; what are they?

Dr. WOOLSEY: After pyramidotomy they are very similar, maybe somewhat higher postcentrally. But before section, the thresholds are considerably higher postcentrally than precentrally.

Dr. KUYPERS: I think that on the basis of your findings, your suggestion of a relay from the motor cortex downstream to brain stem structures is very attractive. Your results obtained by stimulation of the supplementary motor cortex may be explained by the findings that this area also projects to the reticular formation and the red nucleus. However, as far as my anatomical knowledge goes, it has not been possible to demonstrate in the monkey that the supplementary motor cortex contributes to the pyramidal tracts.

Dr. DENNY-BROWN: To go back to Foerster's concepts, I would like to know whether the flexor and extensor synergies are all mixed up on the cortex or is there a separate area for each?

Dr. WOOLSEY: I have not seen any separate areas for each. But I am not even sure whether you would call the types of movements we get "synergies". They seemed to be more often single joint movements rather than movements of the whole limb. We always tried to avoid overstimulation. Perhaps if we had raised the current values still higher we could have produced more massive effects and then we would have had what you might call a synergy.

Pyramidal and Parapyramidal Motor Systems in Man

K. J. Zülch¹

The localization of function in the brain started with the observation of dramatic forms of paralysis of motor movements and this dates back to ancient history. The development of our knowledge is well documented in our introductory chapter. In this paper a general view of our own observations and interpretations in man following localized lesions, both in surgical operations and in trauma and cerebrovascular accidents, will be given (ZÜLCH, 1942-1974).

The highest standard of motor skill is probably reached by man in the art of speaking and also in the development of his finger movements, where he can perform in one second as many as 32 different isolated consecutive flexions or extensions using 10 digits while playing the piano. This ultimate degree of isolated movements seems to be achieved only in man and is probably a result of the high concentration of corticospinal motor fibers in the "pyramidal pathway" which may be defined as consisting of all fibers running through the "pyramid". This partly includes the neurons of the Betz cells but mainly those of the "adversive" cortical fields. Apart from this pyramidal ("ventral") motor pathway, which is integrated into the circuits to the oral and caudal basal ganglia including the thalamus (the Papez circuit), a "dorsal" system also probably exists. This could descend from the mesencephalic region (substantia reticularis?) and run by interconnections to the spinal level. We may call this part the "parapyramidal" system.

This paper will deal with the potential capacity for movement following impairment of the pyramidal pathways and the patterns of function restored by supplementary systems, i.e. the pattern of the "parapyramidal synergies".

After any massive injury to the pyramidal pathway - in its cortical region in the internal capsule or in the mesencephalo-pontine segment - a flaccid hemiplegia usually results. This will later become spastic, when reflexes recur and become exaggerated. The first "voluntary" movements return around the fourth to the sixth week of recovery. They usually have a precursor: the reflex or semireflex associated movements (ZÜLCH, 1942, 1956; ZÜLCH and MÜLLER, 1969). These consist of flexion movements in the leg during sneezing or extension movements in the arms and fingers

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while sprawling or yawning in the morning. The first voluntary movements, however, are shortening synergies in the leg. These eventually develop into the flexor synergies of OTFRID FOERSTER, which in turn correspond to the movements referred to in classical neurology as the "predilection type" of WERNICKE-MANN.

The pattern of the ultimate synergic movements consists of flexion of the hip with abduction, bending of the knee, dorsiflexion of the foot in supination and a slight inward rotation of the leg, i.e. the flexor synergy. In the upper limb, the supplementary movements are manifested as a flexor synergy, with flexion of the elbow in pronation, dorsiflexion of the hand and bending of all of the fingers into a fist, and also abduction and elevation of the arm and shoulder.

Extensor synergy of the lower limb consists of extension and abduction of the thigh, extension at the knee and plantar flexion of the foot and toes. Extensor synergy of the upper limbs consists of depression of the shoulder, adduction of the arm, extension at the elbow, and slight abduction of the fingers.

No isolated voluntary movements return in the distal parts of the extremities, particularly in the fingers. The thumb cannot be extended if the other fingers form a fist and the index finger cannot be moved in isolation. Abduction-adduction movements of the fingers cannot be accomplished because only those movements are available which are predetermined in the pattern of flexor and extensor synergy. It is important to bear in mind that these global synergies consist of fractions of movements, with each component coupled inseparably to the others. It is very characteristic of these synergistic movements, particularly in the elderly, that - when intended - they start with a certain time latency and their whole course may be slower than normal voluntary movement and also only poorly coordinated.

It is important to recognize that, as a general rule, the synergies, usually so strictly linked in their pattern, are less rigid and better developed the earlier they develop, in other words the earlier the destruction of the pyramidal pathway occurs. In elderly people after a stroke, there may be an extensor synergy possible in the leg, with, however, extensive abduction of the hip, with slight bending of the knee, and even less dorsiflexion of the foot in flexor synergy. This results in a gross circumduction, with dragging of the tip of the foot along the ground. However, flexorextensor synergies of the leg in the elderly are commonly restored to a degree which permits ambulation. At the same time, adequate flexor synergy is usually restored in the arm, although it may be virtually useless for any practical purpose. However, in those cases where a substantial portion of the basal ganglia is destroyed - as often occurs after embolism or thrombosis, in which the arterial supply of the basal ganglia is frequently involved - flexor synergy of the arm will be almost absent; sometimes a supination position in the elbow is seen instead of the ordinary pronation.

When lesions of the pyramidal pathways occur in children or young adults (ZÜLCH, 1954, 1969), e.g. in the patient with infantile

cerebral hemiplegia, synergies may be very well developed. The hemispastic child may thus have an excellent synergy for extension and flexion of the arm which may even be sufficient for the simplest routine performances, such as turning over the page in a book or carrying a briefcase under the arm (as will be later shown in a film). Satisfactory extensor synergies of the arms are also occasionally seen in young subjects wounded while in military service (ZÜLCH, 1942).

Generally speaking, extensor synergies appear to develop better the earlier they are called into action due to the so-called "plasticity" of the nervous system (ZÜLCH, 1963, 1969). Moreover, synergies are less firmly coupled in young patients with infantile hemiplegia than in older ones and the proximal segment of the limb is particularly less strictly fixed.

However, I do not believe that even for the patient with the best functions the statement of GOODY and MCKISSOCK is correct "after a young patient's right hemisphere has been removed his left hand can be used for everyday purposes (though perhaps not as well as normally)." Even in the best case (see ZÜLCH, 1974) the synergies give a very poor substitute of normal motor performances, in the majority of patients the remaining motility is of use only for very gross performances.

We have come to appreciate, however, that even in the young therapeutic exercise will not dissociate the isolated components of the synergies. Naturally, where there is any spontaneous recovery, exercises will improve movement and provide optimal limb utilization while failure to perform them will have the opposite effects (ZÜLCH, 1955). FOERSTER believed that firmly interlocked synergies could be broken by exercise and he published an illustration (FOERSTER, 1936, Fig. 226) showing recovery of the isolated mobility thus obtained. In our own experience this has not been possible: one need only study patients in whom no further structural recovery is to be expected, that is to say those in whom there has been a total lesion of the pyramidal tract present for at least six months - in these cases only pure synergic mobility is available.

To test this hypothesis, during World War II, I had functional training carried out on patients continuously under my personal supervision for nine months; no success was achieved. Dissolution of synergies by functional training in such circumstances, especially in younger patients even if their cerebral lesion does not date from early childhood, would have confirmed the validity of FOERSTER's contention. We can only repeat that in our experience, this has not been possible (ZÜLCH, 1956, 1969).

It is interesting to see that, in the face, mimic movements do not disappear or decrease following pure pyramidal destruction, and this can be shown particularly in patients after hemispherectomy. In these patients the effect may even become exaggerated and "hypermimic", as MONRAD-KROHN (1954) has shown for laughing and as I myself have seen in the mourning face (1954, Fig. 2).

Due to the work of NOTNAGEL and NAUNYN (1887) the mimic movements have been "located" (if we can use this term here) in the thalamus and basal ganglia. In the second case in my paper on hemispherectomy (1954, 1974), practically the whole thalamus had been removed by operation and yet the child had almost equal mimics on both sides of the face during the slightest emotion (1969, p. 80).

We must mention at this point, some deviations from the most common types of parapyramidal movement which develop under certain specific conditions: *Partial patterns of global synergies in partial cerebral lesions.* If the lesion is cortical and focal, for instance a contusion restricted to the "hand area", the isolated voluntary motility may be preserved in the entire upper extremity except in the hand and fingers, where only a synergic "flexion-extension movement" (opening and closing of the fist) may be possible (ZÜLCH, 1956).

Patterns in pontine lesions. In contrast, a pontine lesion may produce the reverse pattern, where isolated movements are preserved distally and the paresis is mostly manifested proximally in the shoulder and hip, wherein the synergic movements may develop (ZÜLCH, 1967, 1975) (see Fig. 1).

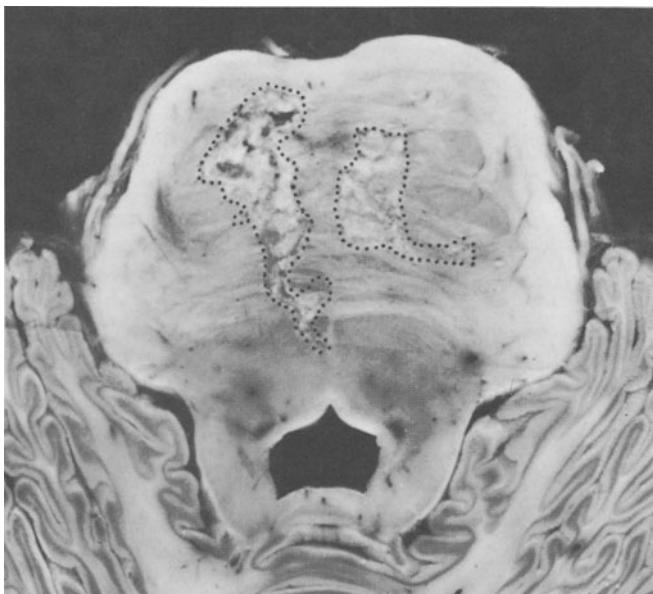


Fig. 1. Larger right and smaller left paramedian infarcts in the pons

Meanwhile we had the opportunity to prove this clinical observation by autopsy findings. In a 60-year-old "stroke" patient whose clinical course was characterized by a left-sided hemiparesis with the preservation of "isolated" movements in his fingers and

toes and a subsequent tetraplegia, at autopsy two paramedian pontine infarcts were found: one right sided, larger and older, and a left-sided, smaller and more recent infarct. The cortex and internal capsule of the corresponding pyramidal pathway were not severed (ZÜLCH, 1975).

Bilateral patterns in cerebral paraplegia. In the common paralysis of "Little's disease", a cerebral paraplegia with typical synergic voluntary movements is observed (ZÜLCH, 1963). Marked adduction of the thighs and slight flexion of the knee joints also frequently occurs, leading to permanent rubbing together of the medial aspects of both knees. At the same time the legs take on a marked medial rotation.

The associated movements. In analyzing the normal physiology of movement, we should cover briefly the so-called "associated movements". These interested the English, French, and German schools of neurology before and particularly after the first world war. Associated movements occur involuntarily or reflexly in the activated part of the body or its immediate neighborhood, or even in different parts of the body (ZÜLCH, 1942; ZÜLCH and MÜLLER, 1969).

Examples of associated movements are the pendular movements of the hand in clenching the fist, etc. Apart from the physiologically associated movements, there are pathological ones, comprising of: 1. Global associated movements or mass movements. These may be either of central or of peripheral origin, the latter are seen, for instance, after facial paralysis. Returning to the global associated movement of central origin; here we find the synergies described earlier. If, for instance, the patient wants to clench his fist, there will be an associated flexion of the elbow, pronation of the fore-arm, abduction of the shoulder, and dorsiflexion of the hand. This rigid pattern of the total synergy is produced whenever the patient wants to perform any of the single parts of that strictly linked pattern of the synergy. 2. The second type of pathologically associated movements is even more interesting. These are isolated movements which are called "identical" or "homologous" or "mirror" associated movements and they occur, for instance, in a patient with infantile spastic hemiplegia, and particularly after hemispherectomy. The patient produces an identical movement on the paralyzed side when he wants to perform a particular movement of the healthy extremity. Thus, if he wants to bend his index finger against resistance, an isolated bending or flexion of the finger in the paralyzed side takes place. This only relates to active, never to passive movements.

I would like to end the discussion of the synergic movements with the statement that these patterns seem to resist any physical therapy when one tries to modify them and restore normal isolated voluntary movement.

It would be easy to stop the description here and renounce any further attempts to analyze pathophysiology. However, some thoughts about the evolution and dissolution of movement in man should be mentioned using the terms employed by HUGHINGS JACKSON (1875), because these may help in understanding the problem.

The evolution of movement in the newborn: When one analyzes the evolution of movement in the human subject, considering specifically the maturation of pyramidal motor performances, one finds that man is born with a "choreo-athetotic-ballistic" pattern of kicking movements: Initially, he cannot perform willed movements.

The motor performance of the newborn seems to indicate that the first higher brain function to develop during the first eight months is vision. This leads to movements of the head and eyes; next comes grasping, i.e. the action of the arms and hands, and the last is standing and walking, i.e. movement of the legs. These three functional units have been crudely described by psychologists and analyzed by GESELL (1952) from the psychological standpoint. However, by meticulous examination, one can observe a distinct chronological sequence of these three important functions of seeing, grasping, and marching. The eyes are brought into operation first and the child begins after only three weeks to fix its eyes upon the bottle of milk for instance. Thereafter, the possibility of voluntary motor performance spreads from the head downwards in a very precise oro-caudal pattern. At the third week, the child may also begin to lift its head. Between the fourth and sixth week voluntary movements of the shoulders appear. In the 10th - 12th week willed movements of the arms occur, and the child begins to grasp. By the 17th week the thoracic segments begin to function and the child learns to sit. From the 22nd to the 42nd week in a rostral-caudal sequence (Fig. 2) the other segments of the voluntary motor system come under the influence of the pyramidal pathway, and finally the child learns to stand and then after about ten months to walk (for details see ZÜLCH, 1955).

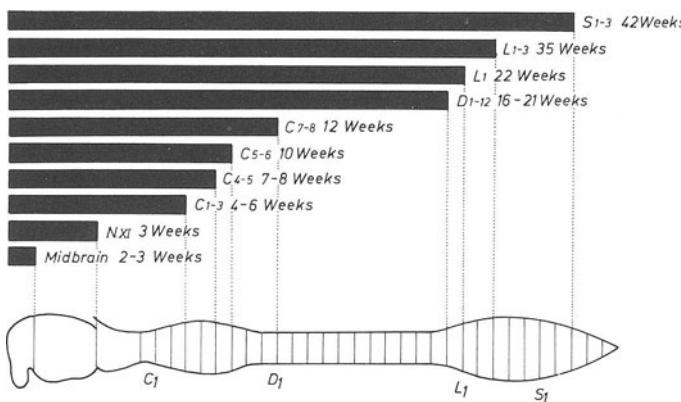


Fig. 2. Progressive oro-caudal "maturation" of skilled voluntary movement in the child during first year

This rostro-caudal functional "maturation of movement", according to our own investigations, corresponds to the myelination of the appropriate segments of the pyramidal pathway, which apparently follow this same pattern and time sequence. Unfortunately, there are as yet no exact descriptions of the spinal myelination in the literature. Yet, there is a curious analogy with observations made by the late Lord BRAIN and WILKINSON (1959). They examined the reflex zones of the Babinski reflex at and after birth and found that these diminished in an oro-caudal pattern in an exactly parallel time sequence to that which we had observed for motor development. This is quite logical if one interprets the Babinski reflex as a release phenomenon following pyramidal tract destruction or nonfunction. Lord BRAIN included our timetable (Fig. 2) in his description as his first figure.

Which are the centers responsible for the initially uncontrolled movements of the newborn and by what process are they inactivated? When the involuntary kicking movements are present - i.e. immediately after birth - only the "extrapyramidal" pathways caudal to the pallidum are myelinated and therefore able to function. There are no myelinated direct corticospinal pathways present at this time. As was first described by FLECHSIG (1927), only those pathways which pass from the motor cortex down to the mesencephalic level are already myelinated. At the spinal level, the pyramidal pathway is also not yet myelinated and this was demonstrated as early as 1899 by CHRISTFRIED JAKOB (Fig. 3).

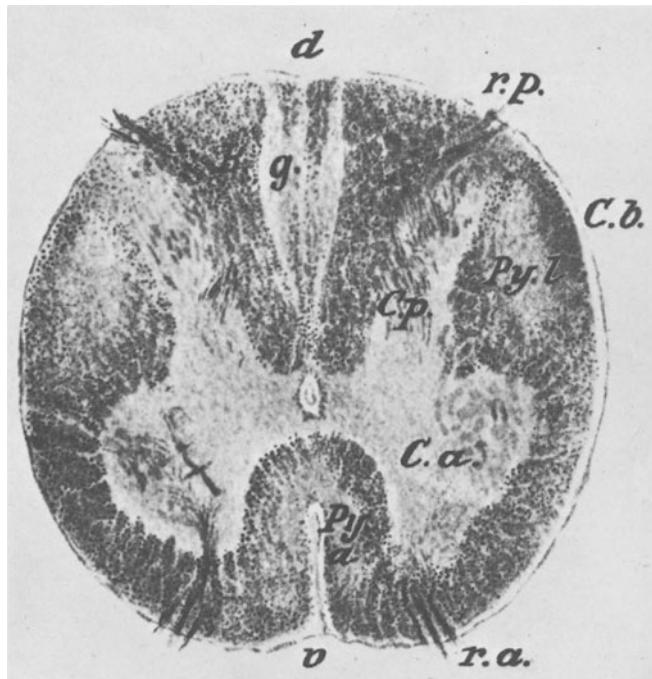


Fig. 3. Both "pyramidal tracts" are unmyelinated in the newborn (from CHRISTFRIED JAKOB)

The uncoordinated motor pattern of the newborn must therefore be subserved by a morphological substratum which is already myelinated and consists of the extrapyramidal motor nuclei, including the globus pallidus, the subthalamic nucleus, and substantia reticularis together with their descending pathways. Simultaneously however, the same motor performance may also be achieved by a morphological apparatus, present caudally in the mesencephalon, as GAMPER (1926) has shown in his "Mittelhirnwesen" (mesencephalic being), a newborn child who reached the age of 3 months. In this little creature the highest nucleus which could be seen was the red nucleus; even the substantia nigra was absent, so that naturally there were no pyramidal pathways. GAMPER found that the motor performance of this child did not differ from those of a normal newborn. The movements consisted of synergies which GAMPER likened to the synergies described by FOERSTER.

The evidence suggests then that immediately after birth, the motor patterns are initiated by an "archaic" apparatus which is later suppressed by the higher "voluntary" functions of the pyramidal pathway in an oro-caudal sequence whereby these voluntary movements are facilitated.

The pathways for the "Ersatzbewegungen" (supplementary motor functions); the ipsilateral part of the pyramidal pathway; the "deep" motor systems: We have now to answer the question: in what way are the voluntary movements of the compensatory motor systems (synergies) brought into function after destruction of the pyramidal pathway? It is most useful to start with the morphological analysis of the central nervous system in a child with spastic hemiplegia. In this case the cause of the destruction of the pyramidal pathway is usually a huge porencephaly: here the pyramid on the side of the lesion is not present and the contralateral pyramid may seem to be enlarged (Fig. 4). According to old examinations, this is not due to an increase in the number of fibers, but to an enlargement of the myelin sheaths. The compensatory motor system thus cannot use the fibers of the pyramidal pathway, only the so-called "parapyramidal" part of the great motor systems - described above - is available. The question arises as to whether: 1) an ipsilateral system, i.e. the (up to) 10% of the pyramidal fibers which go in the anteromedial spinal cord or the 1% uncrossed in the posterolateral, could be responsible for these compensatory motor function (a concept put forward by GLEES and COLE, 1952); or 2) whether there is a system of archaic motor centers which are now providing vicarious functions; this seems to me the most likely explanation, corresponding to what we would like to call the "parapyramidal pathway" (see above). This would correlate well with WOOLSEY's observations in the monkey (see p. 27) and the concept of OBRADOR (1964) or KUYPERS (see p. 324).

The discussion of this question goes back to ANTON (1906, 1926) and ROTHMAN (1914) and particularly to OTFRID FOERSTER (1936). The latter believed that these supplementary movements were derived from the cortical "adversive fields", and he particularly stressed this when he read the memorial lecture on the occasion of the 100th anniversary of JACKSON during the International Neu-



Fig. 4. Medulla oblongata of porencephalic child with typical lack of one pyramid

rological Congress of 1935. There are, however, two observations which contradict this concept. 1. A child with spastic hemiplegia has no "pyramid" (Fig. 4) in which would run the pathways from the adversive fields, and yet it can walk. 2. After hemispherectomy, with loss of all the existing adversive fields, the synergic motor functions are not altered but are even better than before operation; this can be explained by a certain loss of spasticity. The possibility that the "contralateral" (with regard to the pyramid) adversive fields could provide motor impulses, for instance through the median commissures to the contralateral (hemispherectomized) side is thus excluded. Furthermore these fields cannot add to the action of the basal ganglia of the hemispherectomized side, since these were excised in a patient who was still able to walk (ZÜLCH, 1956): no part of the contralateral hemisphere could in this case provide "centers" for willed movements!

The contribution of the ipsilateral pyramidal pathway. Is the compensatory mobility subserved by the ipsilateral pyramidal pathway? Observations in humans tend to contradict this proposition. After bilateral destruction of the motor cortex near the sagittal sinus, as seen occasionally in war wounds where both areas for lower limb movement had been destroyed, in many cases walking was still possible, since sufficient supplementary function for the legs was provided. Obviously this preservation of movement could not have been the function of an ipsilateral motor pathway, since both cortical substrata had been destroyed, at least for the leg. This example has been cited frequently by RITCHIE RUSSELL in support

of the concept of an ipsilateral contribution, but our own experience with war wounds differs from what he has reported. I have never observed a difference in the contralateral side in cases of unilateral lesions or in both sides where the cortical lesion was bilateral. This seems to fit the observation that children with spastic infantile diplegia of the "Little" type can usually walk, provided spasticity is not too marked, and yet they have no functioning motor cortical areas for the legs (ZÜLCH, 1963).

It is reasonable to conclude that the likelihood that ipsilateral pyramidal action provides compensatory motor function can practically be excluded, if my interpretation of these clinical observations is correct. This does not imply that one must deny any function of the ipsilateral pyramidal pathway. We can, for instance, assume that in eye movements the proportion of crossed and uncrossed pyramidal fibers is, most probably, almost equal; hemispherectomy remains without influence. However, from the observation that in one of our cases a squint disappeared after hemispherectomy, it may be deduced that relatively, the crossing fibers predominate. This could probably be accounted for by the influence of the paretic side. An even better example of the action of the uncrossed part of the ipsilateral pyramidal pathway is the so-called "identical associated movements" (see p. 5) which can clearly be seen after hemispherectomy (ZÜLCH, 1954, 1956). These are probably elicited through the ipsilateral pyramidal pathway.

The results of animal experimentation. The question now arises as to how this phenomenon of strictly linked patterns of synergy coincides with our knowledge of the motor systems in the primates. Investigations of these synergies have been undertaken after cortectomies in monkeys. This is the only species in the "evolutionary ladder" which can be used experimentally, because they have similar pyramidal, extrapyramidal, and parapyramidal systems. It seems that the monkey principally uses a synergic motility (KENNARD, 1938), which, however, can be improved at any time to attain the highest isolated voluntary performances. The latter are abolished by corresponding cortectomies, the former - as in climbing trees, clinging, jumping etc. - do not show much alteration whether the cortex is removed in the infant or later on in life. Unfortunately time does not permit me to go into the details of the fascinating wealth of comparative observations (see ZÜLCH, 1969) obtained from cortectomy, pyramidotomy and even hemispherectomy in experimental animals (WOOLSEY, p. 17ff.; GLEES, p. 48ff.; DENNY-BROWN, p. 62ff.). It must mention, however, that I would hesitate to subscribe to the statements of BUCY (1949), SARA TOWER (1949), and HINES (1949); I have always had some doubts as to whether the same methods of neurological examination are being applied in man and in these monkeys for the detection of alterations of motor skill after pyramidal lesions. Furthermore, most of the experiments at that time were "acute" and not "chronic". In this opinion I am in the company of neurologists such as Sir FRANCIS WALSHE (1961) and DEREK DENNY-BROWN (1966), the latter himself having a broad experience in monkey experimentation. The disturbance of isolated movements - as I would define it - can be

recognized in the monkey only under very stringent test conditions and we were glad to have these excellently described in the experiments of Dr. WOOLSEY (see p. 27). I find no basic contradictions in Dr. WOOLSEY's experiments and feel that LAWRENCE and KUYPERS (1968, a, b) and KUYPERS (1973) arrive at very similar concepts in their monkey experiments. They describe the synergic type of motility after double pyramidotomies ("brain stem pathways acting on the spinal cord... the capacity for individual finger movements never returns...").

Pathophysiology of supplementary movement after destruction of the pyramidal pathway: Let us now go on to the final part of this presentation and deal with three remaining problems:

1. What is the anatomic substratum for the compensatory motility observed in man?
2. What triggers this compensatory motility following destruction of the pyramidal pathway?
3. How is the compensatory motility, which at first is completely reflex, transformed into voluntary movements?

ad 1.: The anatomic apparatus probably exists somewhere in the mesencephalic structures (red nucleus, reticular substance) (Fig. 5) as an "archaic motor system"¹ which becomes available after destruction or failure of development of the pyramidal pathways (ZÜLCH, 1954, 1956, 1969). Stimulation experiments in animals point in this direction and here I can cite KUYPERS (p. 324). There is also a certain amount of proof by analogy: the posture and function of the hand of a child with spastic hemiplegia (Fig. 6) and the type of motility existing in the arm, resemble that of the reptile's paw (ZÜLCH, 1969); the brain of the "tiger salamander" (HERRICK, 1948) in its organization grossly corresponds to a mesencephalic level in mammals. We therefore repeat our working hypothesis, i.e. the anatomic substratum for the compensatory movements after destruction of the pyramidal pathway may be situated in the mesencephalon and more caudally (see also OBRADOR, 1964; KUYPERS, 1973). The statement of D. G. LAWRENCE and H. G. J. M. KUYPERS (1968) that "on the basis of our observations we conclude that in the absence of the corticospinal pathways, the descending subcorticospinal pathways are capable of guiding a range of activity, which includes limb movements in addition to total body-limb activity. The corticospinal pathways superimpose speed and agility upon these subcortical mechanisms, and, in addition provide the capacity

² ROTHMANN (1901) refers to the work of MUNK (1890, 1892) in writing: "... Immerhin zeigten die Extirpationsversuche der Extremitätenregionen als der Ursprungsstätten der Pyramidenbahnen bei Hund und Affe, wie sie besonders HERMANN MUNK in exactester Weise ausgeführt hat, dass sich bei diesen Thieren ... Ausfallserscheinungen, besonders bei den gerade beim Affen sehr ausgebildeten Greifbewegungen zeigen. Es sind also, wie MUNK gelehrt hat, die isolirten oder Sonderbewegungen, die ausgefallen sind, bei Erhaltung der Gemeinschaftsbewegungen ...". ROTHMANN, M.: Berl. Klin. Wschr. 21, 575 (1901).

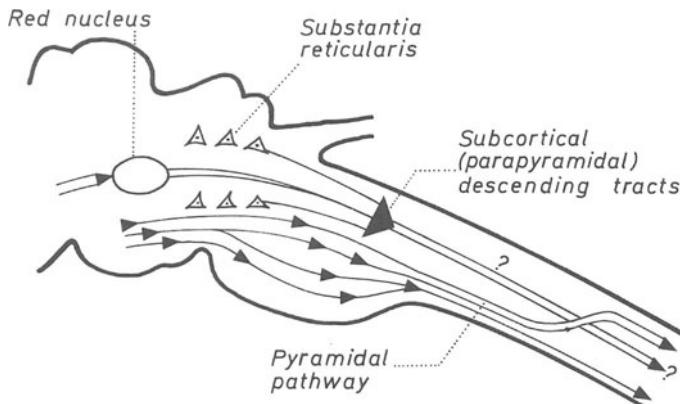


Fig. 5. Dorsal subcortical descending "parapyramidal" and ventral "pyramidal" pathways for "motion"



Fig. 6. Hyperextended ("bayonet-like") fingers in infantile spastic hemiplegia. Similarity to the paw of reptiles

for a high degree of fractionation of movements as exemplified by "individual finger movements...", expresses the same concept and interpretation on the ground of experimental findings.

ad 2.: Triggering the compensatory motility: when we consider what might trigger compensatory motility, we are in the midst of the problem of the organization of the nervous system in man. What is triggering motility when one intends to perform a special movement? The answer must encompass information from many fields of knowledge from philosophy to cell physiology. Our particular problem is the nonexistence of cortical areas to which we ascribe

the triggering capacity of the special type of movements which come from area 4 and the aversive fields. There have been some interesting stimulation experiments by BATES (1953), DENNY-BROWN (1966), and WOOLSEY (1958), which seem to shed some light on this problem. Triggering may come from the contra-, but also from somewhere in the ipsilateral cortex, yet the anatomical substratum for the synergies probably lies deep in the mesencephalon and oblongata. However, electrical stimulation and physiological triggering of a movement are two different modalities, and the final solution to this problem may have to wait until more comprehensive information becomes available.

ad 3.: Reflex or willed movement: our third question is related to the observation that after catastrophic destruction of the pyramidal pathway, the first movements to return are "reflex". Later, "semireflex" movements reappear but the reintroduction of voluntary motility occurs considerably later. Perhaps in this process, descending long gamma systems may play a role, since the process of activation of reflexes by "Jendrassik's manoeuvre" (ZÜLCH and HOSSMANN, 1966) and the appearance of the first semireflex movements after activation of the gamma systems are closely approximated.

As a final test for the functioning of this ipsilateral system we measured evoked potentials (median nerve) in one of our cases (1st case of 1954 who had not the "best" level of sensory performances) and we definitely found them in the parietal region EEG pattern analysis (averaging).

The sensory findings after hemispherectomy: Finally, I will now summarize the sensory findings (ZÜLCH, 1974) which I have demonstrated in the film of a girl aged 12 when she was hemispherectomized. She had been thoroughly examined before and after the operation and again this summer (10 years post-operatively). I have just summarized the findings in 6 hemispherectomized patients, of whom she had gained the highest standard of recovery, whereas in the other 5 patients sensory performance was greatly variable. Without much exaggeration, one can say that she lost practically no sensory capability because of the operation: She could perceive all the stimuli from cotton wool or fine nylon thread at the most distant periphery of the fingers and toes. The quantity of perception changes from proximal to distal. There was deep pressure perception with "Nachdauer" (persistence). Topical perception was best by deep pressure stimuli but also possible with cotton wool or a pinprick. Errors at the index 1/2 - 1 cm (!). All pain stimuli of a sufficient strength were perceived and well localized. There was, however, "hyperpathy" (using the definition given earlier, see ZÜLCH and SCHMID, 1953), which was also true for temperature stimuli, these being easily distinguished (ice-water, and 40°). Graphesthesia was surprisingly good in the face with figures of 1 cm size and at the fingertips with those of 1.5 cm. Position sense was fairly good except at the distal fingers, movement perception was similar. Vibration sense was normal (8/8) proximally, with a slight decrease towards the periphery

(7/8). Stereognosis was never present, just as before the operation; in contrast, two point discrimination was fairly well preserved (1.5 cm on the cheek, 10 cm on the leg, 15 cm on the arm). There were, curiously enough, no extinction phenomena. Using this case as an example, it is difficult to formulate a concept about the anatomical substratum. The whole cortex and also 2/3 of the thalamus was removed in a 5-year-old child and (see ZÜLCH, 1954) the topognosis was excellent. I doubt here that, after healing, parts of the ipsilateral thalamus remained which were still functioning; only an ipsilateral system would in fact be available (POWELL, 1952).

There then follows an enormous amount of sensory perception in various modalities - except stereognosis - which can be performed after hemispherectomy. However, the concept of an ipsilateral system seems particularly hard to envisage because both systems would have to work simultaneously and yet at the same time separately for both sides (see the discrimination of two simultaneous and topographically identical stimuli in the "extinction" test). Since the thalamus probably does not play an essential role in this case, one has to think in terms of two separate but almost identical systems on each side which work for both sides. These may be in a certain collaboration normally but not, however, after hemispherectomy.

The possible role of plasticity in the process of reorganization after birth lesions will be discussed later (p. 319).

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Contra- and Ipsilateral Motor and Sensory Representation in the Cerebral Cortex of Monkey and Man

P. Glees¹

Introduction

Localization of cerebral function is based on experimental and clinical studies. Many of these investigations have one common assumption, namely, that the loss of a particular sensory-motor skill is due to the removal or the disease of a circumscribed cortical region. In addition to this indirect evidence, direct neurophysiological methods of stimulation or recording of cortical potentials have given further direct support for the classical view that some cerebral function is localized (SCHALTENBRAND and WOOLSEY, 1954; GLEES, 1961). Localization of function, at least in the great channels of sensory input and motor output, is strongly supported by anatomical data with special fiber degeneration methods or radioactive methods for demonstrating axonic flow terminations (cf. NAUTA and EBBESON, 1970). These morphological methods demonstrate clearly that circumscribed neural interconnections are the basis for functional localization.

Localization of function is most easily shown in sensory-motor channels, in particular in the relationship of brain and muscle (LIDDELL, 1955). But localization of function is relative, depending on the experimental conditions and the viewpoint the observer is taking. The experiments described below confirm that the pre- and postcentral gyrus in primates has a somato-topic arrangement and, if any of these subdivisions are removed, significant motor or sensory impairments appear; but impressive degrees of recovery of primary functional losses do occur, although such recovery is difficult to reconcile with the detailed localization of muscle response or finer subdivisions of dermatoms in the cerebral cortex.

An even more challenging finding is the preservation of voluntary motor control and sensory awareness and the ability of touch and pain location and shape recognition in the contra-lateral limbs after hemispherectomy. This is contrary to the classical concepts in neurology stating that motor and sensory pathways are entirely crossed. While a research associate to the late Professor of Neurosurgery at Oxford, Sir HUGH CAIRNS, I studied a number of patients for motor and sensory performance before and after hemispherectomy. Two cases (D. W. and D. C.) in particular were fol-

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lowed up extensively and will be discussed after reporting the experimental findings. Further studies of hemispherectomy cases in recent years were made possible through the kindness of Prof. BUSHE, Dept. of Neurosurgery, Göttingen and Dr. med H. BOEHNCKE, Hamburg (his cases were operated on by Prof. KAUTZKY). One main aspect of this contribution concerns therefore the relatively high degree of sensory and motor integration in that half of the human body which would normally be carried out by the now ablated hemisphere. The important question arises as to whether this motor and sensory function has been taken over by the other hemisphere (mainly by the cortex) or is due to a functional takeover of subcortical structures (ZÜLCH, 1954).

GOODDY and MCKISOCK (1951), discussing the retention of some function in the contralateral limbs after hemispherectomy, point out that "residual function must depend on residual cerebral tissue". Like some earlier workers, they suggest that "lower motor structures" play a part in maintaining the patient's use of his limbs contra-lateral to his lesion. To the assistance of these ill-defined subcortical structures come normal cortical and subcortical structures from the intact hemisphere. Intellectual and behavioral changes in a long term follows up have been reported by GRIFFITH and DAVIDSON (1966) and should be consulted.

Experimental Studies in Primates

To gain more insight into the preservation and recovery of somatic functions after cortical lesions, a number of different experiments were performed in macaques and baboons previously trained for a number of dexterity and recognition tasks. In these animals single, repeated and multiple lesions were caused in the sensory-motor cortex (GLEES, 1952, 1953, 1960, 1961; GLEES et al. 1950 a, 1950 b, 1951, 1952, 1958, 1973). Electrical stimulation of the pre-central gyrus or primary somatic area in the normal animal reveals the repeatable somatotopic organization well known to all investigators of cortical motor function (reviewed by GLEES, 1956). E.g. in every primate subject studied by stimulation, the thumb area is sharply separated from the face area and the boundary is outlined by a small artery. Taking the constant and reliable motor responses into account, no surprise is felt when, after ablation of the hand area, disability of hand skill is very evident. Our studies of sensory-motor skill were mainly concentrated on hand skill; we used the problem box, the dexterity board, a shape-discriminating board, and differently shaped objects hidden in a bag (Fig. 1). These tests have been described by GLEES (1961). The significance of the cortical control of hand has recently been reviewed by PHILLIPS (1970). However, when making qualitative and quantitative investigations by stimulation of the previously lesioned cerebral cortex (small lesions in area 4), after the recovery of motor function (GLEES and COLE, 1950) we found that neighboring portions of the same motor cortex had taken over the functional properties of an ablated area. At the same time, our studies strengthened our assumption that the motor cortex, when experimentally interfered with, can no longer be regarded to solely act as a mosaic-like structure. Stimula-

tion experiments by LIDDELL and PHILLIPS (1951) confirmed and amplified this view.

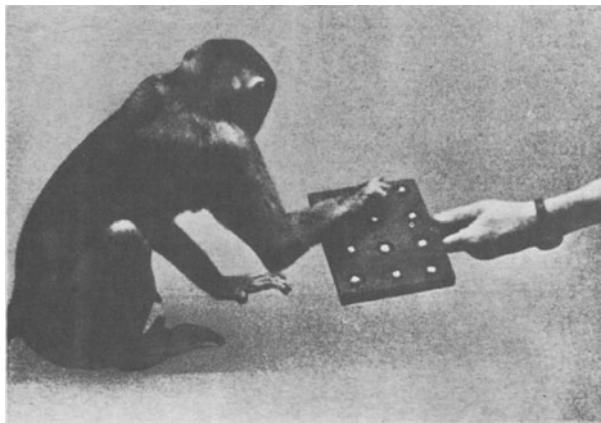


Fig. 1. *Macaca nemestrina*, dexterity test on Klüver board

We also concluded from the study of degenerative cortical fibers that, though a particular subdivision (e.g. the hand area) of the motor cortex sends most of its descending fibers to the appropriate segments of the cervical cord, a minority of fibers are connected with other levels as well. This is true for all subdivisions of area 4. These plurisegmental connections of the major subdivisions of the motor cortex within the cord offer an explanation of motor recovery subsequent to small lesions in area 4. The concept of plurisegmental connections arises from the study of fiber degeneration after causing small cortical lesions in sensory-motor cortex (Figs. 2a, 2b). I am well aware that a critical reviewer of this concept must consider that even small cortical lesions limited to the grey matter may cause additional vascular damage to the underlying white matter and by this causing contaminating fiber degeneration. This identical damage cannot be entirely excluded, but having considered this implication carefully in serial sections, there is little evidence for a contamination of cortical degeneration by subcortically damaged fibers originating in cortical areas not purposely interfered with. In particular, lesions of the foot area cannot damage subcortical white matter of 'face or arm neurons' projecting to medullary or spinal nuclei, for a fair number of degenerated 'foot fibers' terminate already at medullary and motor cervical levels.

The concept of plurisegmental connections from the cortex explains most readily functional recovery and would do more justice to the embryological downgrowth of cortico-fugal fibers, which appear to connect with all levels initially and achieve a more selected mode of projection during maturation. I recall in this connection the

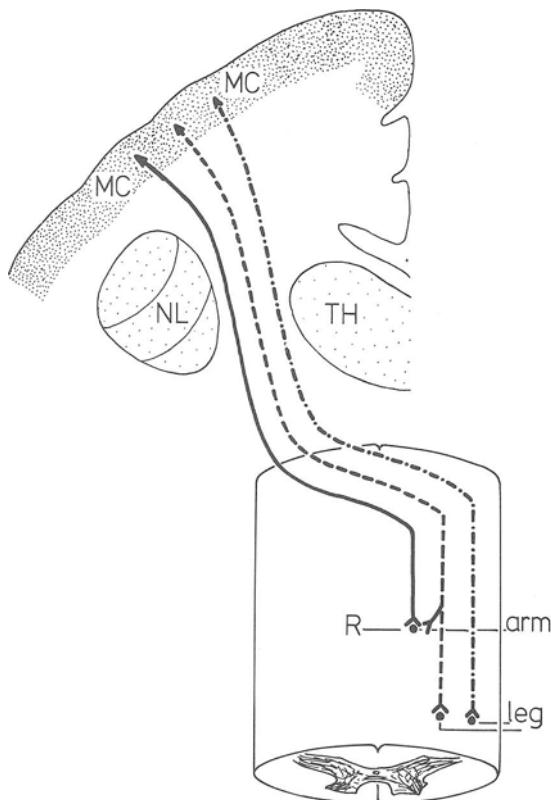


Fig. 2a. Diagrammatic representation of plurisegmental connections of the motor cortex, based on the study of degenerating pyramidal fibers following small cortical lesions. Fibers from a given subdivision of the motor cortex (MC), e.g. arm area, drawn in a continuous line, terminate on cervical relay cells (R) but some fibers either descend directly to lumbar pools or supply collaterals to cervical pools. This neuro-anatomical plurisegmental pattern explains motor recovery for all spinal levels following lesions in a subdivision

NL = Nucleus lentiformis

Th = Thalamus

classical paper by HINES and BOYNTON (1940), who stimulated the cerebral cortex of monkeys at different stages of pre- and postnatal development. They emphasized the holokinetic response pattern at early stages in contrast to highly selective motor points later on. Further physiological support for the diffuse anatomical arrangement of pyramidal fibers in their descending course seems to lie in the finding that cortical lesions in infant monkeys between 3 weeks to 4 months old reveal a great capacity for motor reorganization (KENNARD, 1942). These observations appear to favor the view that cortical connections at the spinal level are initially widespread and become more selected during maturation.

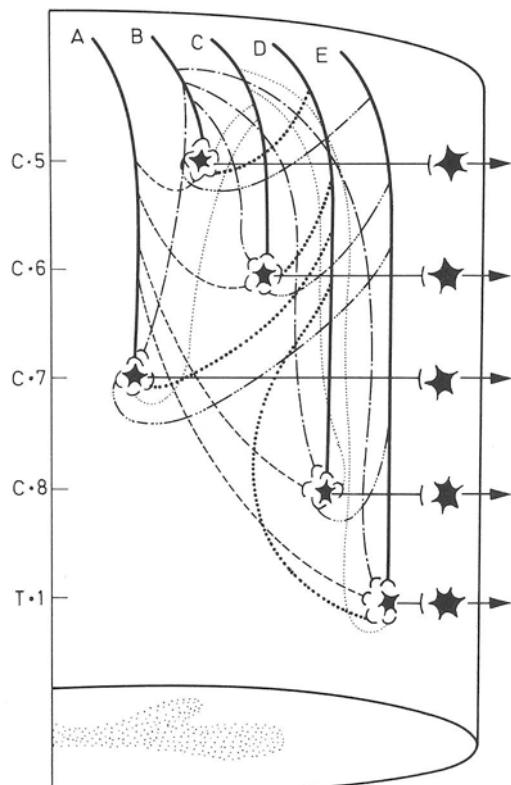


Fig. 2b. Diagrammatic representation of multiple innervation at cervical motor neuron pool. The stem fibers A, B, C, D, E send collaterals to other motor neurons. A possible explanation for motor recovery following minute lesions in hand area

Ipsilateral Fibers from Area 4

In the work summarized above we had developed quantitative tests for measuring the loss and recovery of power and dexterity in the hand contralateral to the lesion (COLE, 1952). When we came to study ipsilateral impairment after lesions in area 4, we were able, by means of the same tests, to state such impairment in quantitative terms (Figs. 3 and 4). Thus we obtained evidence:

1. that cortical areas adjacent to a lesion play a part in the recovery of function in a contralateral limb, as was demonstrated by our earlier work, and
2. that fibers from the *ipsilateral* hemisphere participate in the motor activity of a limb. This latter finding suggests that ipsilateral fibers play an important part in residual function in limbs after a hemispherectomy (Figs. 5 and 6).

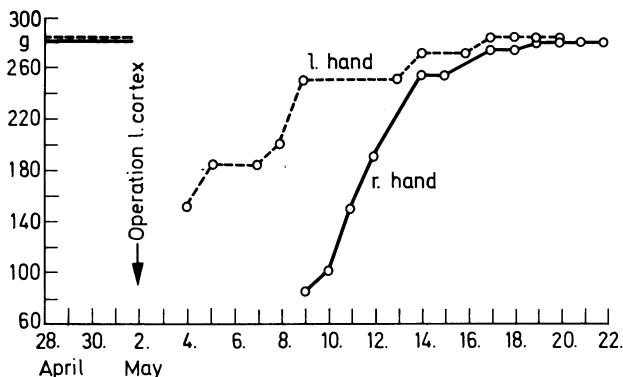


Fig. 3. Depression and recovery of motor power in both hands after multiple small lesions in left area 4

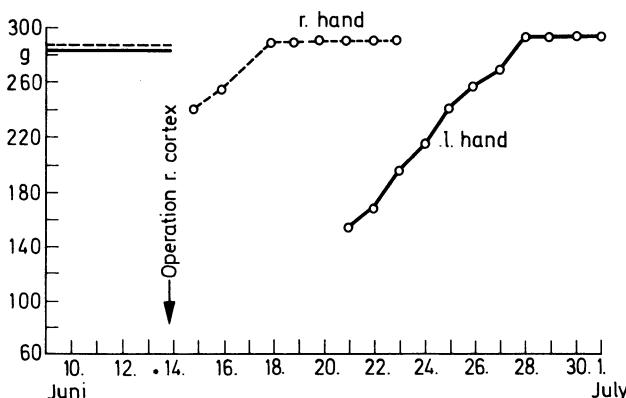


Fig. 4. Depression and recovery of motor power in both hands after multiple small lesions in right area 4

Sensory Cortex

The initial effects of lesions made in the sensory cortex in monkeys involve loss of dexterity and the power to discriminate between different shapes. There is also a loss of tone in the arms; some animals do not seem to be aware of the position of their arms and will hold them for a considerable time in unusual or uncomfortable positions.

There is, however, a considerable degree of recovery from these disabilities, which can be measured by using monkeys trained before operation and again tested on their performance postoperatively. Motor power returns to normal although dexterity remains permanently affected, but the most striking recovery is the complete return of stereognosis, even after ablation of the hand region, the monkeys being able to differentiate by touch between a cone and a pyramid after only a few weeks (COLE and GLEES, 1953). This confirms the findings of RUCH (1935) that a monkey (*Cerco-*

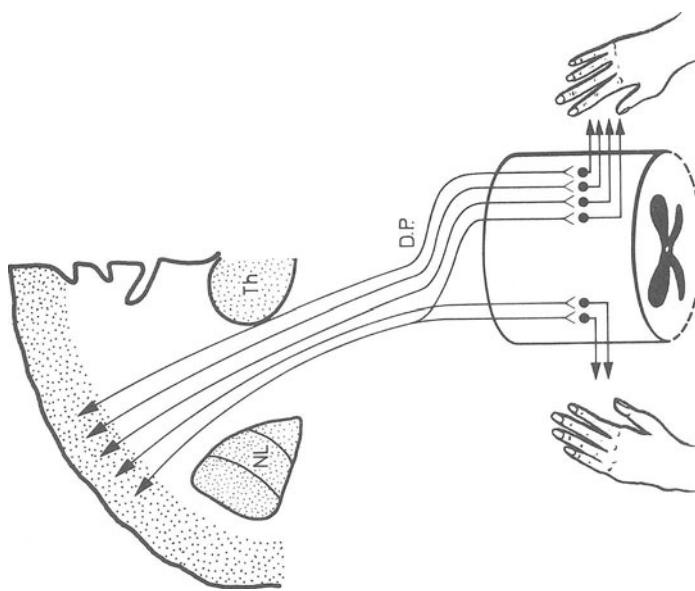


Fig. 6. Ipsilateral contribution to left hand.
These fibers may be collaterals or stem fibers.
NL = Nucleus lentiformis, TH = Thalamus,
D.P. = Decussatio pyramidalis

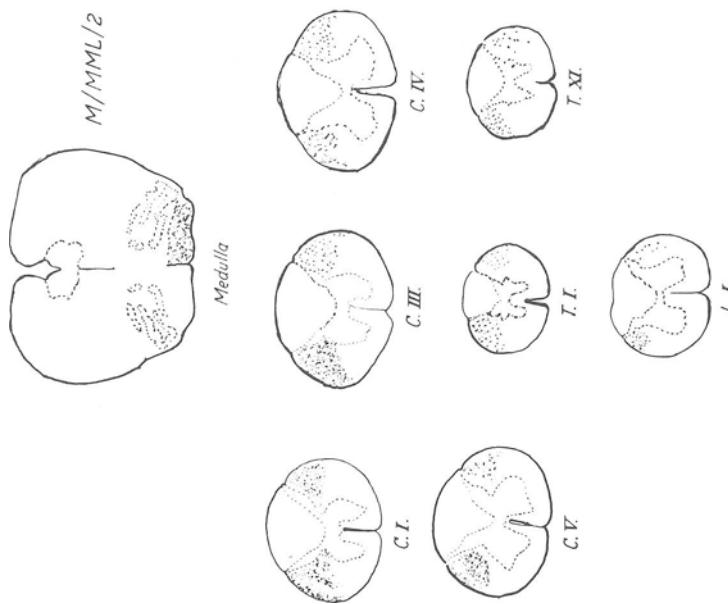


Fig. 5. Fiber degeneration after multiple small lesions in left motor cortex. Note ipsilateral fibers

cebus torquatus atys) trained to discriminate between different weights was still able to do so after ablation of the sensory cortical region.

If sensory impulses from the periphery were projected solely through selected regions of the thalamus onto the sensory cortex, no such recovery of function would be possible. There must therefore be additional pathways which, through facilitation effected by postoperative training, are brought into functional contact with other intact portions of the cortex. After ablation of the hand region of the sensory cortex, the peripheral impulses from the hand may be transmitted from the hand region of the thalamus to another, intact, part of the sensory cortex, or there may be alternative pathways which take impulses from the hand to regions of the thalamus other than the hand region, whence the normal pathway to the appropriate region of the sensory cortex takes over. Other reserve or unspecific pathways must also exist to enable the sensory signals to reach the motor cortex by an alternative route (see Fig. 7) (GLEES, 1953). It is also possible that the motor cortex receives sensory information from the thalamus via the superior cerebellar peduncle (WEINSTEIN et al., 1940). Since the alternative route will normally be used very little, postoperative training is of the utmost importance for its re-activation. The operated animal will refuse to use its impaired arm unless there is some incentive to do so, and its co-operation must be gained by appropriate gastronomic enticement. If these observations are applied to clinical neurology it is most likely that persistent physiotherapy may be the means of producing a certain degree of functional recovery after cortical injury; no doubt the patient will be more willing to co-operate than some operated monkeys, but will be hindered by concomitant spasticity.

The loss of function caused by cortical ablation can be explained by the destruction of the projections with the shortest latent periods, and the recovery of function by use of adjacent cortical areas which receive the same impulses as those destroyed by the lesion, but only after a longer latency. That means that the projection with the shortest latent period is normally in use, but that, if this is destroyed, the equivalent areas with longer latency can take over.

If this explanation of sensory discrimination and function represents the true state of affairs - and it must be remembered that we are a long way from finding the complete answer to all the inherent problems - then we have certainly travelled far from the original conception of the cortex as a mosaic and sensory projection as a point-for-point arrangement. It was said at the beginning of this chapter that the improvement of stimulating technique and the employment of the evoked potential method for mapping sensory projecting has done much to clear up many of the problems, but not all the results gained by better techniques have necessarily supported the view that the difference in latency of the impulses projected to the cortex is the key to sensory discrimination in an intricate pattern of overlapping areas. The older idea of point-for-point projection could not be reconciled with many of the observations made, but the cortical points

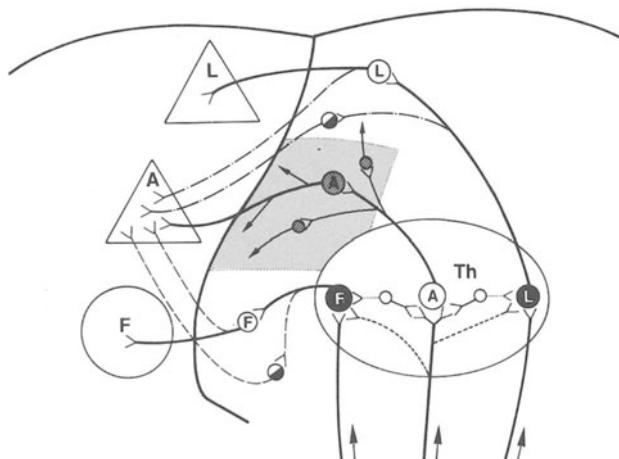


Fig. 7. Diagram explaining the recovery of function after sensory cortex lesions. The arrows indicate the afferent fibers (Medial fillet and spinothalamic fibers) to the thalamus. A = arm area, F = Face area, L = Leg area, Th = thalamus. Alternative routes occur either at thalamic level or at the level of the sensory cortex and are indicated by the interrupted lines (From GLEES, Mschr. Psychiat. Neurol. 125, 129, 1953)

- Thalamic relay
- Intrathalamic relay
- Sensory relay-cortical level
- Additional sensory relay-cortical level
- Normal arm area relays (knocked out by operation)
- △ Motor cortex (Sub-divisions)
- Sensory arm area

involved were all situated on the surface of the cortex and the deeper parts of the postcentral gyrus were disregarded, chiefly for the excellent reason that it is difficult to record accurately below the surface. By using fine microelectrodes this has now become possible and has been the means of disclosing other possible methods of sensory organization. MOUNTCASTLE has published his conclusions from microelectrode experiments, the results of which showed that within the primary sensory cortex different types of sensory receptors project onto the different subdivisions: proprioceptors send impulses to area 2, cutaneous receptors to area 3 (MOUNTCASTLE et al., 1957). Mountcastle tends towards the point-for-point theory, for he reports that within each area of the primary sensory cortex each neurone receives on-

ly one type of stimulus from one specified area of the skin, with no overlap involved, and that all projection is contralateral. But it is not only the neurones on the surface of the cortex which respond; peripheral stimulation initially causes activity in vertically orientated columns of cells, which all fire simultaneously (POWELL and MOUNTCASTLE, 1959 b). Each column of cells in the sensory cortex is therefore related to a restricted peripheral receptor area, an arrangement which is justified by Mountcastle's view of the anatomical pathways via dorsal column nuclei and thalamus. The very restricted area of discharge is explained by the presence of a zone of inhibition round the excited area, which MOUNTCASTLE and POWELL (1959) found to exist not only at the periphery but at all levels in the ascending pathway. A center of excitation is thus surrounded by an area which prevents the discharge of neighboring cells and may even limit the projection of impulses from a nearby cutaneous site to a smaller area, if two sites are stimulated simultaneously. The simultaneous response of a whole column of cells to stimulation of a restricted area of the skin implies a point-for-point projection for spatial stimulation, but does not suggest the means of discriminating different types of stimuli applied to the same spot. It was mentioned in the previous chapter that the postero-medial ventral nucleus of the thalamus may relay taste as well as other sensory modalities to the sensory cortex, and there is some evidence that both taste and touch are projected onto the same area in the sensory cortex of the cat (COHEN et al., 1957). The only topographical difference in the neurones responding seemed to be the slightly more superficial position of 'touch' cells. Other neurones, however, showed no inclination to restrict their response to any particular type of stimulus and discharged equally strongly to thermal, tactile, and taste stimuli (LANDGREN, 1957, 1959). This would mean that projection to the sensory cortex is both by pathways concerned with one modality only and by pathways common to a number of different sensations.

How the convergence of different pathways onto the same neurone, as evidenced by overlap, the return of function, or the difference in latencies, can be combined with the organization of columns of cells with a restricted zone of discharge and a point-for-point projection is difficult to say. We are in fact far from finding the definite answer to the question of sensory function, and this can only be done by either abandoning one or other of the two points of view or reconciling the two; in either case the information available so far is much too scanty. However, the above reported experiments in primates should be helpful in understanding residual motor power and sensory awareness in those regions of the patient's body deprived of normal cortical control and receiving areas. The film (shown at the meeting) of a patient, R. L., who was closely followed up after undergoing a hemispherectomy operation at the age of 10 and who died aged 21 of persistent cranial bleeding (OPPENHEIMER and GRIFFITH, 1966) is typical for the preservation of some voluntary motor power and sensory awareness.

The patient having lost the right hemisphere is still capable of raising his left arm, flexing it in one elbow joint and flexing his thumb when this was

extended previously. Tongue, eye, and facial movements are all practically normal. Obviously the range of movements in the left arm would be greater if considerable spasticity did not prevail. Location of pain and tactile stimuli is misjudged but repetition improves accuracy. Weight measurement is grossly impaired but the patient has a relative judgement of weights. Shape discrimination, e.g. the values of coins, is not accurate but again relative evaluations are possible and a number of objects can be identified (cf. BÖHM, 1962). There seems to me no doubt that residual motor power and sensory recognition is controlled and perceived in the remaining ipsilateral cerebral cortex.

Finally I would like to point out that the main emphasis of this paper lies on the cortical control of motor and sensory performance. For this reason subcortical integrative properties of the pyramidal system cannot be considered, however the review of WIESENDANGER and TARNECKI (1966) should be consulted on this aspect and the paper by HEPP-REMOND and WIESENDANGER (1971) and FELIX and WIESENDANGER (1971) deal with the sensory motor skill of trained monkeys after sectioning of one pyramidal tract.

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Discussion

Dr. WOOLSEY: Do you have any information about where the ipsilateral corticospinal tract terminates when it reaches the cord?

Dr. GLEES: The fibers terminate on internuncial neurons in the dorsomedial portion of the cord on the ipsilateral side. However, we know now that even contralateral fibers re-cross at spinal level.

Dr. WOOLSEY: Has anyone ever done experiments to demonstrate the motor aspect of these ipsilateral components, especially those coming from the arm area and going to the leg portion of the cord? Could they have inhibitory actions on other functions of the cord involving the lumbar level?

Dr. GLEES: This is possible, but I cannot give any answer to this point.

Dr. KUYPERS: In respect to the question of Dr. Woolsey I would like to point out that according to the findings of LIU and CHAMBERS (1964)² as well as those of KUYPERS and BRINKMAN (1970)³ it appears that the ipsilateral descending cortico-spinal fibers terminate both ipsilaterally and contralaterally. Moreover, the contralaterally descending cortico-spinal fibers likewise terminate not only contralaterally but also ipsilaterally. The ventral ipsilaterally descending cortico-spinal tract may therefore be regarded as a group of cortico-spinal fibers which undergo a delayed decussation. Further Miss BRINKMAN and I have extended Dr. GLEES' observations by making lesions in the different parts of the precentral motor cortex and counting the degenerating elements in the different spinal segments. From these findings it appeared that the cortical projections to the motoneurons and to the dorsolateral part of the intermediate zone and those to its ventromedial parts of the intermediate come from different cortical areas. For example the projections to the low cervical motoneu-

² LIU, C. N., and CHAMBERS, W. W.: An experiment study of the cortico-spinal system in the monkey (*Macaca mulatta*). *J. comp. Neurol.* 123, 257-284 (1964).

³ KUYPERS, H. G. J. M., and BRINKMAN, J.: Precentral projections to different parts of the spinal intermediate zone in the rhesus monkey. *Brain Research* 24, 29-48 (1970).

rons have a very restricted origin in the hand area of the motor cortex. However, the projections to the ventromedial part of the intermediate zone of the cervical segments have a less restricted origin and come for example from an area along the central sulcus immediately dorsal to the hand area as well as from more rostral parts of the precentral gyrus. Thus the areas of Dr. WOOLSEY's map which carry representations of more proximal movements seem to distribute fibers preferentially to the ventromedial parts of the intermediate zone, while the areas which carry hand and foot representation are the main sources of the cortical fibers to motoneuronal cell groups of the low cervical and lumbosacral segments respectively.

Dr. ZÜLCH: With regard to the motoraction of the ipsilateral pathway, I have a quite different opinion to that of Dr. GLEES; you have noticed that (p. 32). Here I would like to mention a clinical example for the ipsilateral action of the pyramidal pathway: the "identical" or "mirror" movements, a particular kind of associated movement. If, for instance, you have a patient with a right-sided spastic infantile paralysis and if you try to have the patient flex the index of the normal side against resistance, then the index on the paretic side will do an identical movement. This to me is one of the actions of the ipsilateral pyramidal pathway.⁴

Dr. OBRADOR: I want to support what Dr. ZÜLCH has said; in a review I made of our first twenty cases with hemispherectomy some years ago⁵, we were able also to see what has been said here. Moreover, in those patients with cerebral infantile hemiplegia with a long-lasting lesion, removal of the hemisphere did not greatly affect the myotonic reflex and the cutaneous responses, probably because they were isolated already for a long time. Therefore, it seems to me that the section of the hemisphere with lesions already established for a long time is different from the experimentation in monkeys.

Dr. GLEES: You must motivate the ipsilateral component very strongly and this is usually not done, or very difficult to do, in patients. This is also true for monkeys; you have to do it either by tying the intact arm or otherwise immobilize it. We have gone as far as to cut the brachial plexus to motivate the ipsilateral component.

⁴ ZÜLCH, K. J.: Die Mitbewegungen bei Hirnverletzten. Zbl. Neurochir. 7, 160-186 (1942). ZÜLCH, K. J., MÜLLER, N.: Associated movements in man. In: Handbook of Clinical Neurology, Vol. I, pp. 404-426, edit. by VINKEN and BRUYN. Amsterdam: North Holland 1969.

⁵ OBRADOR, S.: Nervous Integration after Hemispherectomy in Man. In: Cerebral Localization and Organization, edit. by G. SCHALTENBRAND and C. WOOLSEY, pp. 133-146. Madison: The University of Wisconsin Press 1964.

The Localization of Hemispheric Mechanisms of Visually Directed Reaching and Grasping¹

D. Denny-Brown², N. Yanagisawa³, and E. J. Kirk⁴

KENNARD (1936) first drew attention to the remarkable potential of the infant macaque monkey for recovery of motor function following removal of the motor cortex from both hemispheres. In later work she found that additional removal of both frontal lobes resulted in greater spasticity, comparable to that produced by removal of motor cortex in the adult monkey. Additional removal of post-central parietal cortex also resulted in the appearance of a spastic overadducted gait. It was concluded that in the very young animal the management of motor function was largely subcortical, and that towards the end of the first year the frontal and parietal lobes had developed some ability to compensate for loss of such cortical motor function as had developed at that age (KENNARD, 1938, 1942; KENNARD and FULTON, 1942).

At the time of KENNARD's reports it had been difficult to maintain survival of the adult macaque monkey after bilateral removal of areas 6 and 4 of BRODMANN, with which the studies on infants were compared. Subsequently, with improved methods of cortical ablation by suction, and particularly with encouragement of the animals to make full use of the limbs, survival of adult macaque monkeys for long periods after much larger extents of cortical ablation has been regularly attained. Thus, TRAVIS and WOOLSEY (1956) found that after removal of the motor and premotor cortex of both sides it was possible for an adult animal to pick up raisins with either hand and carry them to the mouth, though the hands and limbs were spastic, and all fingers and thumb moved together in a clumsy grasp. If in addition the parietal lobes were removed the limbs became malplaced, the hind limbs over adducted, the forelimbs widely abducted, gait unstable and righting very slow and often impossible. Food could no longer be brought to the mouth by hand (TRAVIS and WOOLSEY, 1956, animal 51-47). We ourselves have maintained such an animal with bilateral pre- and post-central ablation for a year with identical findings. The animal could reach for an object, or for support by a wide sweep

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of the arm, which could result in a useful hook-grip of cage wire for righting (CAB 15, Fig. 1a), or even to pull a piece of food towards him, but could not take food to the mouth. The upper limbs could abduct to clasp a pole or other broad object, but not the lower limbs which were very spastic.

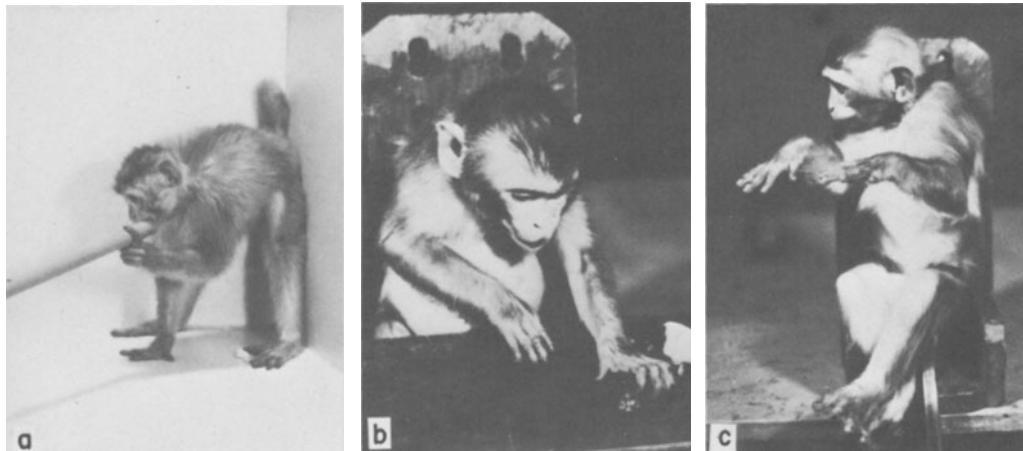


Fig. 1. a, shows the adult monkey CAB 15, 43 days after bilateral ablation of areas 6, 4, and post-central gyrus in the pattern shown for CAB 18, (Fig. 2) biting and hooking the left hand over a stick introduced into his cage. b, shows the animal CAB 52, 181 days after bilateral ablation of area 4 reaching and grasping a piece of food. c, shows the animal CAB 59, 65 days after bilateral ablation of areas 6 and 4

Though the adult monkey can survive more extensive cortical ablations, even complete bilateral decortication sparing the insula, and can right, walk and even exhibit coarse contact placing in the first few days (DENNY-BROWN, 1966) an intense "spastic dystonia" develops between the fifth and tenth day, resulting in complete immobilization. The additional element is a diffuse plastic rigidity that we call "flexion dystonia" associated with great intensification of all body contact reactions (DENNY-BROWN, 1966), and is seen only in primates.

The Motor Status of the Infant Macaque

To appreciate fully the significance of the observations of KENNARD we must also look more closely at the motor behavior of the infant macaque. The development of such behavior in the first year has been reported in the classical study by HINES (1942). In relation to our present thesis it is important to note that though righting, crouching postures, quadripedal progression and standing develop in the first five days after birth, and placing

and hopping in the second week, grasping is limited to a wide sweeping rhythmical clawing movement, with tight closure of the fingers and toes on heavy contact. This movement, used at first for support and righting, becomes adapted to reach for objects after the second week, and to carry them to the mouth by the sixth week. Objects can be held clumsily in the fist as early as the third week. The development of manual dexterity is thereafter very slow. Independent use of digits, and of pronation-supination appear only after four or five months, and the facile use of the hand of the macaque monkey is not fully developed until after the end of the first year.

Bilateral Removal of Area 4 of Brodmann in the Infant

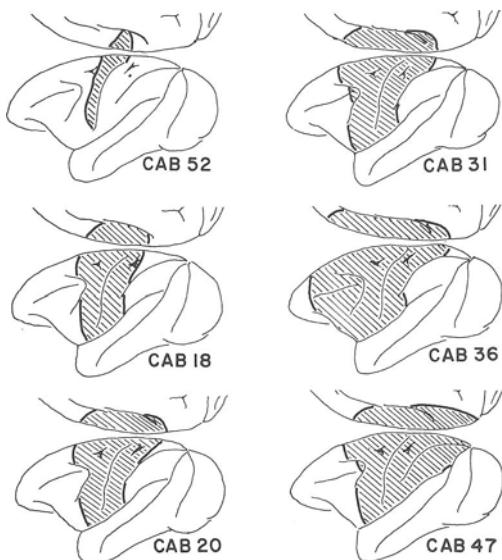


Fig. 2. Diagrams to show the extent of the bilateral ablations described in the text. Each ablation was made first on the left side, then at a second operation on the right, by suction, leaving most of the pia arachnoid intact, after bone flap operation. The extent of the ablation in each case was checked by serial sections stained with Luxol fast blue. When the ablation reached a sulcus the bank of the sulcus was removed to its full depth

Ablation of area 4 by suction two weeks after birth in the pattern shown in CAB 52 in Fig. 2 on the left side, and on the other side on the 33rd day of life, resulted in no defect in natural motor behavior. After the first, unilateral ablation it was evident that the grasp was weaker in the opposite hand, but the difference was very slight. Also, when the animal was supported in a sitting posture and vision excluded a slight contact with the affected hand or foot elicited no reaction, whereas it caused a



Fig. 3. Three frames from moving pictures to show in a, an 18-day-old normal infant teaching for a surface by vision, and in b, CAB 52 reaching for a surface 1 day after removal of the second area 4

small grasp or avoiding movement on the normal side. The biceps and quadriceps jerk were also slightly brisker on the affected side. Five days after the second ablation it was difficult to demonstrate any behavioral defect compared with a control animal (Fig. 3). The traction grasp was excellent in strength on both sides, with very good tilt and hopping reactions. By the end of the first month the tendon reflexes were still very active, with irradiation from biceps to fingers, and quadriceps to toes, but there was no clonus and doubtful, if any constant resistance to passive movement. Extension of the upper limbs as the animal was tilted forward and flexion of the lower limbs as he was held head down were more obvious than in control animals. The slight resistance to passive correction of these postures was very mild in degree. By the end of the second month he could walk on the two hind limbs without use of arms, and showed good visual placing. He could paw at objects and at the end of the third month pick up pieces of grape or apple with either hand and carry them to his mouth. There was a good grasp reflex in hands and feet, and

simple flexion avoiding to noxious stimulus. There was no tactile orientation or tactile placing though on the 123rd day he placed clumsily and slowly to heavy contact displacement. A very slight resistance to passive movement could be felt in wrist and finger flexors, but spasticity was otherwise absent. The condition then remained unchanged until 14 months of age, when further operative procedures were carried out. The animal could reach for a grape by vision, peel it using one hand to hold it, with opposed thumb but no movement of individual fingers (Fig. 1b). When blindfolded the animal remained very flexed, and would grasp only if traction was made on the fingers or toes.

These findings indicate that the motor behavior of the infant macaque monkey is largely made up of visual reaching and placing reactions. In the second half of the first year, when the normal animal develops facile manipulation of objects and tactile orientation to surfaces, CAB 52 failed to acquire these abilities, but did not develop any further spastic change.

In another animal, CAB 59, we removed the whole of areas 4 and 6, left side at 39 days, right at 54 days. There was no defect in visual reaching to objects or surfaces, even on the 1st day after the second operation, but grasping was only a coarse grasp reflex, without tactile orientation. Within a few days all limbs were slightly spastic, and by the 100th day there was an obvious spasticity with a very mechanical stiff gait, and occasional unpredictable jumps. The fingers and toes remained stiffly extended until grasping occurred (Fig. 1c). The tendon jerks were clonic. Placing by vision or contact remained slow. Though he could grasp objects clumsily by vision or contact, spasticity prevented them from being carried to the mouth. There was no defect in movements of head or eyes, though the neck reflexes were exaggerated. Thus, there is no doubt that the infant can develop classical extensor spasticity, but the problem is in the nature of paralysis.

Pre- and Post-Central Ablation

Complete removal of the cortex of areas 6 and 4, together with post-central gyrus, on both sides, left on 24th day, right on 67th day in CAB 18 (Fig. 2), was followed by ability to right and walk from the 2nd day after the second operation. By the 9th day he could right, crouch and run without any apparent difficulty. He could place by vision by a kind of progression movement, as if he walked on to the new surface. There was a strong traction grasp in all limbs, and he could clasp for support by a wide abduction movement of one or both arms. After 2 months he was able to pick up pieces of food with either hand and carry them to his mouth. On the 79th day he picked up a grape by the stalk, held it between fingers and thumb. He was able to transfer a piece of food from one hand to the other. The knee and biceps jerks were very active, but there was no irradiation and no clonus. Finger and toe jerks were not increased. When held head up then head down in air he showed good labyrinthine reversal of hemiplegic posture, which offered only very slight resistance to passive movement. At 289 days he could jump from the floor to a horizontal bar or to the ceiling wire of his cage successfully. When suspended close

to a pillar he embraced it with his arms but not the lower limbs. There was only a very slight spastic clawing of the fingers. A slight grasp reflex with good reinforcement by traction was present in hands and feet. There was no oriented movement to contact. The condition then remained unchanged (Fig. 4a) until the age of 15 months when he was subjected to another procedure.

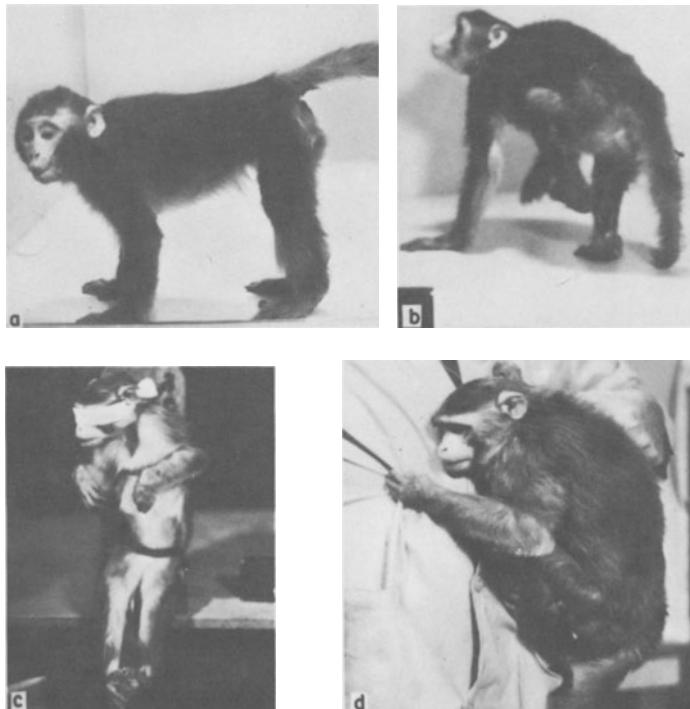


Fig. 4. In a, the animal CAB 18 is shown standing and vocalizing 225 days after bilateral cortical ablation. In b is shown CAB 20, 1176 days after bilateral cortical ablation, in c, CAB 20 blindfolded, and in d, reaching for, and grasping the examiner's coat with her hands, but not using the lower limbs, at the same examination as b

This experiment indicated that the ablation of post-central gyrus (areas 3, 1 and 2), in addition to area 4, added no further motor disability except a difficulty in abduction of lower limbs and slightly increased spastic phenomena, particularly in the lower limbs.

Encroachment on Mid-Parietal Cortex

The animal CAB 20 (Fig. 2) had a more generous ablation of area 6 as well as area 4 and post-central gyrus on both sides, left

at 9th day and right at 23rd day after birth. In the first weeks after bilateral ablation this animal was indistinguishable from normal controls except for an occasional difficulty in relaxing the grasp of either hand, and an inability to place the lower limbs by vision, or to embrace a vertical surface. Also, on moving forward the lower limbs showed occasional jerks of overflexion at the hip joints, with occasional sudden jumps or hops. Nevertheless she was able to stand on the two lower limbs alone and reach high in her cage by the end of the first month. Overflexion of the hips in walking became more troublesome in the second and third months. She was able to grasp a morsel of food clumsily in either hand and carry it to the mouth by the 100th day in the same manner as animals CAB 52 and 18. After the 250th day the lower limbs became continuously overadducted and flexed, with rapid jerky extensions that propelled the animal in kangaroo fashion (Fig. 4b). There was a soft resistance to passive extension, most marked in the flexors and adductors of the hip joints. The tendon reflexes in all limbs were all very rapid, with irradiation to the other joints in the limb, but there was no clonus. Hopping was performed stiffly and visual placing took the form of a repetitive sweep of the arms at a new surface. The feet did not place. When blindfolded the animal held all limbs flexed, with mild rigidity, and did not respond to contacts (Fig. 4c). Righting was accomplished by the upper limbs alone, standing being achieved by a sudden twist of trunk and pelvis. The animal could abduct and embrace a pole or other wide surface (Fig. 4d) with the arms but the lower limbs in these circumstances remained flexed and adducted. The animal was observed for over 3 1/2 years before a further final procedure, without further change. In particular, there was no further development of spasticity. Section of lower medulla showed approximately 2000 medullated fibers remaining in each pyramid.

Bilateral ablation of the anterior half of the parietal lobe, in addition to motor cortex, including the greater part of area 5, was studied in animals CAB 31 and CAB 36 (Fig. 2). CAB 31 was operated on 19th and 37th days, and survived 451 days. CAB 36 was operated 12 and 31st days, and studied for 271 days. CAB 36 had a greater extent of removal of frontal cortex as well as area 5 (upperbank of intraparietal sulcus, Fig. 6). Whereas the animals CAB 52, 18 and 20 had presented no difficulty feeding, both CAB 31 and 36 had great difficulty from spastic closure of the mouth and jaws for the first 3 days, and were very delayed in developing ability to chew solid food. They ultimately showed sucking movement in response to visual stimulus. Both animals walked within a few days but circled to the side of the last ablation for a week or more. For the first 2 months the animals walked on flexed limbs which presented a soft yielding spasticity with very rapid, irradiating and clonic tendon reflexes after the first week. The reaching grasp towards a new surface was rhythmical, and alternated in the four limbs in the manner of quadripedal progression, with clawing of the overextended fingers and toes, but the arms would abduct to an approaching broad surface (Fig. 5b). There was no reaction to objects until the 7th week when an ineffectual hooking of either arm at a piece of food, in a feline manner, first appeared. This movement was most frequently bilateral, mov-

ing food towards the head, but without resulting in carrying food to the mouth. In 16 months CAB 31 was never able to achieve more use of the hands. CAB 36 could make the same modified progression movement to claw at a cloth, but never at particles of food, or even a feeding bottle, in the whole period of survival. Both animals continued to react to an approaching surface by a progression movement, with appropriate turning of the head, eyes, and body, whether in response to visual stimulus or to very coarse contact when blindfolded. There was no visual or contact placing in the sense of a directed support reaction. Both animals righted by extending the upper limbs and then making a body turn.

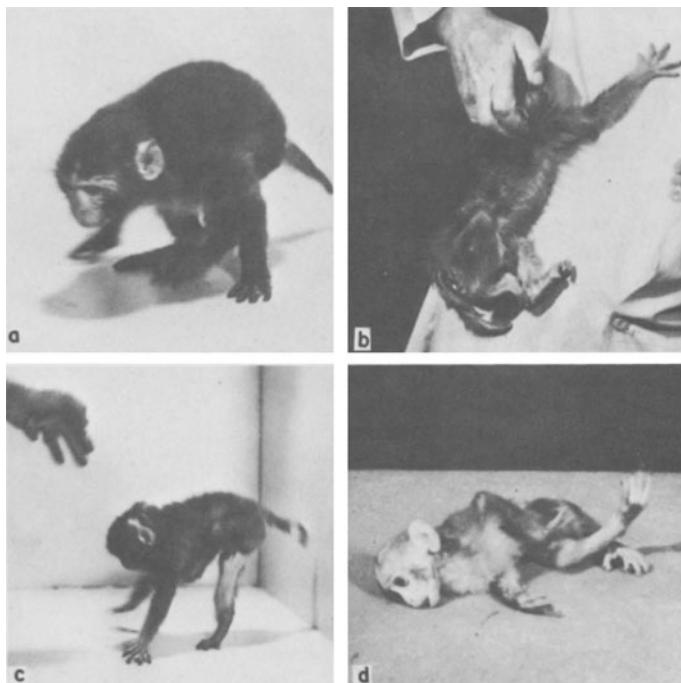


Fig. 5. In a, the animal CAB 31 is shown 395 days after bilateral ablation, in b, CAB 36 grasping the examiner's coat 182 days after bilateral ablation, and in c, CAB 36 walking with dystonic lower limbs 325 days after bilateral ablation. In d is shown CAB 47, 6 days after bilateral ablation, helplessly dystonic

The most remarkable feature of these two animals was the intense flexion posture of the hip joints with over adduction (Fig. 5a and c), and the appearance of sudden prodigious jumps if the animal, while squatting, suddenly extended the neck. In both animals this posture became evident around the 100th day after bilateral ablation, and remained for the rest of survival. Section of medulla showed no surviving medullated fibers in the pyramids (Fig. 6).

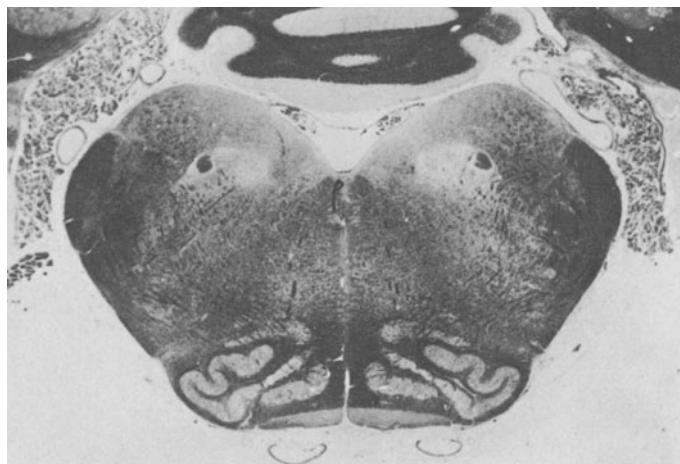


Fig. 6. Upper figure shows the brain of CAB 36 and the lower figure a section of medulla of the same animal, Luxol fast blue stain, to show complete degeneration of the pyramids

The Full Development of Dystonia

In the animal CAB 47 the pattern of bilateral ablation included not only pre- and post-central cortex, but the whole parietal lobe, including the postero-lateral cortex (Fig. 2). The result of such an ablation was indistinguishable from that of complete decortication. The first 3 days after the bilateral ablation the animal could right the head, and showed strong traction reactions of the uppermost limbs. By the 5th day the animal could right from the side of the first operation and walk a short distance on overflexed limbs before falling. Strong flexion dystonia of all four limbs nevertheless rapidly developed, resulting in a fixed posture in trunk and limbs (Fig. 5d), with tonic flexion of hands and feet.

The Relation of Parietal Cortex to Reaching and Grasping

From the experiments described above it may be concluded that the ability to grasp by vision involves at least two components, the direction of the limb to the object and the adjustment of the hand to the object. The former requires the integrity of the posterior parietal cortex, area 7. The movements of the hand require, in addition to orientation of the palm and fingers, for which area 5 appears to be necessary, the basic mechanism of the grasp reflex and related instinctive tactile adjustment of the digits. The part played by these parietal areas has a different aspect when ablation is limited to this part of the cortex.

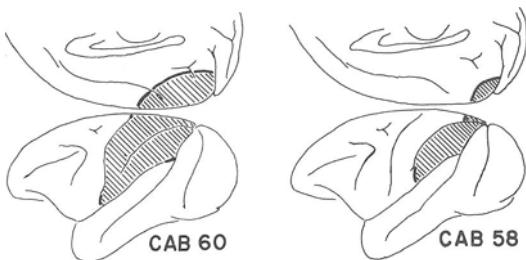


Fig. 7. Diagrams to show extent of ablation in CAB 60 and CAB 58, using same methods as for Fig. 2

We have described elsewhere (DENNY-BROWN and CHAMBERS, 1958) the bias of behavior towards avoiding reactions following parietal ablation in the adult macaque, associated with the loss of optic righting and the adoption of flexed postures. In the infant macaque unilateral parietal ablation leads also to severe inattention in the opposite visual and tactile fields, and circling to the side of the ablation. The opposite limbs are held slightly more flexed with an obvious inability to abduct the affected limb to grasp a cloth or surface. When the ablation was made bilateral (at 49 days of age in CAB 60, Fig. 7) there was an inattention to the opposite field lasting only a week. There was no obvious defect in righting or gait, and orientation of head and eyes to a moving object was excellent. The limbs were held partly flexed when the animal was suspended by head or tail, and lowering him then caused marked extension of fingers and toes. The limb opposite the last ablation failed to reach for moving object or surface contact. After a month the animal could reach for a cloth or an edge by means of a wide swinging progression movement, with strong clumsy grasp following coarse contact. There were facile avoiding reactions to light touch in all limbs. An extremely flexed posture when suspended or sitting remained constant for the next 6 months, with soft dystonic resistance to passive extension. The tendon reflexes were very brisk. He reached by vision for a grape by a wide swinging movement, often inaccurate, with clumsy, poorly oriented grasp.

In view of the critical function that the earlier experiments had indicated for the intraparietal cortex it was of particular interest to examine the effect of removal of this area alone. We have described elsewhere (DENNY-BROWN and CHAMBERS, 1958) the severe dislocation of visual orientation in the adult macaque after removal of the posterior walls of the intraparietal sulcus. Removal of the postero-lateral parietal cortex in the infant macaque in the pattern shown in Fig. 7, CAB 58 (removal left side at 15 days, right side at 48 days of age) resulted in circling to the side of the last ablation, lasting only a few days. A sweeping clawing movement to an approaching object or surface appeared on the 10th day. After the bilateral removal a tightly clasped dystonic flexion of all limbs appeared during the first week. When the animal was lying, sitting or suspended all limbs clasped tightly to the body and to each other, with a moderately intense soft, pliable resistance to passive extension (Fig. 8a and b). A limb making contact with a surface slowly extended and applied to the surface, but only after a very coarse contact. There was no visual placing (Fig. 8c), no reaching for objects, and only very poor tactile placing in the first 4 weeks. Eye and head movement followed an object in the visual field. There was no optic righting and no extension of limbs with a simulated fall. After 9 weeks the animal became able to reach for and claw at a surface by vision or contact, slowly extending one lower limb to do so, but was still extremely dystonic, even after 6 months, and still showed no placing of the hands. Visual grasp with the hands was very delayed, but accurate. Tactile avoiding was very facile in all limbs, with good orientation to stimulus (i.e. the limb withdrew, adducted or abducted appropriately). The gait remained very flexed, but the animal could run and jump, and by 6 months could walk on 2 legs, and could hop from one table to another. The eye movements were not disordered at any time.

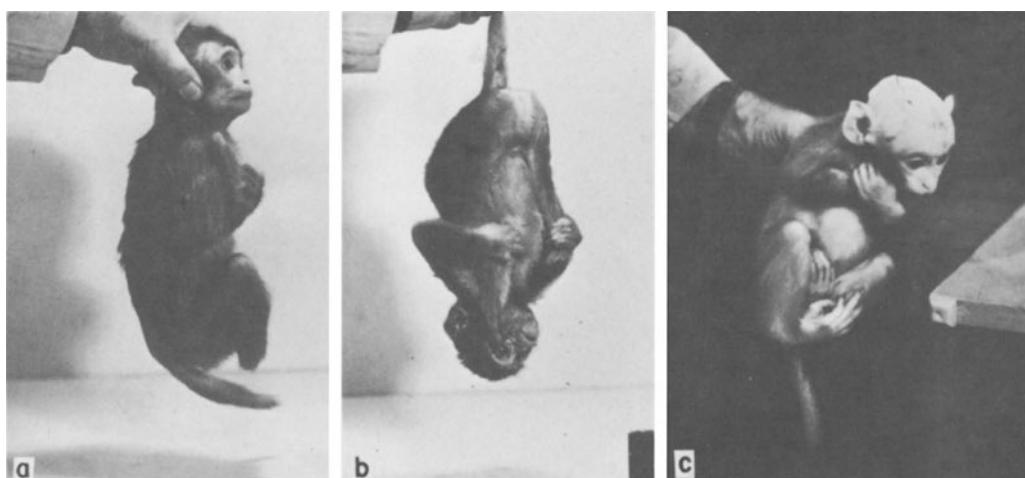


Fig. 8. To show the dystonic, overflexed postures of the animal CAB 58, suspended by head and tail so as to avoid stimulation by body contact, at 182 days, and lack of visual placing (taken at 6 days)

It is of special interest that this "mummified" flexed dystonic posture was later found by us to result also from bilateral coagulation of posterior putamen (DENNY-BROWN and YANAGISAWA, 1972), indicating that though a few fibers in the pyramid are derived from the midparietal area the pathway for visually directed projection of movement of the limbs is indeed extrapyramidal.

Conclusions

Our findings do not support the view that there is reorganization of function in the cerebral cortex of the infant deprived of motor areas. In the absence of area 4 the use of the limbs is visually directed. Movement becomes extremely adept, but the placing and grasping reactions retain their poor adaptation to the shape of the object or surface. Unless the other limb is occupied in some postural reaction it tends to exhibit mirror movement. Spasticity remains minimal even in the second year, but the difference can probably be fully accounted for by the more effective use of the limbs than occurs in an animal operated at that age.

The type of visually directed grasping and placing that forms the greater part of motor behavior in the infant is dependent upon the integrity of the parietal cortex. Abduction of the lower limbs, as in embracing, requires medial parietal cortex. Visual direction of the grasp of the hand requires the integrity of area 5, of the larger movements of reaching and placing of the upper limb requires the integrity of area 7. In the absence of these areas vision can still direct quadripedal progression which can then be adapted for coarse placing and reaching. If area 4 remains intact, and particularly if post-central gyrus is also intact, the instinctive tactile orienting movements of the hand that remain can be effective for grasping, even though the reaching component has been downgraded to the status of directed progression. The experiments reported do not completely exclude the possibility of later maturation of some visual direction of reaching movement by area 8 in frontal cortex (DENNY-BROWN, 1966, pp. 190-191).

Loss of visual direction of movement results in great overaction of tactile reactions, particularly those leading to flexion of the limbs, as in contact righting. The release of such reactions provides a postural bias that heightens all other aspects of dystonia.

The motor reactions of the parietal lobe are mediated by extrapyramidal projections, like those of the premotor areas, the importance of which were first appreciated by OTFRID FOERSTER (1936), who also described the simple flexion and extension synergies resulting from irritation or epileptic discharge of these areas. FOERSTER proposed that the pyramidal system normally suppressed extrapyramidal functions, and that positive release symptoms resulted from loss of this interaction. Our own experiments indicate a normal equilibrium between these two systems, release symptoms being the result of overaction of the different labyrinthine, proprioceptive (neck reflex) or body contact components of subcortical righting reflexes that are normally modified by the cortex.

Acknowledgement. The authors wish to express their indebtedness to the staff of the Infant Nursery of the New England Primate Center, headed by ELLEN NEWHOUSE, B.A., whose skill in rearing infant macaques made this study possible.

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Discussion

Dr. GLEES: After which lesion do you see a retardation in body-growth, because you are working with the infant and you should eventually get atrophy of leg or arm; do you observe this?

Dr. DENNY-BROWN: Regularly we do but we have not made an analysis of it. The totally decorticated animal which we kept alive for 3 months was smaller than a normal 3-month-old monkey, but he grew quite considerably.

Dr. GAZZANIGA: I may have missed the central point: are you suggesting that if there are early putamen lesions there is not this adaptation and compensation? You have that in your data? Cortex versus putamen?

Dr. DENNY-BROWN: Dystonia is more prominent in adult animals, but there have not been enough experiments of this type to enable a truly significant comparison. The defect following putamen lesions appears to be more completely compensated in the infant. In the

infant the residual visual reaching movement can prevent dystonia, which would otherwise occur in the absence of such movement.

Dr. GAZZANIGA: Well, what is your suggestion as to where the compensation occurs in the early cortical brain damage?

Dr. DENNY-BROWN: In the parietal lobe in the infant. In the adult the frontal lobe undoubtedly participates.

Dr. PREILOWSKI: I would like to ask how these young monkeys were raised, on surrogates or with their natural mothers or in isolation?

Dr. DENNY-BROWN: No, they are separated from their mothers and fed by bottle.

Dr. PREILOWSKI: Despite the fact that you get such really dramatic differences I would like to point out that some of the behavior as shown by your animals appears to be very much like that of isolated monkeys. This is not meant to be an alternative explanation to your findings, but I think it may be a disturbing factor.

Dr. DENNY-BROWN: There is an infant colony in the primate center where there are a large number of other infants of the same age reared in the same way and they have not shown this phenomenon, that is all that I can say.

Dr. WOOLSEY: I was struck by one thing which you reported, Dr. DENNY-BROWN: by adding to the precentral-postcentral lesions the removal of the posterior parietal - if I understood correctly - you then got a very incapacitated animal. Was this common finding? I recall our totally decorticate fully adult monkey in which we first removed both precentral convolutions, followed by the supplementary motor cortex except for one face area, and then both parietal lobes simultaneously; this caused relatively little additional disturbance except for some ataxia. After this we removed both occipital and both temporal lobes and the animal was still walking around and had relatively slight spasticity. When we finally removed all the rest of the cortex it still walked. I wonder, how you would account for the difference?

Dr. DENNY-BROWN: We had the same experience in adults, but not in infants.

Dr. WOOLSEY: What do you think is the explanation for the difference?

Dr. DENNY-BROWN: Learning.

Occipito-Frontal Connections, a Possible Sensory-Motor Link for Visually Guided Hand and Finger Movements¹

H. Kuypers and R. Haaxma²

An attempt was made to elucidate the role of the occipito-frontal cortico-cortical connections in visual guidance of relatively independent hand and finger movements which seem to critically depend upon the activity of the precentral motor cortex.

Rhesus monkeys were tested by requiring them to remove food pellets with their fingers from a well in the center of a disc. The well was surrounded by eight radially oriented grooves, only two of which - situated opposite each other and painted white - gave access to the well, the others ending blindly. The orientation of the white grooves could be varied by rotating the disc. When presented with a food pellet not protruding above the disc's surface the index was inserted into one of the white grooves and dislodged the pellet with aid of the thumb (Fig. 1). In six animals one occipital lobe (areas 17, 18 and 19) was removed, followed later by a telencephalic commissurotomy. These operations only affected the performance of the hand and fingers contralateral to the lobectomy. This arm brought the hand to the disc but the hand did not adapt to the orientation of the white grooves and the index generally was not inserted into the white grooves, reaching them only indirectly after exploration of the disc.

A similar defect was observed in six other animals in which, instead of an occipital lobectomy, a unilateral transection of the occipito-frontal connections was performed by a leucotomy at the junction of the parietal and occipital lobes, according to the procedure of MYERS et al. (1962). This defect, which persisted throughout the survival period up to 21 months, does not appear to represent a visual defect since it has been demonstrated in two animals that the half of the brain containing the leucotomy was still capable of visually discriminating the orientations of the white grooves. In addition, it was found in three other animals that ablation of the postcentral gyrus did not produce the above defect. The results obtained in these various animals, which are still alive, therefore strongly suggest that occipito-frontal cortico-cortical connection play an important role in visual steering of the precentral motor cortex.

¹ Since the text of the paper which was read verbally had already been submitted for publication in "Brain Research" and could not be repeated here, we felt it, however, necessary to give at least an extract of this valuable contribution.

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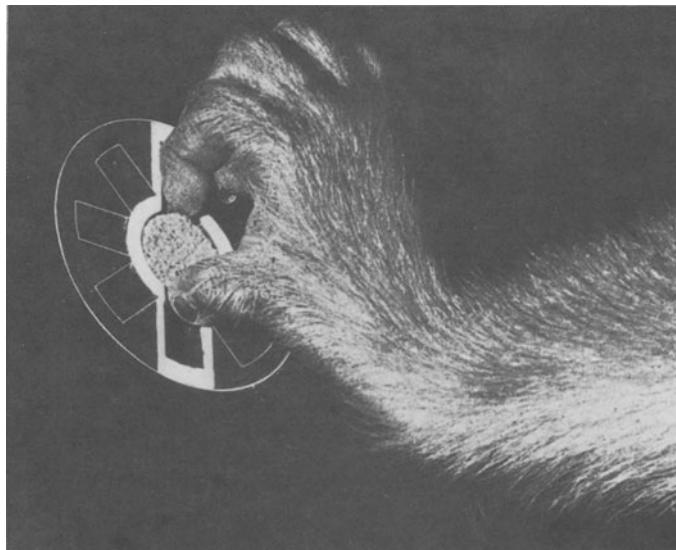


Fig. 1. A photograph showing the hand and fingers of a normal rhesus monkey dislodging a food pellet from the disc. Note the adaptation of the hand to the orientation of the white grooves (To be published in Brain Research, used with permission)

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Discussion

Dr. HECAEN: Do you think that the defect of your monkeys has some relation to apraxia or optic ataxia?

Dr. KUYPERS: One could argue that the defect which Dr. Haaxma and I observed in our monkeys resembles apraxia more than visual ataxia, since the defect was rather restricted to the visual guidance of hand and finger movements and after a recovery period of two weeks was not accompanied by any obvious signs of misreaching. Misreaching was observed only initially immediately after the operation but in a few weeks had disappeared. The arm contralateral to the leucotomy also persistently showed another phenomenon in that it was rather reluctant to adopt unusual and somewhat complicated movement strategies in order to retrieve food. For example when a food morsel was held in front of the cage the intact arm and hand quickly learned to reach for it through an opening in the cage front 10 to 5 cm above the cage floor. However, the arm and hand contralateral to the leucotomy generally kept trying to reach, at the cost of much effort, straightforward

through the spaces between the cage bars. These findings suggest to me that the defect resembles an apraxia rather than visual ataxia.

Dr. MYERS: Does an intact commissure help the contralateral hand?

Dr. KUYPERS: In the animals with an occipital lobectomy but the commissures intact, the contralateral hand makes a lower score of correct placements than the intact hand. After the commissurotomy the score of the contralateral hand tends to drop further and the hand made only 1 or 2 correct placements out of twelve.

Dr. HASSLER: Is there any difference between the use of the contralateral and of the ipsilateral eye in your experiments with the interruption of the fronto-occipital and occipito-frontal lobe connections?

Dr. KUYPERS: You mean in the figure showing transection of the chiasm and enucleation of the eye contralateral to the leucotomy? Yes, under these circumstances we see a difference between the performance of the two hands. The hand ipsilateral to the intact eye behaves in roughly the same manner as the ipsilateral eye-hand combination in our split-brain monkeys and shows a more pronounced deficit in visually guided, relatively independent hand and finger movements than the hand contralateral to the leucotomy. After some practice the latter makes properly directed correcting movements after misplacement of the index on the disc more frequently than the former and thus seems to be "less blind" than the former.

The Central Organization of Adversive Movements as the Main Direction of Locomotion on Land

R. Hassler¹

Since cortical localization studies were initiated by FRITSCH and HITZIG (1870) and FERRIER (1876), movements of the head and of the trunk to the contralateral side accompanied by binocular movements have frequently been demonstrated to be elicited by circumscribed electrical stimulation of different fields of the cerebral cortex. HUGHLINGS JACKSON related such combined movements to the contralateral side to epileptic foci in different parts of the cerebral cortex. After C. and O. VOGT (1907) demonstrated local specific stimulation effects of different cortical areas in the form of adversive movements, FOERSTER (1923, 1926) described adversive movements as resulting either from epileptic discharges or electrical stimulation of various cortical fields in the human.

OTFRID FOERSTER (1936 a,b,c) would have understood adversive movements to mean turning movements to the contralateral side of the head, trunk, and eyes in combination with flexor synergy of the contralateral arm and leg, sometimes followed by an extensor synergy. This can be produced either by stimulation or epileptic discharges (1926, 1936), as is demonstrated in Fig. 1a, by a patient at the beginning of an adversive seizure which originated from a traumatic lesion in area 5b (Fig. 1b). The foci from which FOERSTER (1936²) could produce these adversive movements are: area 6a β , 8 $\alpha\beta\delta$, 5a, 5b, 19, 22, as reproduced in WOOLSEY, Fig. 1 (see p. 18), where area 6a β on the medial aspect of the hemisphere is today differentiated as supplementary area 6a.

FOERSTER made this map by relating the excitatory effects elicited from different cortical locations to the cytoarchitectonic cortical fields discriminated by BRODMANN in the human which can be homologized with those of the architectonic map of the cortex of cercopithecus made by C. and O. VOGT (1919). C. and O. VOGT in 1907 and 1919, however, also described among these fields with *adversio* (latin) area 9a and 9b, 9c, and 9d of the granular pre-frontal cortex, the parietal areas 7a and 7b, area 19b, and differentiated area 22 into three subfields: area 22a α , 22a β , and 22a γ (Fig. 2). They expanded the field-specific stimulation effects by the description of the directing of attention to, or advertence toward the contralateral side as a local specific reaction of different cortical areas. The correspondence of the maps for adversive movements, as demonstrated in 1926 by OTFRID FOERSTER and by C. and O. VOGT for the human, is striking if one considers the different material and methods.

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² Handbuch Neurologie Bd. VI, Fig. 69 a and b.



Fig. 1 a

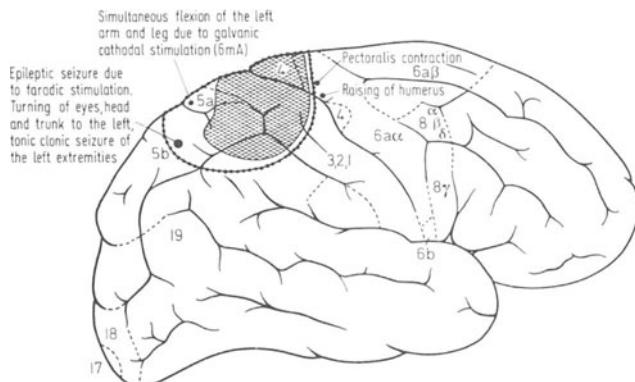


Fig. 1 b

Fig. 1 a, b. Epileptic adversive seizure due to a traumatic lesion (hatched in Fig. 1b) of the postcentral and anterior parietal cortex. Turning of the eyes, the head, and trunk to the left side, tonic-clonic convulsions to the left extremities; the same seizure has been produced during the operation by faradic stimulation of the cortical point near 5b. The dotted line in Fig. 1b marks the cortical excision during the operation (after FOERSTER, 1936b)

Twenty five years later, W. R. HESS et al. (1951/52) produced very similar effects by stimulation of the orbital and anterior cingulate gyri in the cat (Fig. 3). Here the adversive or contraversive movements (a term preferred by HESS and also less equivocal in English language) are further characterized by the dilation of the pupils and palpebral fissures, and the directing of attention to the contralateral side, which is very prominent. Thus, adversive movements must no longer be considered to be purely motor phenomena but also psychomotor. The first to consider this psychic implication in the sense of advertance was probably DARWIN (1872), and it has since been further substantiated by stimulation and coagulation effects in the human patient (HASSELER, 1957, 1967). KAADA (1951), KAADA and URSIN (1957),

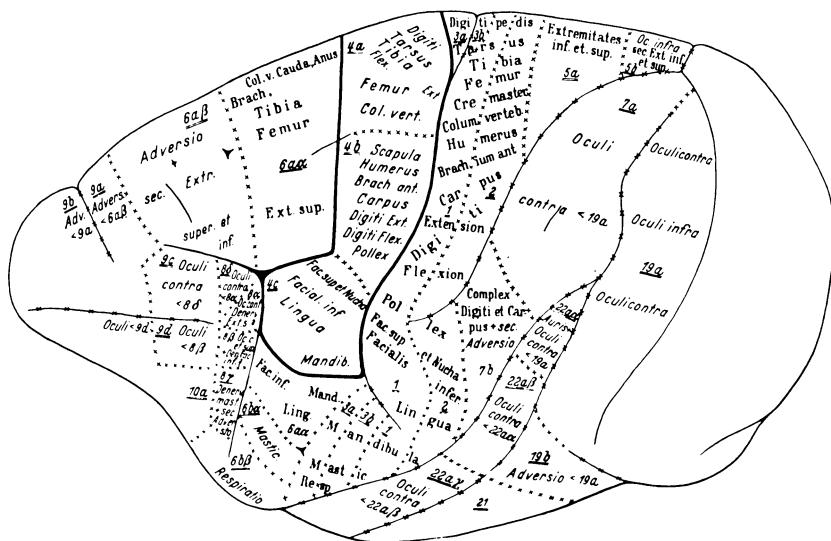


Fig. 2a

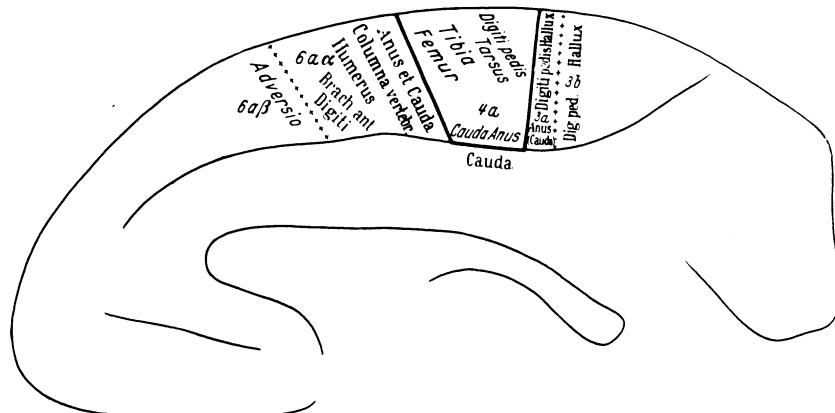


Fig. 2b

Fig. 2. a Map of stimulation effects on the convexity of the hemisphere in cercopithecus drawn by C. and O. VOGT (1918) with additional notes in collaboration with BARANY (1924). Note that the cercopithecus map includes many more adressive fields than the human map of Fig. 1 (article of WOOLSEY, s. p. 17), mainly in area 7a, 7b, 9 a, b, c, d, and the sub-fields of area 22. Fig. 2 b Field organization of the medial aspect of the left hemisphere of cercopithecus demonstrating the effects of faradic stimulation (according to C. and O. VOGT, 1926)

GASTAUT et al. (1959), and URGIN and KAADA (1960) called the same stimulation effects "attention and arousal" or "searching" response. The term "arrest-reaction" is not justified for these movements because in the true arrest-reaction, no movements occur in the direction to the contralateral side and spontaneous movements are suppressed as a result of putamen stimulation (DIECKMANN and HASSLER, 1968). The adversive (or contraversive) movements are instead a part of locomotor movements (HASSLER, 1964); they form the main part, at least in terrestrial animals, because locomotion on land occurs mainly in the horizontal plane.

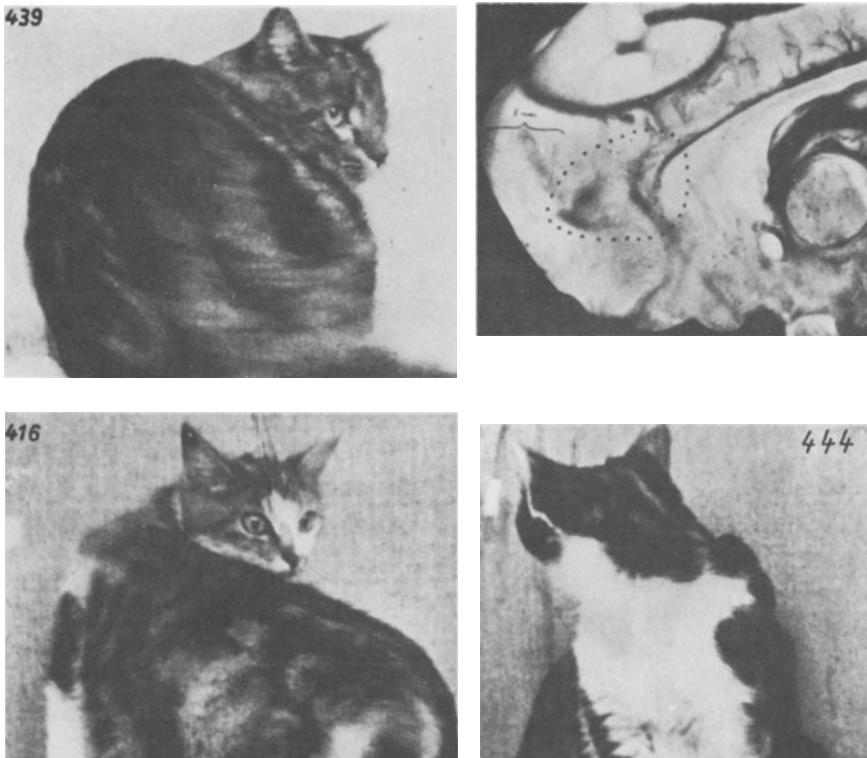


Fig. 3. Three stimulation effects with contraversive turning of the head almost without participation of the forebody. The stimulation points are situated in the anterior cingular area as shown on the medial aspect of the hemisphere (right upper). (According to HESS, AKERT and MACDONALD, 1951)

"Locomotor movements" is a frequently used term; the central regulation or programming for these movements, however, has been totally neglected. In fact a search through the locomotion literature for the problem of the central programming for these movements is utterly frustrating. Even in neurological circles, it is clear that walking is a peculiar form of movement, but the common belief is that it is regulated by the common (central) upper motor neuron of the pyramidal tract.

The research progression after the studies of W. R. HESS was to first investigate further parts of the basal ganglia, the stimulation of which resulted in direction-selective movements, mainly in the horizontal plane (HASSELER, 1956, 1957; MONTANELLI and HASSELER, 1964; DIECKMANN and HASSELER, 1968; and HASSELER and DIECKMANN, 1969). Secondly, together with Dr. WAGNER we investigated the frontal pole of cat brain as well as the somatosensory region (including the extensive cortex hidden in the cruciate sulcus) by stimulating the freely moving unanaesthetized cat with a slightly modified Hess technique (HASSELER, 1960, 1966). The stimulation effects have been classified according to their localization in

the cyto-myeloarchitectonic maps for the cat's sensory-motor cortex by HASSLER and MUHS-CLEMENT (1964).

From these physiological stimulation experiments it resulted surprisingly that the threshold stimulation of the extrapyramidal motor center pallidum (externum) as well as its inner segment (Fig. 4) - in the cat identical with the entopeduncular nucleus - as well as of its efferent pathways the H_1 (Fig. 5) and H_2 bundles of FOREL with their processes to the mid-brain, like the Q bundle of SANO, elicited the contraversive movement of the head, the eyes, the trunk and the whole body (MONTANELLI and HASSLER, 1964; HASSLER, 1956). DIECKMANN and HASSLER (1968, 1969) showed that, in respect to the direction-selective movements, the stimulation of the putamen produces either turning of the head and eyes to the ipsilateral side or an inhibition of the contraversive turning elicited either by pallidum stimulation or occurring spontaneously (HASSLER and DIECKMANN, 1969). Thereby the earlier established subcortical system of direction-selective movements (Fig. 4) has been completed.

In the cat's frontal cortex, the excitation of field 6a δ resulted in ipsiversive movements (Fig. 6), of the area 6a.if.fu. in combined rotating (around the longitudinal axis) and contraversive movements and of the area 6a β particularly in contraversive movements. These are more pronounced when elicited from the walls of the sulcus praesylvius (Fig. 7a). The point is that direction-selective head movements can be elicited not only from neuronal systems of the mid-brain but also from different cortical areas. As in the subcortical system, the eye movements will be elicited on stimulation if the head movement in the same direction is suppressed (Fig. 7b). The connections between these cortical and mid-brain systems are made by ascending collaterals of different direction-selective midbrain neurons; for example, praestitial, praecommissural, and interstitial (HASSLER and HESS, 1954) nuclei connected with certain thalamic nuclei (like V.o.i and V.o.m) which project to cortical fields in the somatosensory and frontal region.

O. FOERSTER has stated that after destruction of the cortical adversive fields in the human, all mirror turning of the head or eyes toward the contralateral side disappears quickly. This happens even faster in experimental animals. If, however, the putamen is affected by an extensive lesion, its ipsiversive action is destroyed, thereby releasing the pallidum to exert its contraversive influence uninhibited for a long time. This seems to be the neurophysiological basis of horizontal torticollis, which is due to a gross lesion in the putamen (GLASER and PUTNAM, 1942) or in the center median nucleus, the afferent neuronal system of the putamen (HASSLER and DIECKMANN, 1969), whereby the contraversive movements originating in the pallidum are disinhibited (Fig. 8). On the basis of this concept, we developed a treatment of horizontal torticollis consisting of the interruption of the efferent pathway of the pallidum internum in the H_1 bundle in the base of the thalamus by stereotactic procedure (HASSLER and DIECKMANN, 1970). Such an operation is successful in about 80% of the patients, and at present it seems to be the most effective (Fig. 9 a-h) and

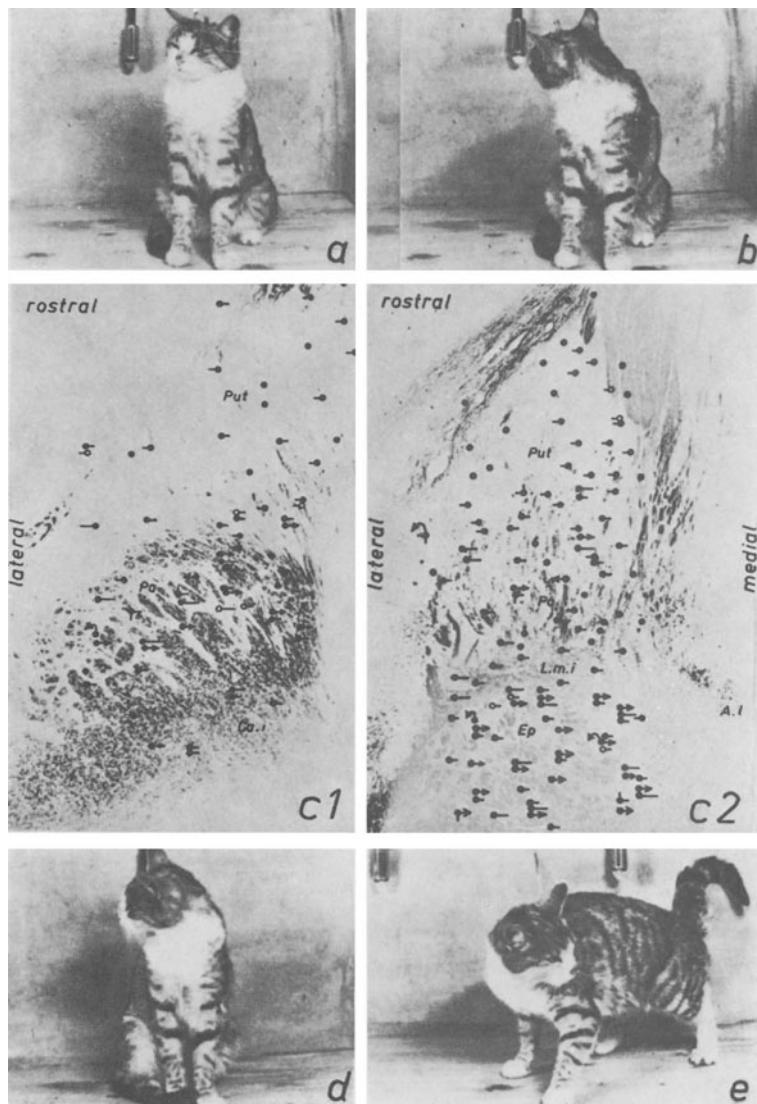


Fig. 4. Stimulation within the putamen (Put) results in ipsiversive turning of the head (b). Stimulation of electrode position (Bru) on the border between putamen and pallidum has the same ipsiversive effect (d) in comparison to the rest position (a). Stimulation of the electrode position (Cru) in the entopeduncular nucleus (Ep) (which afterwards has been coagulated) results in a contraversive turning of the head (e). (After DIECKMANN and HASSLER, 1968.) c₁ and c₂: Horizontal sections through the pallidum at 2 different levels showing the sites of stimulation which have produced direction-specific movements. Contraversive turning and circling are elicited by stimulation of the entopeduncular nucleus (Ep) and (external) pallidum (Pa). Stimulation of the putamen has elicited, for the most part, ipsiversive turning. (After HASSLER and DIECKMANN, 1968)

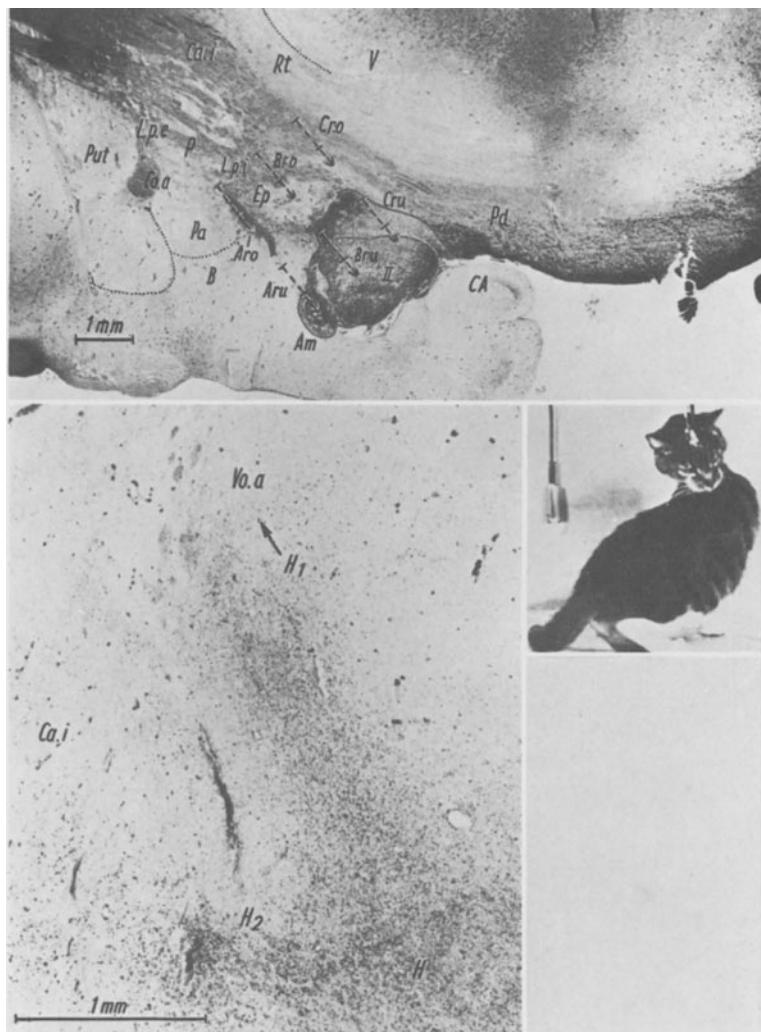


Fig. 5. Stimulation in the position (Aro) in the border between pallidum (Pa) and entopeduncular nucleus (Ep) resulted in a contraversive turning of the head and body in a spiral-like manner. The coagulation around Bru in the ansa lenticularis produced the antero-grade Marchi degeneration through H_2 , curving up in the H field of Forel and terminating through H_1 in the V.o.a nucleus of the thalamus

least complicated method for relief of spasmodic torticollis in the horizontal direction, which, however, requires an intensive physiotherapeutic posttreatment.

The central programming of these horizontal movements is coincidental with the neuronal programming apparatus of the binocular eye movements in the horizontal plane. This apparatus, along with

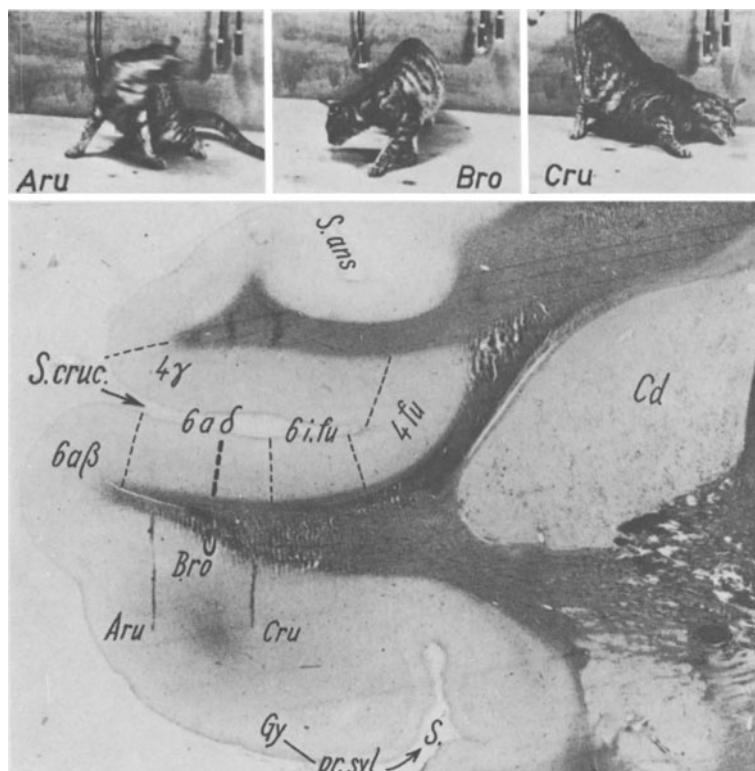


Fig. 6 a

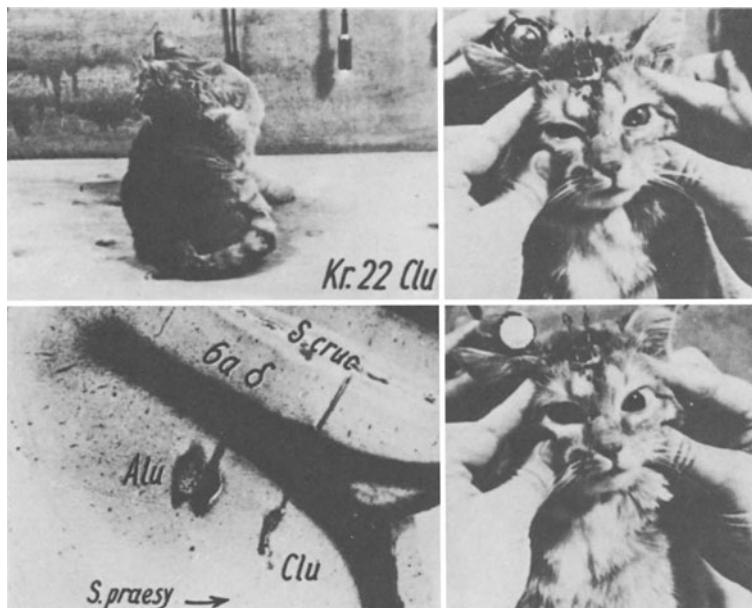


Fig. 6 b

◀ Fig. 6. a Turning movements to the contralateral side elicited by stimulation of electrode position (Aru) in the anterior part of gyrus praesylvius. Ipsiversive turning elicited from the electrode (Bro) which mainly has excited the area 6a δ . Contraversive turning combined with lowered posture of the head and forebody elicited by stimulation of electrode position (Cru) in the posterior part of gyrus praesylvius. The frontal pole of the right hemisphere of the same cat with the positions of the stimulation electrodes.
 Fig. 6. b Stimulation effect of the superior wall of praesylvian sulcus (Clu) is a spiral-like contraversive turning of the head. If the head is fixed during stimulation, only the eyes perform the contraversive turning (lower right)

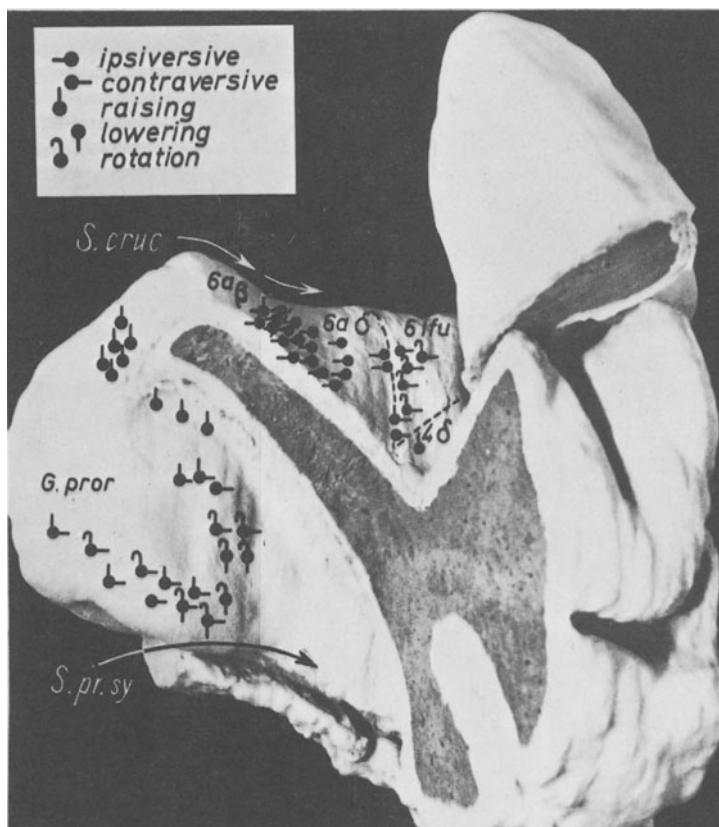


Fig. 7 a. Reconstruction of cat's frontal pole with electrode positions. The upper lip of the cruciate sulcus has been removed to expose its lower lip with the sub-fields 6 β , 6 δ , and 6 i.fu. The lateral wall of the sulcus praesylvius is also removed to expose the medial wall and the gyrus proreus. Clear distribution of direction-specific stimulation effects

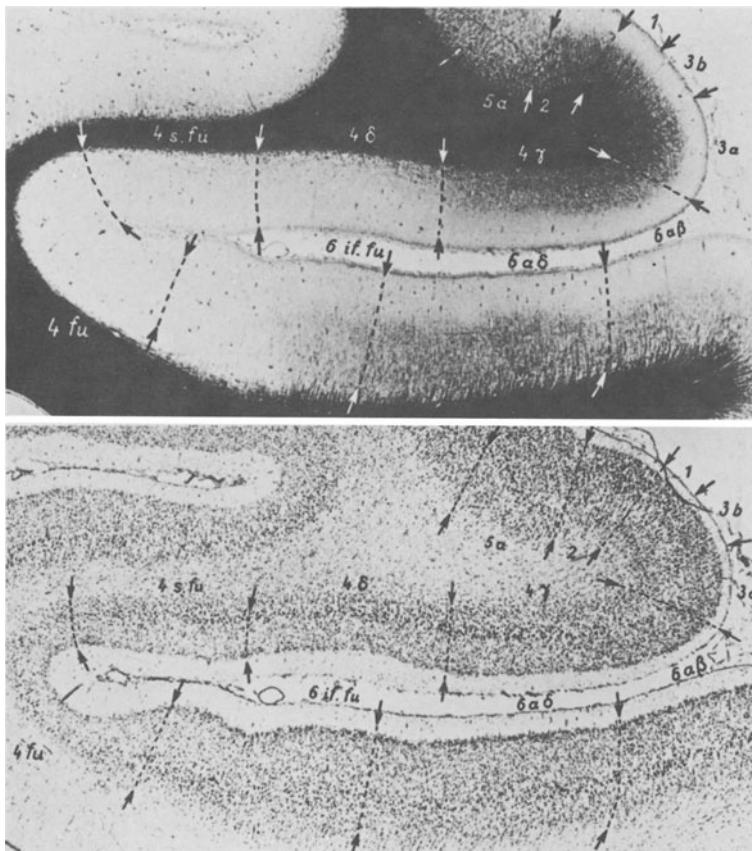


Fig. 7. b Myeloarchitectonic picture of the sensory-motor cortex of the cat on a sagittal section in fiber-staining. The subfields of area 6 and area 4 are differentiated. c The same in Nissl-stain (after HASSLER, 1966)

the central apparatus for the other direction, forms the system of direction selective movements in which either the eyes and head (BIZZI et al., 1972) or the trunk and whole body (locomotor movements) participate. Each of the programming systems for a specific direction is composed of: 1) a subcortical neuronal circuit which becomes tonic in the awake state, therefore giving mirror movements or postures after a circumscribed lesion, and 2) a thalamo-cortical neuronal circle, the elimination of which results in only a very slight and short-lived mirror effect, if any at all.

Motor activities which are not simple reflexes need a complicated computation process to adapt the impulses adequate for the given situation and for regulating the right movement in space and time. In the higher vertebrates this computation is worked out by cerebellar structures. The efferent pathway for each specialized motor activity requires a cerebellar input. If we follow these cer-

ebellar neuronal pathways back, we are able to discriminate 7 motor pathways (Fig. 10).

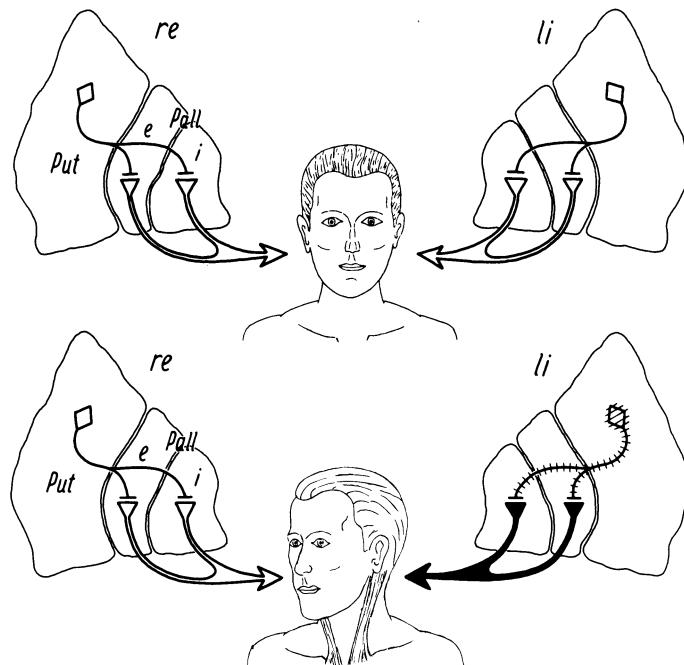


Fig. 8. Scheme of action mechanism of the turning system in horizontal torticollis. In the normal (above), the pallidial systems of the right and left sides are in a balance which produces the normal position of the head. If the inhibitory influence of the left putamen is lost by a lesion, the left pallidum is disinhibited and overactive and turns the head to the contralateral side. The hyper-activity of the left pallidum should be restricted or abolished to relieve the horizontal torticollis (after HASSSLER and DIECKMANN, 1970)

The most simple of these is the vestibulo-spinal pathway for corrective movements against passive deviations of the start position; its cerebellar input runs from the posterior vermis through a part of the fastigial nucleus to the vestibular nuclei, mainly the dorsal part of the Deiters nucleus, from which the vestibulo-spinal neurons arise (Fig. 10). This pathway is still present and functioning in human beings but is inhibited during active direction-selective movements which produce the same deviation.

The next pathway with cerebellar regulation through the fastigial nucleus is the reticulospinal tract (Fig. 10). This tract represents the turning movements to the ipsilateral side which are facilitated and mostly initiated by afferents from the contralateral pallidum externum (pa.rt.spi in Fig. 10). The stimulation of the latter causes adversive, or perhaps better, contraversive movements (Fig. 4). These are represented in the pallido-thalamic fibers crossing the lowest fibers of the internal capsule where they merge in the cerebral peduncle. After the decussation in the

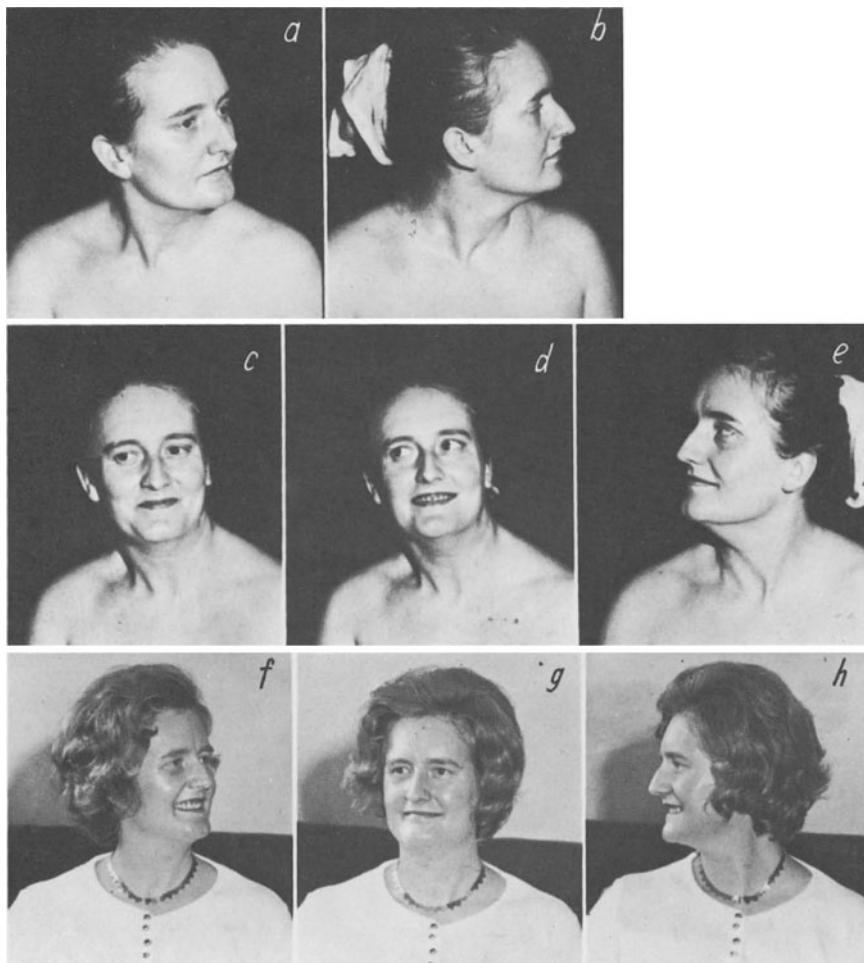


Fig. 9 a-h. A patient with horizontal torticollis before operation. a: spontaneous posture, b: during active turning of the head to the left. c: In an attempt to turn to the right on command, the head is first turned to the zero position, d: secondly, the eyes are turned to the right, e: finally, the active turning to the right is accomplished. f: The patient, one year after the operation, during active turning to the left, g: resting position, and h: during active turning to the right side which was almost impossible before the operation.

rostral midbrain, the Q bundle (of SANO, 1910) connects with the descending reticular systems, which forms the main locomotor system in the horizontal plane for turning the head, eyes, and body in the same direction (ipsiversive) even to the point of circling.

The control of other directions, such as raising, lowering and rotation, also belongs to the locomotor movements. Each of the next three efferent pathways represents a different direction, with vestibular input and cerebellar regulation occurring through the globosus nuclei (Fig. 10). The interstitio-spinal pathway, for

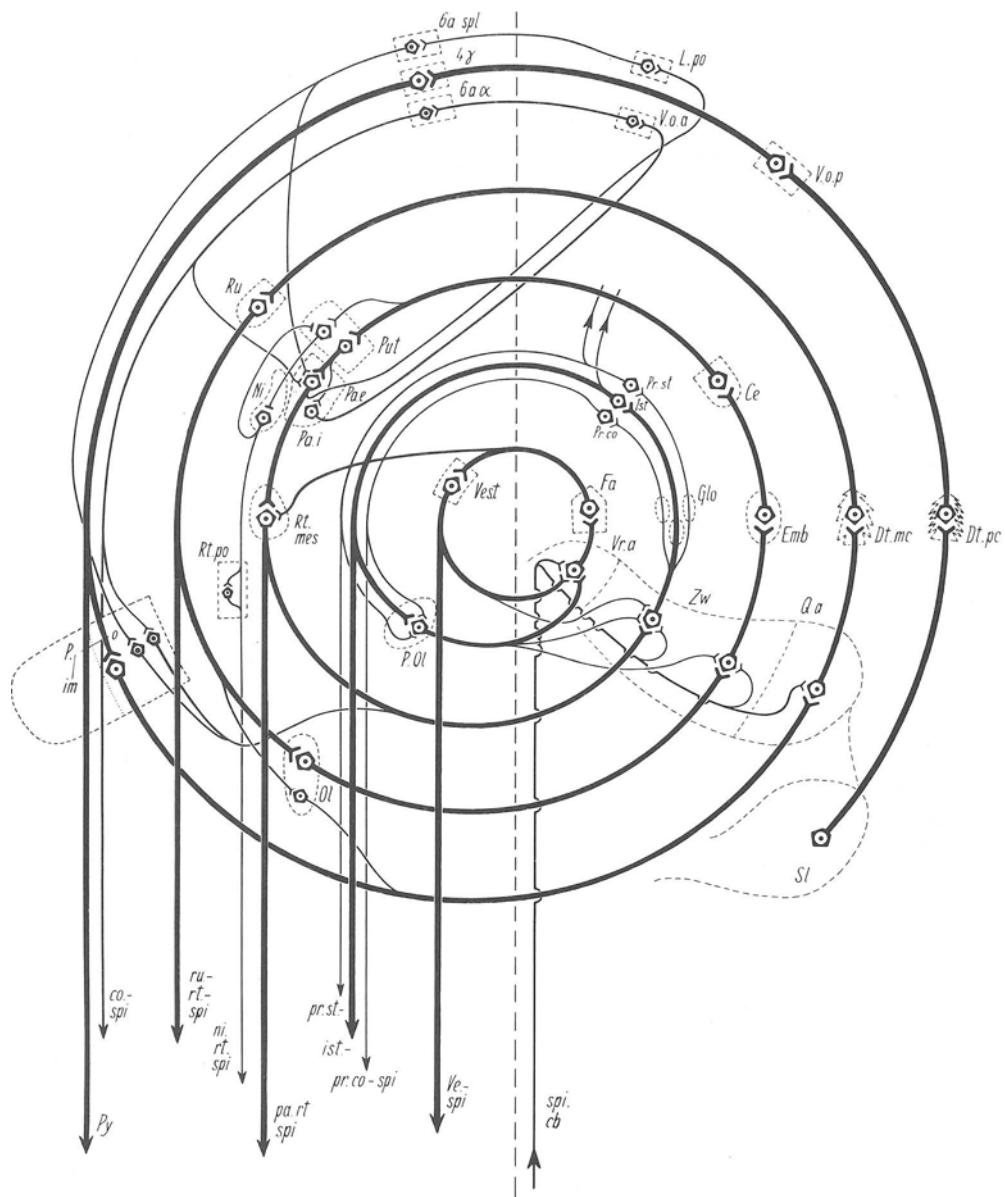


Fig. 10. Schematic snail of motor control systems. Explanation: see text

instance, included in the posterior longitudinal bundle, has the largest fiber diameter and regulates the rotational movements around the longitudinal axis. The praestitio-spinal neurons originate in the posterior wall of the third ventricle and control the raising movements of the head and the eyes (Fig. 10). The pre-commissuro-medullary fibers (*pr.co-spi*) arising from the nucleus of the posterior commissure control the lowering movements of the head and the eyes.

These three different nuclei of the posterior commissure send a bundle of ascending collaterals through parts of the ventro-oral thalamic nuclei (V.o.i and V.o.m) to premotor fields, i.e. area 6 if.fu for the rotatory movements, different parts of area 8 on the gyrus proreus (for raising) and on the gyrus praesylvius (for lowering movements). These cortical representations of different directions of movements project downward to the rostral pontine nuclei but also send direct feedback pathways to their mesencephalic centers, namely the nuclei interstitialis, praestitialis, and praecommissuralis, respectively. These nuclei send efference copies of their discharges to the parolivary nuclei, which feed them back to the cerebellum especially to the intermediate part of the anterior lobe, from which the cerebellar afferents to the three nuclei of the posterior commissure arise.

The parolivary nuclei also send afferents to the lateral part of the intermediate anterior cerebellar lobe (Zw. in Fig. 10); from there the impulses are conducted to the emboliform part (Emb) of the interpositus nucleus. This deep cerebellar nucleus projects to the centrum medianum (Ce) and further to the putamen. The putamen exerts inhibitory effects by GABA-ergic synapses on both segments of the pallidum (Pa.e, Pa.i) and on the substantia nigra (Ni). Reticulo-spinal fibers mediate the influence on the spinal motor neurons. The further spiral revolutions of their motor control snail can be seen in Fig. 10.

The last pathway is very important as the adversive movement starts from the inner segment of the pallidum to the thalamic nucleus V.o.a, which projects to area 6a α and from the outer pallidar segment to the most rostral thalamic nucleus L.po and to the supplementary motor area (6spl) on the medial aspect of the hemisphere. Both are adversive fields.

The structures and pathways regulating the contraversive movements of the head and body as well as of the binocular eye movements and advertence of attention in the horizontal plane are organized in a complicated manner as demonstrated by the schematic drawing of Fig. 11. The thalamo-cortical adversive systems (---;—) run from the V.o.a of the thalamus to area 6a α , from the L.po to area 8 and to area 6spl, from the anterior nucleus to the area 32 on the cingular gyrus. All these cortical fields have synaptic contacts with the outer segment of the pallidum, which is also reached by descending fibers from area 22 and probably area 5 whereas a part of the fibers are projecting back through the pallidum internum to V.o.a. The main descending pathway for contraversive movements runs from Pallidum e through the Q bundle, crosses the midline and terminates in a circumscribed periaqueductal strip of reticular formation (Rt.); from it the dorsolateral tegmental tract descends, the stimulation or excitation of which results in ipsiversive movements. The influence on the limb movements and the binocular eye movements is exerted by descending reticulospinal (bulbo-) spinal and vestibulo-spinal fibers, partly after switching in the vestibular nuclei (Ve).

The ipsiversive system in the forebrain (-|-|-|) starts from the center median nucleus to the putamen and from the vestibular-supplied nucleus V.im.i to area 6a δ (left side of Fig. 11).

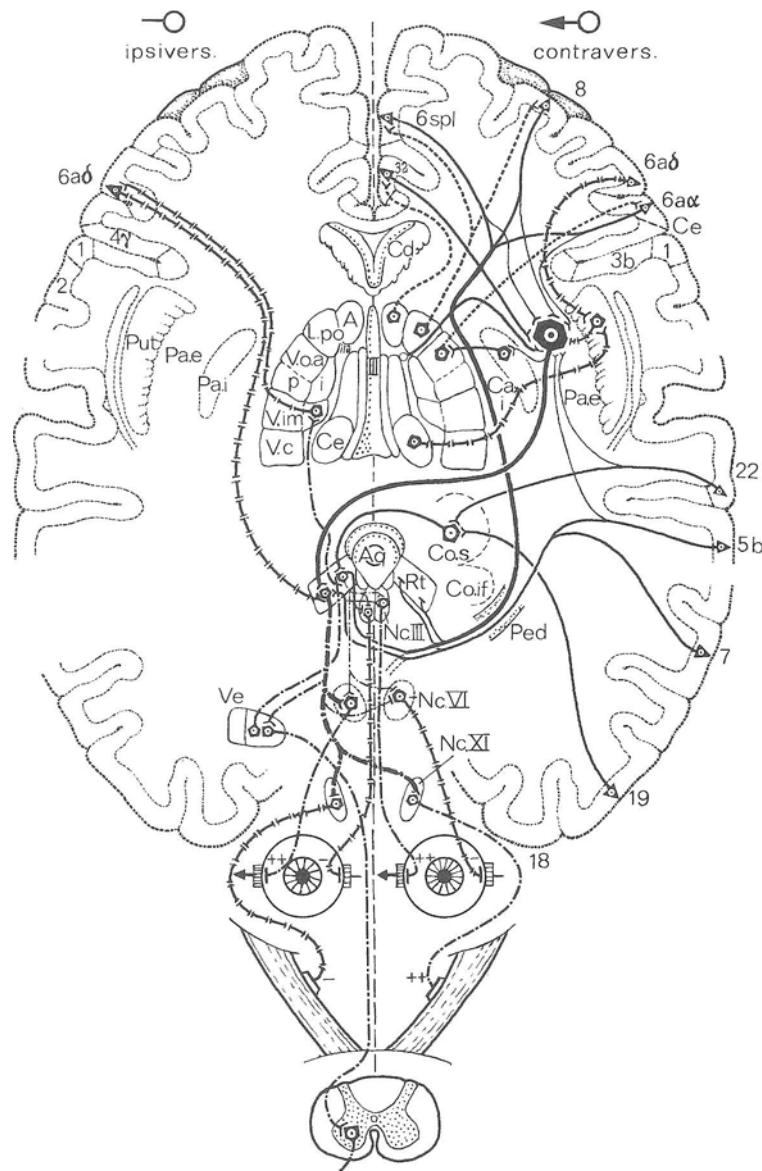


Fig. 11. Diagram of the contraversive (—) and ipsiversive (-|-|-) turning systems with their conduction mechanism to the descending reticular pathway: see text

Some other thalamo-cortical contraversive systems as that of area 19 and perhaps 22 converge to the superior colliculus (Co.s), which also projects to the contralateral mid-brain reticular formation. The contraversive system in the frontal as well as parietal lobe (area 5b, area 7) have direct descending fibers through the internal capsule and cerebral peduncle (Ped) to cross the mid-line of mid-brain and to connect to the mid-brain reticular formation (Rt).

Summary

As described by C. and O. VOGT and OTFRID FOERSTER, at least 10 cortical fields with adversive functions have been revealed by electrical stimulation: areas 6a β , 6 spl, 8, 5a, 5b, 7a, 7b, 19, 22, and 32 (anterior cingular gyrus). In the unanaesthetized human patient as well as experimental animals, the threshold stimulation of these cortical fields results in a contraversive turning of the eyes, head and trunk and an advertence of attention in the same direction. In the cat's frontal cortex, the local stimulation of area 6a β produces contraversive movements, and of area 6a.if.fu produces contraversive movements combined with predominate rotation, whereas stimulation of area 6a δ produces ipsiversive movements.

All these cortical fields, except the area 19 and perhaps 22 which conduct to the superior colliculus, convey to the outer segment of the pallidum, the bottle neck for adversive movements. Stimulation of both segments of pallidum in the unanaesthetized cat results in contraversive movements. They are under the inhibitory action of putamen, the stimulation of which produces ipsiversive or arrests contraversive movements. The two efferent pallidum systems are contraversive and act as well: one ascends through the V.o.a. of the thalamus to the area 6a α , and the other descends through the zona incerta to the mid-brain reticular formation of the contralateral side. Pathological alterations of the putamen system are the cause of the horizontal torticollis which can be relieved by stereotactic coagulation of the efferent pallidar system which is overactive due to disinhibition.

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Discussion

Dr. WOOLSEY: It seems to me that some of your results from stimulating the rostral bank of the cruciate sulcus fall into the supplementary motor area. This has now been worked out in the case of the cat, though less strictly than in the dog and raccoon, and it covers most of the rostral bank of this sulcus. I might have mentioned in my own discussion that some of the adverse movements, which were represented in the past as coming from the area 6aa apparently are due to the fact that the axial musculature of the body in the precentral motor field is represented there, and of course the same thing applies again in the supplementary motor area. When you saw no defect from coagulating the cortex, I wonder if this could be due to the wider spread size of the focus in the cortex, and thus only a part of the area was removed. I know, from earlier experiments in monkeys where we removed area 8 and the frontal eye-field, that the animal subsequently turned to the ipsilateral side and the eyes deviated in that direction.

Moreover, BATES³ pointed out in his observations on man that some of the movements are ipsilateral, some are contralateral, and some are bilateral, so I assume that some subdivision of the center may exist.

³ Brain 76, 405-447 (1953).

Analysis of the Sequential Motor Events in Oral Apraxia¹

K. Poeck and M. Kerschensteiner²

Although movement is a mode of human expression and communication comparable to speech, apraxia, unlike aphasia, has been devoted little or no study with respect to the structure of the disorder, e.g. the type of single components within a given motor sequence, so to speak the "vocabulary", or the sequential order (the "syntax") of the pathologically distorted movements. We have initiated a program aimed at the quantitative and qualitative assessment of the single components that constitute apraxic movements, and, hopefully, we also plan to study the problem whether or not there are regularities existing in their sequential order. For the purpose of this presentation I am going to limit myself to the syndrome of oral apraxia.

Patients presenting with this type of motor disorder are impaired in their ability to perform, on command by the examiner or on imitation, facial or oral movements, such as sticking out the tongue, whistling, holding the mouth wide open. The apraxic nature of this motor disturbance is easily recognized by the fact that the patient does not simply abstain from the movement or perform it in a clumsy way. Rather, the paramount feature is a type of faulty performance which LIEPMANN (1900, 1905) termed parapraxic, and this old term is self-explanatory in its analogy to the term paraphasia.

These parapraxias occur when the movements are required by the examiner. In contrast, they are not, or very rarely, observed in spontaneous actions. This holds true for apraxia in general, as well as for many other neuropsychological symptoms.

Patients and Methods

The experimental group consisted of 66 aphasic patients presenting with oral apraxia. Table 1 shows the subtypes of aphasia represented in this population. You will notice the remarkably high proportion of patients with other types of aphasia than BROCA's. In fact the subgroup with amnesic aphasia is the largest. Duration of aphasia varied between one week and 7 1/2 years. Etiology was vascular in the majority of the patients.

¹ This study was supported by the Deutsche Forschungsgemeinschaft.

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Table 1

Aphasic Syndromes	
amnesic	n = 27
Broca	n = 21
Wernicke	n = 9
global	n = 9
total	n = 66

In a study on rather unfamiliar movements in aphasic patients it is also mandatory to examine two groups of controls: Patients with right-sided brain damage without aphasia (20 patients) and persons without brain damage of varying educational level (20 subjects). The performance of these control groups provided a cut-off score for the diagnosis of oral apraxia in the experimental group.

Table 2

whistle	smack lips
wiggle nose	smack, lips puckered
show teeth	smack lips, mouth held wide
stick out tongue	click tongue like horse gallop
lick upper lip	pucker lips
lick lower lip	hiss
blow out cheeks	clear throat

The tasks for oral apraxia are given in Table 2. Every movement was required first on verbal command and then on imitation. Execution of the movements was either described on the spot scrupulously in the protocol or we took a videotape and described the recorded performance later. These descriptions were then coded in such a way as to indicate clearly the characteristics of the single components of the motor sequence. This code had been developed empirically in a pilot study on patients with oral apraxia. The code and its significance is explained in the following tables. The common features are:

Table 3

1. Substitution

- s = semantically different buccofac. movement or noise
 - sb = body movements
 - t = talks instead of moving
 - n = makes noise instead of moving
 - on = onomatopoetic noise
-

1. *Substitutions* (Table 3) implies that the required buccofacial movement was replaced by a definite motor, verbal, or acoustic reaction.

s = semantically different buccofacial movement or noise

Example: pucker lips instead of wiggle nose or singing instead of whistling.

sb = body movement

Instead of clicking the tongue to imitate the sound of a galloping horse, the patient moves his whole body like in horse-riding or claps his hands rhythmically.

t = talks instead of moving

Instead of hissing, which is "zischen" in German, the patient repeatedly says "tschischen", "tschichen". When the task included a noise, the patient characteristically would approach that noise by adapting the spoken word to its character.

n = makes noise instead of moving

Example: Whistling instead of puckering lips.

on = onomatopoetic noise

Example: Patient says "hop, hop, hop" or: "clap, clap, clap" instead of clicking tongue like a galloping horse.

Table 4

2. Augmentation

mao = motor augmentation (oral)

mab = motor augmentation (body)

an = additional noise

2. In *augmentation* (Table 4), the patient produced additional movements or noises.

mao = motor augmentation (oral)

Example: When the patient wiggled his nose, he also puckered his lips, or when he whistled, he closed his eyes firmly.

mab = motor augmentation (body)

Example: When asked to stick out his tongue, the patient tried to pull it out with his left hand, or when blowing out cheeks, the patient also pulled his mouth wide open with his hands.

an = additional noise

Example: A sipping noise, when showing teeth.

Table 5

3. Deficient Performance

\emptyset = no reaction
 f = fragmentary execution

4. Other

ca = "conduites d'approche"
 a = amorphous movement

3. Deficient performance (Table 5)

\emptyset = no reaction
 f = fragmentary execution

Instead of puckering and smacking his lips, the patient just puckers his lips without producing any noise.

4. Others

The "Conduites d'approche" correspond to the language behavior in some aphasics, when they correct a phonemic paraphasia through several stages of approach.

Example: The patient is told to imitate the act of hissing. At first he whistles several times, then alternates between whistling and a movement of sucking air through half closed lips before finally succeeding in hissing.

Amorphous movements could not be described adequately in one of the above-mentioned categories.

Perseverations were given the symbol p, not referring to the perseveration of a whole movement, but to the appearance of perseveratory elements within a parapraxia. Consequently, p was not coded to indicate perseveration as such but the perseveration of one of the above-described elements of a movement. So if the patient repeated part of the movement inadequately within the motor sequence of task number 11, which had been correct previously within the execution of task number 10, it was coded as sp1.

Table 6

Task: smack lips

$\overbrace{\text{Patient blows out cheeks,}}^{\text{sp1}}$ $\overbrace{\text{says: "mack mack",}}^{\text{t}}$
 $\overbrace{\text{opens and closes mouth repeatedly without any noise}}^{\text{f}}$
 $\overbrace{\text{while pulling his lower lip with left hand}}^{\text{mab p2}}$

Table 6 gives an example of how we transcribed the descriptive text of the protocol into the code. The actual sequence of motor elements appears now as a sequence of symbols, in this case: s p1/t/f/mab p2. These symbols could then be subjected to mathematical analysis, the first results of which are described under "results" in this paper. Details of the method were also described by KER-SCHENSTEINER and POECK (1973).

Results and Discussion

Apraxia, and in particular oral apraxia, is often considered a transitory symptom. ALAJOUANINE and LHERMITTE (1960) have assumed that the movements of oral praxis are less complex than the movements required to articulate speech. DE RENZI et al. (1966) referred to this interpretation when faced with some cases of BROCA's aphasia without oral apraxia. Our finding is at variance with these assumptions (Table 7). Acute and long-standing aphasia were divided at the end of the third month. Severity of oral apraxia was judged, as in DE RENZI's study, according to the items failed. The table gives the values found as compared to the values expected. A correlation between duration of aphasia and severity of oral apraxia clearly shows: the longer aphasia lasted at the time of examination, the more errors were made, i.e. the more severe was the oral apraxia.

Table 7

Duration of Aphasia at Date of Exam. (months)					
	0-3	4-90			
Incorrect Performance (v+i)	0 - 11 12 - 30	15 (11)	18 (22)	33	
		7 (11)	26 (22)	33	
		22	44	66	
Phi = 0,257 Chi ² = 4,3636 df = 1 p < 0,05 Expected values in parentheses					

It is remarkable that in our group of 66 aphasics there were 30 patients with BROCA's and global aphasia, whose expressive speech is notoriously similar (i.e. non-fluent), versus 36 patients with WERNICKE's and amnesic aphasia whose fluent expressive language behavior is quite different from the former two subgroups. Evidently, the gross clinical type of aphasia is not a critical variable for the appearance of oral apraxia. Neither is the localization of brain lesion, because it is known from the brain-scan studies of FRANK BENSON (1967) that non-fluent (=BROCA's) and

fluent (=WERNICKE + the majority of amnesic) aphasia have a differential localization as illustrated in Figs. 1 and 2.

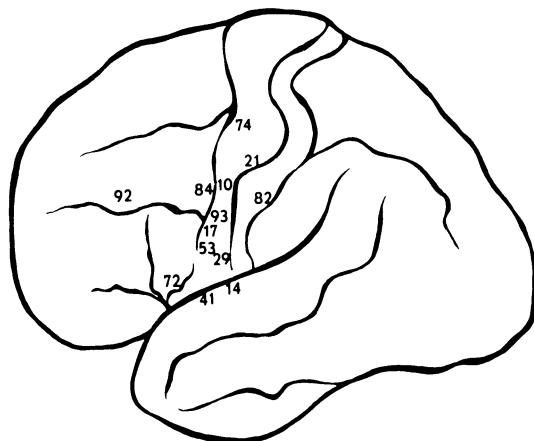


Fig. 1. Brain-scan localization of lesion in non-fluent aphasics (cf. BENSON, 1967)

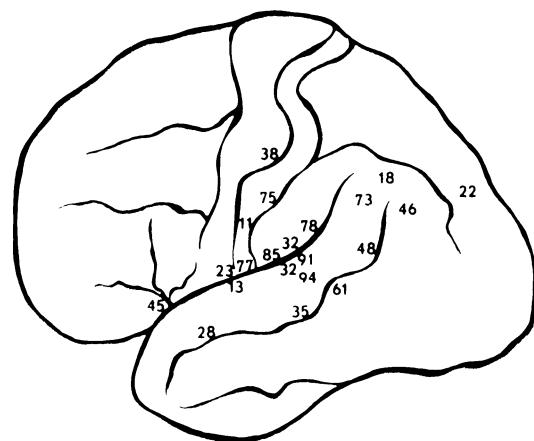


Fig. 2. Brain-scan localization of lesion in fluent aphasia (cf. BENSON, 1967)

One feature, however, stands out quite clearly: GESCHWIND (1965) has pointed out the high frequency of oral apraxia in conduction aphasia, in which the patient produces a wealth of phonemic paraphasias. DE RENZI et al. (1966) demonstrated a statistically significant relationship between phonemic paraphasias (considered across the clinical subtypes) and oral apraxia. We have confirmed

this correlation, comparing frequency of errors in imitation, such as in the study of DE RENZI et al. with severity of phonemic paraphasias (Table 8). This correlation is still positive (Table 9) when the comparison is made for both, that is, errors occurring on verbal command and on imitation.

Table 8

		Phonemic Paraphasia	
		1	2-3
Imitation Errors	0-1	17 (10.23)	8 (14.77)
	2-12	10 (16.77)	31 (24.23)
		27	39
		66	
phi = .430		$\chi^2 = 12.22$	df = 1 p < .001

Table 9

		Phonemic Paraphasia	
		1	2-3
v + i Errors	0-7	15 (9.82)	9 (14.18)
	8-26	12 (17.18)	30 (24.82)
		27	39
		66	
phi = .332		$\chi^2 = 7.27$	df = 1 p < .01

These correlations suggest that particularly precise verbal and non-verbal movements are subserved by similar brain mechanisms. To our knowledge, however, the localization of lesions producing phonemic paraphasias within the language area is not completely understood, although GESCHWIND (1965) ventured some speculation in this respect in his discussion on conduction aphasia.

Our 66 patients with oral apraxia made a total of 1076 errors in our 2 x 14 tasks. The distribution of these errors over the 12 possible modes of failure is given in Fig. 3. The substitution "s" (=semantic parapraxia) is clearly the forerunner, followed by the deficient symptom of fragmentary execution. In the third place, there is the substitution "t" (talk instead of movement). This is an interesting parallel to the observation that aphasic patients often side-step a naming task and replace the required answer by pantomime, i.e. they move instead of talking. This be-

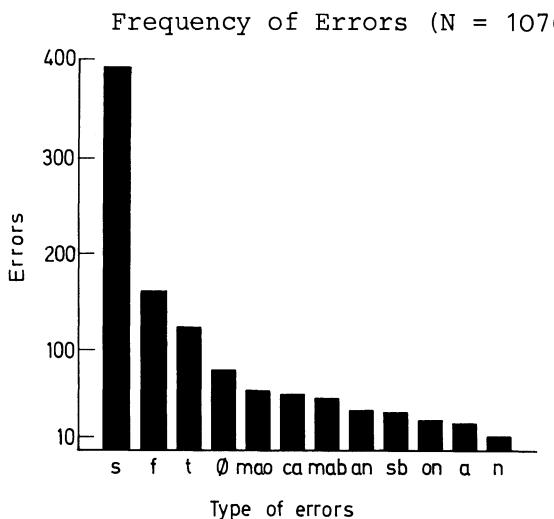


Fig. 3. Qualitative distribution of errors. For symbols for type of errors see page

havior is very frequent in patients with amnesic aphasia. It is interesting to note that the parapraxic error "t" is also relatively more frequent in amnesic aphasia than in any other aphasic subgroup.

In the literature it is a common assumption that amorphous movements are a particularly impressive feature of apraxia. If we apply our qualitative analysis, however, these only take the next to the last position.

Of particular interest was the problem whether or not the distribution of errors in the 4 subtypes of aphasia was different, possibly to such an extent as to yield characteristic profiles. In other words, we asked ourselves if distinctive subtypes of oral apraxia existed, and if these then corresponded to the subtypes of aphasia, which they are usually considered to be.

Fig. 4 shows that the answer clearly was in the negative: we found no typical profiles. The finding, however, only warrants the conclusion that not every clinical subtype of aphasia has its counterpart in oral apraxia. The problem as to whether "natural subgroups" of apraxia might eventually emerge, characterized by a syndrome of typical errors, cannot be solved by this simple type of evaluation. This would require a cluster analysis of the kind we applied in our study on fluency in aphasia (KERSCHENSTEINER et al., 1972), i.e. considering the single errors independently.

The fact that the tasks were given verbally and on imitation raises the question to what extent oral apraxia is dependent on language comprehension. We do not feel that language comprehension plays a critical role. This statement is supported by our

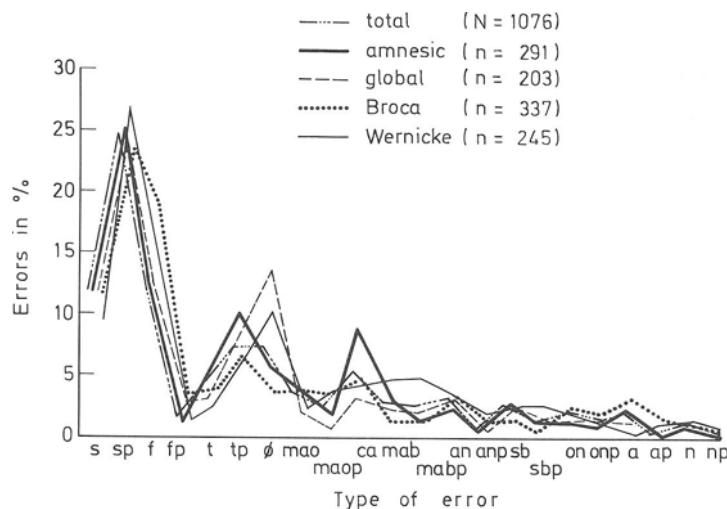


Fig. 4. Percentage of type of errors within each subgroup of aphasia. The lines give the error profiles

coding system, which enabled us to recognize that errors on verbal command and on imitation were not different in quality. The similarity in motor behavior, which in both situations was characterized by parapraxic elements in the faulty movements, strongly suggests that oral apraxia is a disorder of the organization and output of movement, relatively independent of the input channel, auditory or visual, and also of the verbal or non-verbal nature of the stimulus.

Table 10

Relation of v- to i-Errors $N_{tot} = 1076$

Aphasia	verb.	imit.	v/i
amnesic	248	43	5,77
global	129	74	1,74
Broca	210	127	1,65
Wernicke	157	88	1,78

It was also demonstrated (Table 10) that it was not the subgroup of patients with Wernicke's aphasia who made relatively more errors in the verbal than in the imitative situation, but rather the subgroup with amnesic aphasia. These made about six times as many errors on verbal command than on imitation. This finding cannot be explained by a particularly severe disturbance of language

comprehension in this subgroup. Instead, we are inclined to offer the following speculation: the tasks in our examination for apraxia are in some way comparable to the naming tasks in the aphasia examination. It is well known that patients with amnesic aphasia have particular problems in the precise verbal expression of a concept in a given situation. On the contrary, they are much less impaired in the repetition of words, that is, when they are to imitate an acoustic verbal stimulus while the concept is provided by the examiner. In spontaneous language, the words that the patient lacks during examination are more readily at his disposal. If these same aphasic patients fail more in verbal than in imitative tasks of oral praxis, this seems to bring into focus a similar neuropsychological disturbance which has to do with the realization of a concept out of its natural context. Consequently, it is not only justified, but helpful to consider the information provided by verbal command.

In the analysis of certain types of errors, we were particularly interested in evaluating the role of perseveration. If we compare from our 14 items the number of errors with and without an element of perseveration, we arrive at an extremely high proportion of perseveratory errors: 467 out of a total of 1076. I repeat that this statement does not refer to the perseveration of the entire movement - this would add little to common knowledge - but to perseveratory elements within a complex motor sequence.

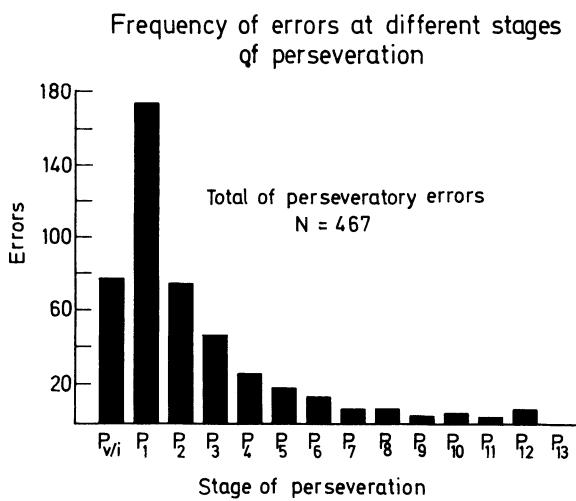


Fig. 5. Frequency of errors at different stages of perseveration

Fig. 5 illustrates how many steps can be bridged by perseveration. The strength of the perseveratory tendency can be judged by the high rate of P v/i error, which we find in second place. P v/i means that a patient repeats the error he had made in the section

on verbal command immediately afterwards upon imitation. He perseverates against the visual evidence of the correct execution of the movement.

It could be expected that patients with prerolandic lesions (as evidenced by BROCA's and global aphasia) would make more perseveratory errors than patients with retrorolandic lesions, that is those with WERNICKE's and amnesic aphasia. This dichotomy, however, had no bearing on the occurrence of p-errors (Table 11). No subgroup was characterized by a particularly high or low p-error rate. A qualitative comparison was made between p+ and p- errors, that is, perseverated and not perseverated errors in the total sample as well as in each subgroup (vertical columns). It can be seen that only the errors t and s appeared significantly more frequently in the form of a perseveration or a perseveratory element. Fragmentary movements appeared least frequently as perseveration in the total population and in the subgroups with BROCA's and WERNICKE's aphasia.

Table 11

Relation of p+ to p- Errors

	amnes.	global	Broca	Wernicke	total					
	p+	p-	p+	p-	p+	p-	p+	p-	p+	p-
f	3	31	5	26	9	61	3	24	20	142
t	29	14	18	6	21	13	16	6	84	39
n	0	2	0	2	0	3	1	3	1	1
s	73	40	50	24	81	40	66	20	270	124
on	2	4	3	3	6	8	2	4	13	19
sb	3	7	3	7	1	6	6	6	13	26
mao	5	11	1	4	11	12	9	9	26	33
mab	3	9	4	4	4	6	12	11	23	30
an	1	6	1	6	3	11	4	9	9	32
a	0	6	0	2	5	10	2	0	7	8

[] p+ > p- ($p \leq 0,05$)

[] p+ < p- ($p \leq 0,05$)

In conclusion: We had started our study on oral apraxia as part of a larger investigation into the field of apraxia, with the assumption that movements as a mode of expression, communication, and purposeful action should be studied in much the same way as verbal expression and communication. I hope we have demonstrated that such a study is not only feasible but also meaningful, and that it gives at least some of the expected insight into this aspect of symbolic functions. We have developed a method that promises to be helpful in recognizing disturbances in the "lexicon" of movements. Whether or not disturbances also exist in the

"syntax" of movements - in other words, whether the sequencing of distorted movements follows some recognizable rules - that we dare not say on the basis of these preliminary data. However, if regularities of this kind exist they should be detected when we continue this type of study on a larger scale.

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Discussion

Dr. PLOOG: If you calculated your data using a model of Markoff analysis then you would come up with the result - if I understand correctly - that your patients are much more deterministic in their behavior, i.e. that events preceding your stimulus are more powerful in determining their subsequent movement than the actual stimulus.

Dr. POECK: Yes, I think so.

Dr. PLOOG: And this of course is more the contrast in terms of sequential analysis of behavior under pathological conditions, not only for all behavior but for many types of motor behavior.

Dr. POECK: I think this would be revealed in a further analysis of our data. The first thing we have shown is that these para-praxies do not occur at random, and that there are certain types of errors which occur. I think there is only a limited "vocabulary of errors" and there are also "error types" or "configurations of errors" characteristic for one particular patient.

Dr. PLOOG: May I ask one more question? What I do not understand is your statement that the comparison of fluent aphasic patients with nonfluent patients resulted in the same number of errors regardless of whether you presented your stimulus verbally or by

imitating behavior. One would assume that the fluent aphasic patient would not understand your command as well as the nonfluent.

Dr. POECK: Yes, but the results did not show what would generally have been predicted, i.e. that the subgroup of patients with WERNICKE's aphasia would make relatively more errors on verbal command than on imitation. They did not, and in fact it was the subgroup with amnesic aphasia who made relatively more errors on verbal instruction than on imitation. We have speculated - and that is an analogy, as weak as all analogies are - why this is the case. Our reasoning is as follows: If you confront a patient with amnesic aphasia with a task of naming an object, he is likely to fail. If you give him some clue, then he can find or rather produce the name. The apraxia task on verbal command appears to us comparable to the naming situation, whereas in the imitative situation the concept of the movement is provided by the examiner. It might well be that patients with amnesic aphasia have an impairment in the realization of a concept out of its natural context.

Dr. ZANGWILL: I am very interested to hear that you have thought for a long time the difficulty of the amnestic aphasic was by no means how he can find language. Very often the greatest difficulties exist in repeating; the more you limit the task the more defects you can elicit.

Dr. POECK: Yes, it very strongly suggests that the defect in the patients with amnestic aphasia transcends language, it covers larger fields than speech alone.

Dr. RASMUSSEN: I would like to ask you whether any correlations were made in the duration of the aphasia in these patients or was it a rather relative homogeneous group? And secondly, was there any correlation made with the age of the patients?

Dr. POECK: One of the first slides showed that we divided the patients into two subgroups, one with acute aphasia of three months duration and then another with longstanding aphasia. But the series was heavily overweighted towards longstanding aphasias because we carried out the examinations in the clinic of Dr. LEISCHNER in Bonn, where longstanding aphasias are usually treated. The age range was 20 - 62 years, the average age was 57 years.

Dr. RASMUSSEN: You had no young aphasics then?

Dr. POECK: Not younger than around twenty years of age.

Dr. HECAEN: In your test was there any more meaningful gesture, e.g. smile, cry or astonishment?

Dr. POECK: Not yet; you know our "battery" of tests, if I may call it so. We selected it from the literature. We read papers on oral apraxia and chose any oral apraxia test given to aphasic patients. However, we should reshape it in the future.

Dr. ZANGWILL: At the end we seem to be concerned not just with the localization of movement or with the localization of either sensory or motor function, which was the earlier dichotomy, but with the localization of skilled performance. We are now moving toward a conception of localization which is more realistic. I may say that as psychologists standing between human physiology and experimental psychology, we are obviously working towards an understanding of the correlations of the two hemispheres in sensory/motor performance. We are looking at another very important question: The age factor in relation to defects produced by lesions of motor function. In fact, the whole question of motor function seems to be advancing fast in a very challenging way.

II. Interhemispheric Connection

Bilateral Motor Interaction: Perceptual-Motor Performance of Partial and Complete "Split-Brain" Patients

B. Preilowski¹

In recent years VOGEL and BOGEN, both neurosurgeons at the White Memorial Hospital in Los Angeles, have used surgical division of the neocommissures to treat a number of patients for intractable epilepsy. This measure was always a last effort to alleviate advancing, life-threatening convulsions and for most patients so far has brought remarkable improvements (BOGEN et al., 1965; BOGEN and VOGEL, 1962). This review is based on tests with ten of these patients, eight of whom underwent a complete commissurotomy, i.e. the corpus callosum in its entirety, the anterior and hippocampal commissure, as well as the massa intermedia (when present) were sectioned in a single operation. In the other two patients (N. F., D. M.) only a partial division of the neocommissures, including the anterior two thirds of the callosum and the anterior commissure, was performed (case histories: BOGEN, 1969; GORDON et al., 1971).

Special tests with the so-called complete split-brain patients reveal that their two hemispheres function separately and independently of each other, each having its own realm of perceptual and cognitive functions (SPERRY et al., 1969; SPERRY and PREILOWSKI, 1972; SPERRY, 1973). Just as spectacular as these experimental findings, is the fact that the split-brain patients show no obvious deficits in daily life. Their motor behavior looks normal. They can button and unbutton clothes, tie shoelaces, ride a bike, swim, and perform various other bimanual² tasks. Among an earlier series of patients in whom an extensive division of the neocommissures was performed, one case was reported to have continued to type and another to play the piano with both hands after surgery (AKELAITIS, 1944; AKELAITIS et al., 1942). At first this may seem somewhat disconcerting to those trying to define motor functions of the cortex. However, as far as basic motor patterns are concerned it seems that coordination takes place in the central nervous system below the cortex anyway. Also, it has been suggested that the control of highly overlearned motor functions

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The experiments were made while the author was a postdoctoral fellow and research associate at the California Institute of Technology. Support was provided through N.I.M.H. Grant MH 03372 to Prof. R. W. SPERRY, to whom the author would like to express his gratitude for all the help and encouragement received. Further thanks to Drs. VOGEL and BOGEN for permission to test the patients, and to BARBARA BONFIG for expert secretarial help.

² Some of the tasks involved arm as well as hand movements. Terms like "bimanual", "bilateral" and "two-hand" are used interchangeably.

may descend to lower brain levels (SPERRY, 1945). In itself the existence of bimanual skills in split-brain patients would of course not exclude the involvement of the cortex in such tasks: Interaction between the hemispheres can still be achieved by various unifying mechanisms, such as through connections of lower brain centers, through extensive ipsilateral representation, as well as by visual feedback, which, due to unrestricted eye movements, is available to both cortical halves.

The difficulty in inferring brain functions from deficits in performance after commissurotomy is due to the same problem encountered everywhere in attempting to localize functions: It is the problem of having to rely mainly on negative evidence and of complexity. There is a multitude of different ways to perform the same motor task. Each possibility may involve different neuronal circuits to a different extent. To be sure, there are probably optimal combinations that lead to optimal performance, and any disturbance in these circuits would show up in a decrease of performance. However, how often, if ever, can we say what the optimal performance is? How often do we tax the upper limits of performance? For obvious reasons the clinician has to be satisfied with lump sum scores and short, economic tests. For research purposes, however, training and testing has to be extensive in order to establish stable limits and to collect refined qualitative as well as quantitative measures. This is especially important in evaluating the cortical and commissural contributions to motor functions. Clearly, loss of the commissures in our patients does not result in the severe praxic defects that have been described earlier in cases with lesions of the commissures due to progressive disease processes (LIEPMANN, 1905; SWEET, 1941). Rather, as I will try to show in the following account, the lasting defects of partial and complete surgical division of neocommissural pathways point to the cortex as the place where sets for motor behavior are developed and where final integration, adaptation, and elaboration of movements take place. In the words of SPERRY (1952): "Cerebration, essentially, serves to bring into motor behavior additional refinement, increased direction toward distant, future goals, and greater over-all adaptiveness and survival value" (p. 299).

This review will start with some of the general sensory transfer deficits relevant to motor functions and then move on to bilateral motor behavior itself. Here again it will be concerned first with those deficits which in general are only visible during the early post-operative period, before going into the permanent impairments which can be ascribed to the lack of neocommissural connections with more confidence (Details of these findings are published by BOGEN, 1969; BOGEN et al., 1969; GAZZANIGA et al., 1967; PREILOWSKI, 1971, 1972; SPERRY et al., 1969; SPERRY and PREILOWSKI, 1972).

Somesthesia

Topognosis. With the exception of head, torso, and proximal parts of the extremities all complete split-brain patients show a lack

of topognostic bilateral transfer. If the fingers of one hand are touched lightly, the patients, with vision excluded, can indicate the stimulated point with the thumb of the same hand. However, they are unable to localize the corresponding finger or points within a finger with the thumb on the opposite hand.

Stereognosis. One of the consistent findings of the complete commissural section is that objects which are identified with one hand by touch only, cannot be found or recognized with the other hand. When the complete split-brain patients are given two different objects to feel, one in each hand, and then are asked to retrieve out of a pile of other objects what they had held in each hand, we can observe the patients searching with both hands at the same time. However, we see the left hand coming across and testing the object which the right hand was looking for and rejecting it, and vice versa, until each hand has found the item which it had held previously. That is, there is no interaction or exchange of information between the two hemispheres. It is as if two people work simultaneously, but independently. With practice some patients have acquired techniques for making intermanual comparisons which seem to utilize ipsilateral pathways. Two patients (A. A., L. B.) have been observed probing objects for sharp points and pressing on these with the finger or palm. Then they would try to do the same with the other hand on all items out of which the target object had to be selected. Apparently pain serves as a relevant cue here. Similarly temperature can be used to differentiate between materials.

Both partial callosal patients in whom the posterior portions of the corpus callosum are preserved perform intermanual topognostic and stereognostic comparisons like normal controls without any obvious problem.

Proprioception. There is interhemispheric transfer of proprioception in the complete split-brain patients unless complicated poses of fingers, which are impressed on one hand by the examiner, have to be copied with the fingers of the other hand. In contrast to this NORRSELL (1970) has described the inability to match gross arm postures of one side with the other in one patient. The same patient (R. Y.) also gave negative results in an experiment testing for separate transfer of muscle and joint sensation (MCCLOSKEY, 1973). During tests administered by the author, R. Y. was quite able to match with one arm (tracking arm) movements imposed on the other arm (target arm) by the experimenter as long as the target arm was actively moved by the patient himself. As soon as R. Y. was asked to relax the target arm which was then supported by the examiner in a certain position, the previously correctly tracking arm drifted off. No systematic aberrations were noted. The inability to transfer seemed least possible for positions of the lower arm and hand. Different poses of the hand were matched with a seemingly random array of postures of the other side including the changing of position of the whole arm. It is interesting to note that the same patient can carry on a conversation and at the same time use both of his hands to go through a well-coordinated procedure of lighting a cigarette and smoking it, only interrupting the motor sequence by a gesture to underline a point in his conversation. It should

be added, however, that observations of this patient have to be regarded with caution. He was reported to have had neurological impairments in bilateral sensory and motor functions before the operation. He is also difficult to test because of constant restlessness and inability to remember the instructions.

In more recent tests with two other patients (N. G., L. B.) MCCLOSKEY (1973) found no abnormalities in proprioceptive matching. Both patients could track movements imposed at the elbow of one arm by the experimenter with the other arm. Furthermore, when the tendon of the biceps or triceps muscle of one arm was vibrated while the arm was gently restrained, both patients fell subject to the illusion of the muscle being lengthened and moved the tracking arm in the appropriate direction. Also, both were able to indicate the direction of movements of the terminal interphalangeal joint of the middle finger with a finger of the opposite hand, supporting the finding of transfer of simple finger postures (SPERRY et al., 1969). During MCCLOSKEY's test the middle finger was maximally flexed at the first interphalangeal joint, while all other fingers of the hand were extended. If held in this position no voluntary movements are possible at the terminal interphalangeal joint of the middle finger. The dissociation from muscular action thus supposedly allows testing for pure joint sensation. The anatomical implications of these results are not quite clear. Both the possibilities of ipsilateral projections and/or lower commissural connections are considered to be responsible. The partial split-brain patients show no difficulties in transferring proprioceptive information under any conditions.

Motor Functions

Dyspraxia. Complete section of the neocommissures was generally followed by praxic disturbances similar to those described by AKELAITIS et al. (1942). The degree and the duration of the impairment were greatly dependent upon the age of the patient at the onset of seizures, on the age at the time of the operation, and on the course of general post-operative recovery as well as on the extent of extracallosal damage as indicated by preoperative neurological tests and observations during surgery. In one patient the inability to use the left hand independently, as in cleaning the fingernails of his right hand, has persisted for several years. However by the fourth post-operative month this same patient could use his two hands together to fold linen and even button his clothes. Similarly, patients unable to make simple movements with their left hand or arm on command during the earlier post-operative period do use the left arm and hand to perform spontaneous, well coordinated movements, for example, when scratching parts of their body or pulling up their bedcovers. It is not clear what happens when the left-sided dyspraxia disappears. It must mean either that the right hemisphere has improved in comprehending verbal instructions or that ipsilateral control from the left hemisphere is being used.

Neither of the two partially commissurotomized patients showed any praxic impairments following the surgery.

Intermanual Conflict. In the previously mentioned study of patients with extensive surgical division of the neocommissures by AKELAITIS and co-workers (1942), two patients were found to demonstrate a conflict between the activities of both hands. Similar instances of the more recently operated patients are described (BOGEN et al., 1969), e.g. a patient trying to remove an object with his right hand while unable to release it with his left hand. In the same patients a forced grasp response could not be elicited by stimulation of the palm and there was also no proximal traction response. It seems possible that synergic movements controlled from one hemisphere are responsible for these apparently conflicting intermanual activities: As the right hand grasps the object to remove it, the left hand performs a simultaneous flexion thus apparently holding on to the object. Unfortunately, a direct study of synergic movements after neocommissurotomy has not been performed. Somewhat in support of the explanation proposed here after the fact, is the tendency of these patients to use their left hand less than usual, sometimes requiring extra prodding to get them to use it. Also, inability to do two different things at the same time as writing with one hand and sorting cards with the other hand was reported to be a most consistent symptom in the AKELAITIS patients (AKELAITIS, 1944). Furthermore, one still gets the impression in most testing situations that the disconnected left hemisphere is in command most of the time.

On the other hand, more dramatic demonstrations of conflict have been described by BOGEN et al. (1969) which seem to require an explanation in terms of both hemispheres being actively involved. In one case the patient (W. J.) would repeatedly pick up a newspaper with his right hand and lay it down with his left hand. This would be performed several times until finally the left hand threw the newspaper on the floor. Another patient (R. Y.) was described by a physiotherapist: "He was buttoning his shirt with his right hand and the left hand was coming along just behind it undoing the buttons just as quickly as he could fasten them" (p. 19). However, as in the praxic impairments described earlier, instances of intermanual conflict were generally confined to the first post-operative months and again seemed related to the age of the patient and extent of extra-callosal damage. It is of interest to note that the same patients while exhibiting these episodes of intermanual conflict were able to use their left hand in a purposeful and cooperative manner when 'not thinking of what they were doing'. For example, they could pour coffee out of a pot held in the right hand into a cup held by its handle with the left hand. The above-mentioned peculiarities in motor functions were observed only in the complete split-brain patients.

Lack of Coordination After Complete Commissurotomy. As has been mentioned earlier, all of the patients are able to perform well-coordinated bimanual skills post-operatively in those skills in which a high degree of overlearning had already been obtained before division of the commissures. In contrast, even simple tasks like simultaneous tapping with fingers of both hands (KREUTER et al., 1972) or simultaneous ab- and adduction movements of the lower arms with the elbows supported present a problem. The patients are unable to maintain synchronous bilateral movements and usually perform at different rates with right- and left-hand fin-

gers or arm. This impairment becomes even more pronounced when the patient is asked to work as fast as possible and when visual control is prevented. When instructed to tap alternately with right- and left-hand fingers, the patients become totally disorganized and their general rate of performance remains much below that of normal controls.

In general, symmetric movements show better performance than asymmetric movements which seems to indicate that, at least periodically, control is exercised by one hemisphere (I shall return to the problem of asymmetric versus symmetric movements later). Another finding supports the possibility of one hemisphere trying to control performance: When the split-brain patient is asked to perform a tactual maze with both hands simultaneously, it is much easier for him if the two mazes are mirror images of each other. Bimanual performance deteriorates when one of the mazes is reduced to one-third of the original size.



Fig. 1. Two-hand coordination apparatus: An X-Y recorder, fitted with two crank handles such that turning of one registers as horizontal movement of the pen and turning of the other as vertical displacement. By turning with both hands simultaneously a line had to be drawn within a narrow track as fast as possible without touching the sidelines. (From PREILOWSKI, 1972)

In an attempt to investigate motor coordination in greater detail a test was applied that required simultaneous, mutually adjusted

movements of both upper limbs, such that in the movement of each limb the action of the contralateral limb had to be continuously taken into account. The test apparatus (Fig. 1) consisted of an upright X-Y recorder which was fitted with two crank handles (turning radius 6 cm), so that turning of one registered as horizontal movement and turning of the other as vertical displacement (360° of rotation = 10 mm of displacement). By simultaneously rotating both handles the pen of the recorder could be moved in any direction. A sheet with four identical patterns which had to be traced was attached to the writing surface of the recorder. The assigned task was to draw a straight line within a narrow track 155 mm long and 5 mm wide as fast as possible without touching the sidelines. The track was presented at different angles. Exactly vertical and horizontal lines only required movements with one hand. At any other angle simultaneous movements of both hands were necessary; the ratio of the required right-hand to left-hand output changed with the angle of the track. Examples of the task which require asymmetric movements are given in Fig. 2.

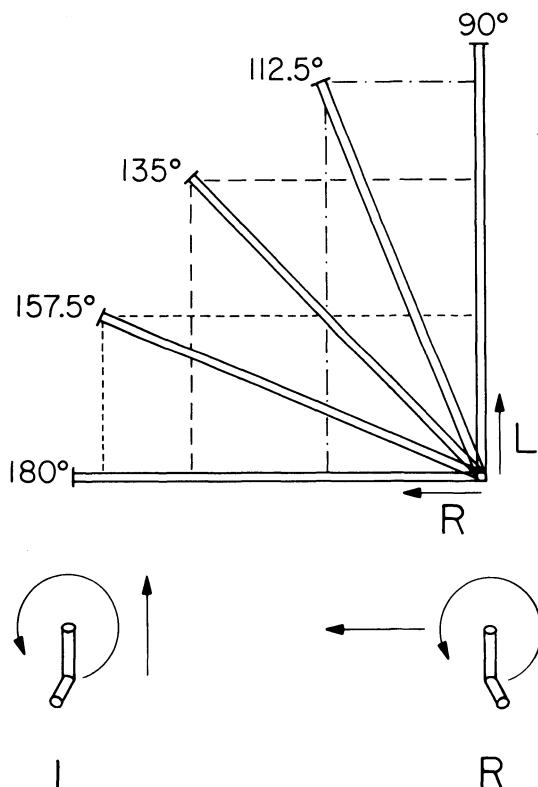


Fig. 2. Schematic representation of the patterns and the bilateral input relationships in asymmetric movements. Note that at 90° and 180° only the left and right hand, respectively, make counterclockwise movements. At 135° both perform identical parallel movements, and at 112.5° and 157.5° the left and right hand, respectively, has to turn more than twice as fast as the other hand. (From PREILOWSKI, 1972)

Similarly, angles of the other four quadrants were used to test for rotary movements in different directions. Time scores were obtained. They were corrected for differences between the amount of output at the single-hand and the different two-hand angles. The two-hand times were then set in relation to the time of that hand, which, under the assumption of independence of both hands, would determine the total time. At 112.5° this would be the left hand, at 157.5° the right hand, and at 135° the slower of both hands would, for example, determine the total time. Thus the amount of interference between both hands during simultaneous action was determined. No interference would mean working with both hands simultaneously as fast as with the slower or speed-determining hand alone. Qualitative aspects of performance were evaluated by inspection of the resulting traces.

In the task described, bilateral coordination can be maintained by using visual and proprioceptive feedback as long as performance is slow. However, in order to obtain high speeds, a faster, more direct, and finer control is necessary such as would be provided by an interhemispheric exchange of corollary or feed-forward discharges arising directly from the motor outflow. Such motor corollary discharges have been proposed by SPERRY (1950) and VON HOLST and MITTELSTAEDT (1950), and more recently by TEUBER (1964), who suggested that such a mechanism may depend on frontal brain structures.

As was hoped, the task did differentiate between performance of normal and epileptic controls with intact commissures and partial as well as complete split-brain patients. The complete commissurotomy patients were unable to perform the task except for two patients (L. B., N. G.) who were able to work only under the conditions requiring equal output from both hands. However, even here their performance remained very slow and erratic. Thus we see, as in the finger tapping and arm movement tasks, that following commissurotomy, in contrast to the survival of previously established bimanual skills, the acquisition and performance of new bilateral coordination is severely impaired. Again it is not clear whether this is due to a lack of interhemispheric sensory-motor transfer or competition between the hemispheres for control of the motor system, or both, since the latter may very well be the result of the former.

Lack of Fine Motor Coordination After Partial Anterior Commissurotomy. Both partial commissurotomy patients were able to perform the two-hand coordination task. However, compared with normal controls and persons with a similarly severe history of epilepsy, they showed less improvement after nearly 500 trials of training, and performed at a consistently inferior level in terms of both quality and speed (Fig. 3). It is suggested that the anterior commissurotomy eliminated a control mechanism involving direct interhemispheric action of motor corollary outflow, forcing these subjects to rely on slower visual and proprioceptive feedback systems. As mentioned earlier, there is no lack of interhemispheric transfer of sensory information in these patients.

In support of this interpretation is the fact that wavy traces persisted in the performance of these patients (Fig. 4). Similar

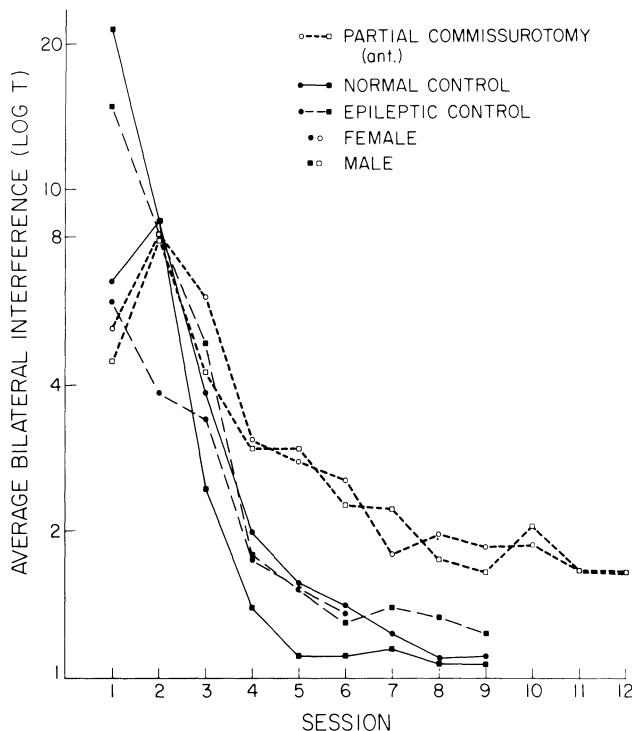


Fig. 3. Average interference (relative speed) during two-hand performance. Each data point represents the arithmetic mean of 48 trials in one weekly session. A T-score of 1 indicates no interference; a T-score of 2 means that two-hand performance was twice as slow as would be predicted on the basis of single-hand performance, i.e. on the performance of the slower hand or that which had to contribute the greater amount of input. Average absolute speeds during bimanual performance ranged from 3.45 (at 135°) to 4.85 (at 157.5°) revolutions per sec for the normal Ss. Epileptic controls: 1.88 (at 135°) to 2.61 (at 112.5°) revolutions per sec. Partial callosal patients: 1.53 (at 135°) to 2.50 (at 157.5°) revolutions per sec. (From PREILOWSKI, 1972)

oscillations are typical for performance with delayed feedback (POULTON, 1966) and result from a lack of fast, anticipatory corrections. When steering a car, for example, a beginner has the tendency to wait until the car is heading in the correct direction before returning the steering wheel to the normal position. Due to his reaction time and the lag in the steering system of the car he will overshoot, and again be forced to correct, repeating the cycle. Or just think of what happens in the shower when it takes several seconds before a turn of the faucet results in a change of water temperature.

The long-term dependency of the partial callosal patients on vision is further demonstrated by the results of withdrawing visual feedback (Fig. 5). While the control subjects are not affected when halfway through the track the lights are turned off or they are asked to continue with closed eyes, the partial callosal patients are unable to maintain uneven output from both arms. Instead they begin to turn at even rates with both hands.

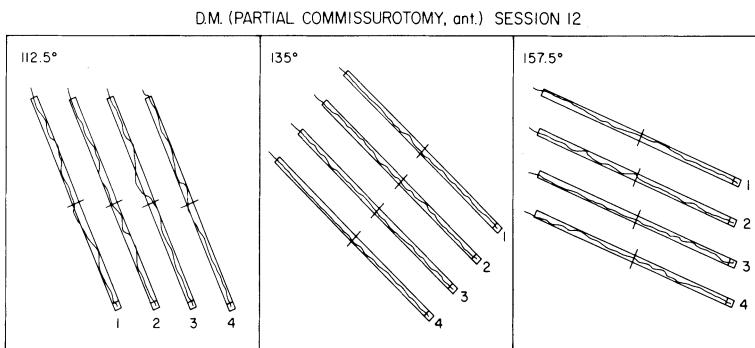
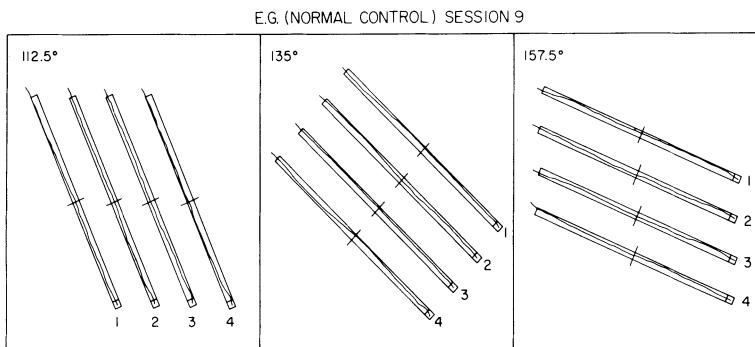


Fig. 4. Performance samples of a partial commissurotomy patient (D. M.) and a normal control (E. G.) from their last session, i.e. 12th and 9th respectively. Note the persistent oscillations in the performance of the partial callosal patient. (From PREILOWSKI, 1972)

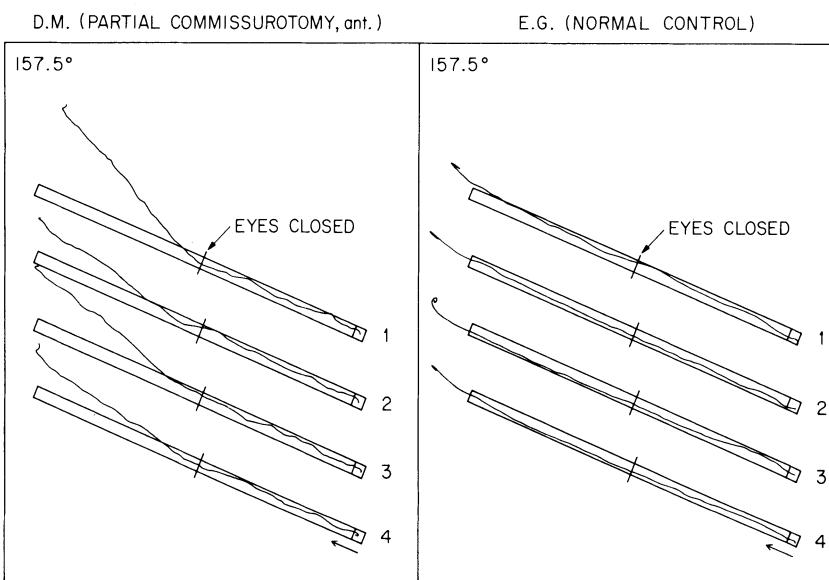


Fig. 5. Performance sample of a partial commissurotomy patient (D. M.) and a normal control (E. G.), when visual feedback was eliminated after crossing the half-way mark. The numbers indicate consecutive trials. (From PREILOWSKI, 1972)

Thus it appears that direct hemispheric interaction through frontal portions of the neocommissures is of importance for the fine regulation of the lower motor system from within each hemisphere.

Besides the significantly lower quality and speed of performance, the partial callosal patients show a persistent asymmetry, such that performance is worst when the left hand has to contribute the greater input (112.5° , see Fig. 2). A tentative explanation of this asymmetry has been proposed in terms of left hemisphere dominance (PREILOWSKI, 1972). This left hemisphere dominance is indicated in several reports about the differences of effects of right and left hemisphere lesions on motor performance (SEMMES, 1968; SEMMES et al., 1960; VAUGHAN and COSTA, 1962; WYKE, 1968, 1971 a, b). In a task requiring mutually adjusted movements of both extremities, total performance cannot exceed that of its weakest contributor. Therefore, if the left hemisphere is dominant, it can be reasoned that the predominant flow of inhibitory impulses through the intact commissures is from the right to the left hemisphere. Hence, at 112.5° , where the right limb, i.e. the left hemisphere, has to be inhibited most in order to stretch its lesser output over the total time taken by the left hand, the lack of control results in the most severe disturbance of quality and speed. As the proportion of the right-limb output to left-limb output increases in favor of the right extremity, the lack of callosal inhibition becomes less detrimental, thus resulting in a seemingly better coordination at 157.5° . Somewhat conflicting with this interpretation is the fact that when visual feedback is withdrawn there is no trend towards greater output by the right hand. Rather, both under conditions of 112.5° and 157.5° the tendency is toward equal output. However, it is possible that synchronous movements with equal output from both hands are controlled by still other mechanisms to which the patients resort when they feel insecure in maintaining unequal hand movements.

Interference During Asymmetric Movements. In normal subjects it has been repeatedly shown that limb movements are negatively influenced by simultaneous action of the contralateral extremity, and one hypothesis has been that the interference takes place at the cortical level via callosal interhemispheric connections (COHEN, 1971). In order to see whether in fact the commissurotomy patients would show interference with simple movements, the previously mentioned abduction and adduction movements of the lower arms were tested. Single arm movements, mirror-image movements, and parallel (asymmetric) movements had to be performed as fast as possible. Visual control was allowed so that the patients could check for synchrony of their movements. Figure 6 shows that with the exception of patients N. W. and R. Y., who were unable to synchronize their movements even with visual control, all patients showed a marked decrease in the number of asymmetric movements compared with the number of mirror-image movements. This definitely seems to exclude the possibility of the neocommissures playing a role in interference during synchronous, asymmetric movements.

Another hypothesis (COHEN, 1970) proposes that interference occurs when the limited capacity of a central processor for movement-generated feedback is exceeded. Thus simultaneous mirror-image movements, involving homologous muscles and supposedly re-

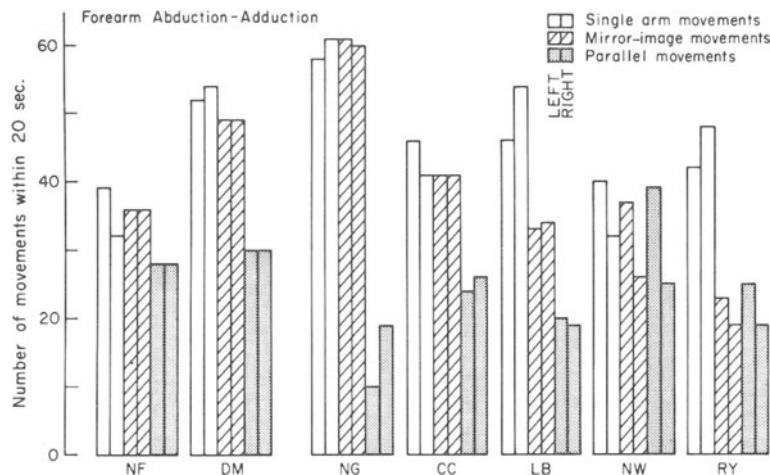


Fig. 6. Average number of single arm movements as well as mirror-image and parallel (asymmetric) bilateral movements of the lower arm of partial commissurotomy patients (N. F., D. M.) and complete split-brain patients (N. G., C. C., L. B., N. W., R. Y.)

dundant feedback, could be handled more easily than parallel movements which involve nonhomologous muscles and generate a greater amount of feedback.

The data which disagree with this theory come from the performance of the controls with intact commissures on the two-hand coordination task. These subjects, after about five sessions, performed with both hands essentially as fast as with one hand alone, except when lines had to be drawn at an angle of 135° . Under this condition, which required parallel motions of equal speed from both limbs, the controls performed significantly worse than at the two angles requiring unequal output from both hands, although here too parallel movements had to be performed. The same trend is at times seen in the performance of the partial commissurotomy patients, but it is difficult to evaluate because of their generally more irregular performance. According to the limited capacity theory the opposite result would have been expected: Movements requiring unequal output should be more impaired than those requiring synchronous output, since the latter should be associated with more redundant feedback.

At present it is felt that the best explanation of bilateral interference is in terms of ipsilateral efferent influences: If the ipsilateral innervation carries the identical information as that transmitted by crossed fibers, movements at each side initiated from one and the same hemisphere would be mirror images of each other. Thus the ipsilateral innervation from one hemisphere could oppose the contralateral outflow from the opposite hemisphere at some lower motor center. Normally this ipsilateral control would be overridden by stronger contralateral innervation. Loss of this overriding control would result in identical synkinesis or mirror-image movements, as they are observed after hemispherectomy or other lateralized cerebral insults (ZÜLCH and MÜLLER, 1969).

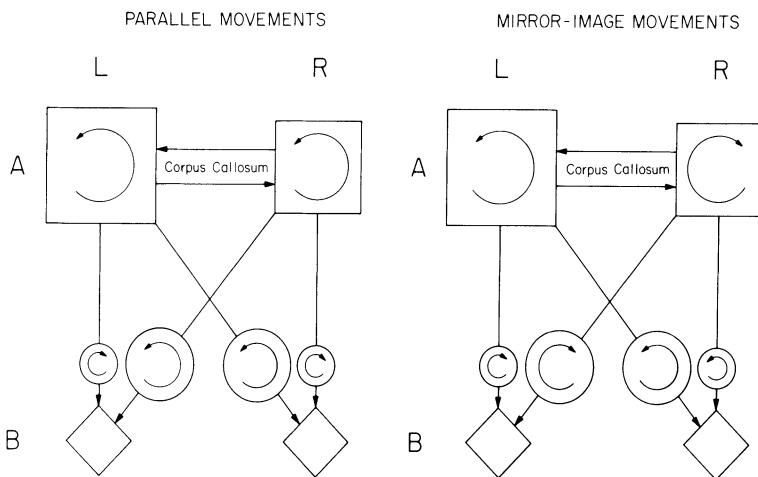


Fig. 7. Schematic representation of proposed interaction between ipsilateral and contralateral motor outflow during bilateral parallel (asymmetric) and mirror-image movements. A represents the cortical level. The circles indicate the type of motor signal transmitted to lower motor centers represented as B

Figure 7 gives a schematic representation of the proposed model. The cortical level is represented at A, with the unequal size of the boxes representing the predominance of the left hemisphere. The circles indicate the type of motor signal transmitted to motor centers at B. The figure illustrates how the influence of ipsilateral control interferes with contralateral signals from the opposite hemisphere during parallel, i.e. asymmetric movements, in comparison with no interference during mirror-image movements.

The finding that with parallel movements unequal output leads to faster performance than synchronous output can also be explained with the model presented here: If we assume that the magnitude of ipsilateral outflow is a function of the magnitude of the innervation of which it is the mirror-image, we can see that parallel movements requiring identical output from each hand such as under condition 135° show the greatest amount of interference of ipsilateral innervation with contralateral signals from the opposite hemisphere. However, if only one hand has to produce a maximal output, as was the case under conditions 112.5° and 157.5° , the strong ipsilateral outflow will interfere with the contralateral innervation to the hand which has to produce less output anyway. In this case bilateral performance will be less affected.

Lack of Interhemispheric Transfer of Motor Set. The results of another study should be mentioned here in order to strengthen the case for an involvement of the frontal cortical areas and its interhemispheric connections in fine motor control and anticipatory motor functions. The task in this experiment was to discriminate weights. The rationale of the task is derived from the evidence of motor involvement in weight comparisons (CHARPENTIER, 1890; PAYNE and DAVIS, 1940): Judgments of weight differences are based

on comparisons of motor output during the lifting of the weights, as well as on comparisons of sensory feedback, and the latter is only possible in relation to the first; of two objects of different size, but equal weight, for example, the smaller one is judged to be heavier (size-weight illusion). This is because more force is applied in lifting the larger object due to the fact that it is expected to be heavier.

Two complete (N. G., L. B.) and two partial commissurotomy patients (N. F., D. M.), as well as two normal controls were tested for their ability to discriminate between weights under three conditions. Firstly, judgments had to be made after successive lifting of weights with the same hand; secondly, after lifting with both hands simultaneously; and thirdly, by lifting first a weight with one hand and then the second weight with the other hand. In each case comparison weights of 150, 175, 200, 225, and 250 g were paired with a standard weight of 200 g according to a counterbalanced schedule.

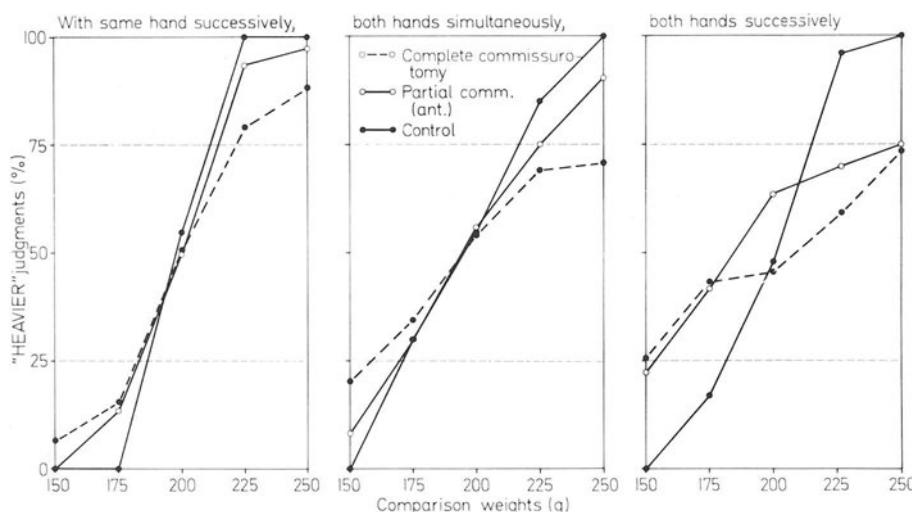


Fig. 8. Gradients of weight discrimination, i.e. average number of heavier judgments for each comparison weight with successive or simultaneous presentation to the same or opposite hand of a standard weight of 200 g

The percentages of heavier judgments, plotted for each of the comparison weights under the three conditions, are shown in Fig. 8. Right-hand and left-hand data were accumulated for the single-hand condition. Poorer performance is indicated in the figure by a flatter gradient. The results show that there is essentially little difference between the three groups of subjects when comparing weights successively with the same hand. When judgments were made after lifting the weights with both hands simultaneously, only the complete commissurotomy subjects showed a significant increase in error. However, when successive intermanual compari-

sons had to be made, the performance of the partial callosal patients fell to the level of the complete split-brain subjects, both groups being significantly inferior to the controls.

Following the rationale mentioned earlier, these results can be explained in terms of the existing interhemispheric cross-connections in the tested persons. The complete commissurotomy patients have lost all neocortical connections for interhemispheric sensory motor comparisons, while the partial anterior commissurotomy patients can still compare sensory feedback under the assumption that the motor output was equal to both hands. If information about motor output cannot be compared interhemispherically, as is proposed to be the case in the partial callosal patients, motor input may still be fairly equal under the simultaneous lifting condition. In successive lifts, however, it is less likely that motor inputs are identical, so that sensory comparisons are probably based on different motor inputs, and therefore lead to a greater number of incorrect judgments.

Summary

In closing, some of the main points arising from the studies of bilateral motor performance in partial and complete split-brain patients should be briefly restated. First, there is preservation of already established and overlearned skills after complete commissural section, and an inability to learn new bimanual coordination tasks: Of interest here of course is the question whether there is any functional reorganization. A specific investigation into this problem with respect to bilateral movements has not yet been undertaken in our patients. There is one of AKELAITIS' patients who showed no evidence of reorganization of motor functions after 27 years: This patient was described in 1942 to demonstrate normal motor behavior after complete surgical division of the neocommissures except for some fibers in the splenium (AKELAITIS et al., 1942). In 1969 the same patient was able to play simple tunes on the piano, embroider, and make lace, as she had been able to do 27 years ago. But she showed deficits in the transfer of training of manual tasks and in crossed visual-tactual identification (GOLDSTEIN and JOYNT, 1969). It is assumed by the authors of the more recent tests that the same deficits were present in 1942 but were overlooked, again illustrating the problem of assessment of "normal" motor behavior.

Secondly, the role of the ipsilateral innervation was discussed. This essentially allows each hemisphere to control the motor system of the body except for fine finger movements of the ipsilateral side. The proposed function of the ipsilateral innervation, checking the contralateral motor outflow, was incorporated in a model to explain interference during asymmetric movements.

Finally, the comparison between performance characteristics of partial and complete split-brain patients gave some indication as to the function of the commissures and the cortical areas, which they connect, in bimanual motor tasks: Visual as well as somesthetic feedback apparently transfers in posterior portions of the corpus callosum. Anticipatory motor information, conceived of as reafferences, corollary discharges or motor sets, are dependent up-

on anterior portions of the neocommissures. Loss of all cerebral commissures leads to excessive dependence upon visual feedback even for gross motor coordination, while disconnection of the frontal cortical areas results in deficits in fine bilateral motor adjustment in new manual tasks.

The investigation of motor performance in split-brain patients is still been carried out at the California Institute of Technology. At the same time experiments are being run with monkeys at the University of Konstanz, using various sized lesions of the callosum, together with physiological and behavioral tests to gain some further insight into the functions of the 'mysterious' frontal lobes and its commissural connections.

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Discussion

Dr. RUSSELL: May I ask a rather naive question which has always interested me: Why is it that the Los Angeles group sees so much more in the split brain than the AKELAITIS³ and SMITH⁴ groups do? This question has been raised many times; is it entirely because the behavioral observations are so much more sophisticated nowadays?

Dr. PREILOWSKI: I would think so; I think Dr. GAZZANIGA will support me in saying that we have indeed used much more sophisticated techniques. We have been very careful to lateralize our input to one or the other hemisphere. This is, I think, the most important aspect.

Dr. RUSSELL: I think that's an interesting suggestion because the reason I mentioned SMITH in association with AKELAITIS is because he had of course quite a sophisticated interest himself.

Dr. GAZZANIGA: You are coming back to lateralization factors, that's an interesting point. That same test, if repeated in these patients shows almost the same result. In addition, if you actually run AKELAITIS' tests in patients following his instructions exactly you obtain similar results to his.

Dr. POECK: ROBERT JOYNT⁵ re-examined one of AKELAITIS' cases and confirmed his findings.

Dr. PREILOWSKI: It may be added that differences may also be due to different surgical techniques used for these two groups of patients. In some of AKELAITIS' cases surgery was performed in successive operations. Also some patients did not have a complete split, but portions of the corpus callosum were left intact.

³ AKELAITIS, A. J.: Psychobiological studies following section of the corpus callosum. A preliminary report. *Amer. J. Psychiat.* 97, 1147-57 (1941).
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⁴ SMITH, K. U., AKELAITIS, A. J.: Studies on the corpus callosum. I. Laterality in behaviour and bilateral motor organization in man before and after section of the corpus callosum. *Arch. Neurol. Psychiat.* 47, 519-543 (1942).

⁵ GOLDSTEIN, M. N., JOYNT, R. J.: Long-term follow-up of a callosal-sectioned patient. *Arch. Neurol.* 20, 96-102 (1969).

Partial Commissurotomy and Cerebral Localization of Function¹

M. S. Gazzaniga²

It is indeed a pleasure and an honor to be included in this symposium in commemoration of OTFRID FOERSTER. Reading over Dr. ZÜLCH's elegant summary of FOERSTER's interests one is reminded of the scope and influence FOERSTER had on brain research. He had, of course, a particular fascination for the problem of localization of function and it is this subject I would like to discuss as it is approached through studies on commissurotomy.

Partial Commissurotomy and Cerebral Localization of Function

Animal Studies: Of the variety of questions raised by split-brain studies, none is more important than determining the effects of partial commissurotomy on inter-hemispheric integration tasks. Animal work has suggested there is a discrete specificity of function within the forebrain commissures. The posterior or splenial areas subserve visual transfer as does the anterior commissure (DOWNER, 1962; BLACK and MYERS, 1964; GAZZANIGA, 1966; SULLIVAN and HAMILTON, 1974). The area slightly anterior to the splenium is responsible for somatosensory transfer (MYERS, 1962). The functional significance of the rest of the callosum remains largely unknown although there is a strong suggestion that it helps, among other things, to maintain a motivational equilibrium between the two hemispheres (GIBSON, 1973). Here, monkeys with posterior section of the corpus callosum as well as unilateral damage to hypothalamic structures showed no eating differences between the hemispheres while completely split monkeys show a marked difference in eating behavior (GIBSON and GAZZANIGA, 1972; GIBSON, 1973).

Perhaps the most improbable and intriguing results from the partial section studies come from a series of reports by HAMILTON and his colleagues (HAMILTON and BRODY, 1973). He has shown that split-brain monkeys, with small segments of the callosum anterior to the splenium left intact, are able to perform an interhemispheric match-to-sample on a pattern discrimination, while simultaneously being unable to transfer interhemispherically pattern discriminations. Thus, a "+" versus "O" discrimination will not transfer through the callosum to the untrained half-brain while the animal can match a "+" or a "O" flashed to one hemisphere with a "+" and "O" sample presented to the other. This remarkable dis-

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sociation shows there is not, contrary to LASHLEY's opinion (1950), a total equivalence within a sensory system.

One interpretation of these data is that as visual information proceeds into the brain, it is constantly being recoded into new forms such that "X" becomes "X'". On the match experiments, the recoded "X'" transfers and as such is recognized by the opposite hemisphere which has performed the same operation on its "X". Thus, the match is possible. In a straight transfer experiment, however, "X'" is transferred but as such is of no assistance to the learning and memory mechanisms of the opposite brain which has had no meaningful experience with "X'". In some sense, the untrained hemisphere has the answer in the form of "X'" continually available to it - but it doesn't know what the question is. In a neurological vein, these data suggest that the learning and memory processes are initiated early in the primary visual system itself.

Human studies: In humans, there are both some classic accounts of neuro-psychological deficits with partial callosal section as well as new reports (GESHWIND and KAPLAN, 1962; GAZZANIGA and FREEDMAN, 1973; GORDON et al., 1971; GAZZANIGA and WILSON, 1973). In the late 30's, MASPES (1934) and TRECHNER and FORD (1937) described cases where a partial posterior callosal lesion resulted in a breakdown in the inter-hemispheric transfer of visual information. Indeed, MASPES reported that while his patients were unable to read in the left visual field, they were able to describe various objects presented in the left visual field.

A striking breakdown in the inter-hemispheric transfer of visual information following splenial section was recently studied by myself and Dr. FREEDMAN (1973). This patient was left-handed and, as a result, was easily able to verbally report left field visual information of all kinds while being unable to report identical stimuli presented to the right visual field. In this patient, there was no breakdown in inter-hemispheric tactile communication. This contrasts markedly with GESHWIND and KAPLAN's (1962) patient who had a dramatic breakdown in tactual function but no inter-hemispheric visual deficits. Their patient had tumor involvement in the anterior portions of the corpus callosum. Comparisons of clinical data such as these allows the determination of where various sensory functions are transferred in the corpus callosum.

In further testing of our patient, we ran a modification of the HAMILTON experiment on inter-hemispheric matching. We found some evidence that the subject could perform a match as to whether two geometric shapes were the same or different, no matter if they were placed in the same or different visual fields. In this test, geometric shapes such as a square, triangle, or circle were flashed in pairs with both appearing in the same visual field or with one presented to the left of fixation and one to the right. The subject was able to correctly judge whether the two were same or different, no matter where they were flashed. Yet, he tended to make errors when verbally describing the stimuli in the right visual field on the "different" trials. In other words, the right hemisphere speech system could not recognize the transferred information in the form it came over but could judge it was differ-

ent from what was being processed in the right. This state of affairs would allow for a correct response of a "same or different" judgment but would not afford the patient's right hemisphere information as to "what" was different about the stimuli.

At quite another level, the same kind of findings was seen in other studies. Engrams laid down in the right hemisphere in the absence of speech and language as the result of the left unilateral injection of amytal cannot be accessed by the language system upon its return to normal functioning (GAZZANIGA, 1972). Again, it would seem information stored in one form or neuronal mechanism is not easily accessible to another form or mechanism such as the language system. A similar result has been recently found by SEAMON and REISS (1973).

Mapping the Flow of Cognitive Information with Commissurotomy

One of the powerful uses of partial commissurotomy, as outlined above, is its application in the examination of where information is transferred in the corpus callosum. Since the area of the projection of the callosal fibers is usually known, this gives a good indication as to what part of the brain is involved in a particular task. It also allows examination of the question of how much backtracking there is in the cerebral flow of information. For example, if the visual areas are disconnected through a splenial section, can a visual-tactual match occur when the stereognostic information is presented exclusively to the hemisphere opposite the one receiving the visual stimulus? Or, conversely, can partial commissurotomy be used to explore the questions of whether lateralized mental duties carried out by specific structures such as, for example, the right frontal or temporal lobes, be carried out by the left hemisphere following frontal or temporal callosal disconnections? Likewise, can olfactory discriminations presented to the right hemisphere be known to the left following anterior commissure section?

These questions and more have been asked of a series of patients, most of whom have been operated on by Dr. DONALD WILSON of Dartmouth Medical School (WILSON, 1973). Dr. WILSON, using a new surgical approach he developed, has operated on several patients with the aim of limiting the interhemispheric spread of epileptic seizures. Encouraged by the medical results of the BOGEN series as well as the LUSSENHOP series (1970), WILSON has carried out both complete and partial sections of the callosal and anterior commissure fibers. We are currently investigating this new series of patients and some of these results will be discussed below.

Visual-tactile matches and vice versa: In the splenial section case described above (GAZZANIGA and FREEDMAN, 1973), who was unable to cross-communicate visual information, visual-tactile matches were easily performed when tactual information was placed in one hand and visual information was presented in either visual field. Since the match was made with split sensory input and since the visual information *per se* did not transfer in this subject, we must conclude the tactual information transferred over to the hemisphere viewing the stimulus. It is not possible, of course, to

say in which domain the actual judgment is made, that is whether the tactial information is made available to the visual system or vice versa. A less simplistic interpretation, of course, would be that the information is funnelled into another brain system within the hemisphere for final processing.

In a patient from the WILSON series, where we have concluded that a portion of the splenial area remained intact while the rest of the forebrain commissures have been sectioned, tactile information could not transfer interhemispherically whereas visual information could. In this case visual-tactile matches which required interhemispheric integration were also easily carried out. Here, it must be assumed that the visual information transferred for processing to the hemisphere exclusively holding stereognostic information.

This kind of data, of course, underlines how important it is to keep in mind the multiple channels that are available for the interexchange of information in the brain. If one channel is blocked another still remains that can do the job. Also, one cannot help but observe that it should not be too long before this kind of analysis could allow for even greater specificity in determining the nature of the interhemispheric codes. Namely, could a lesion that allows the interhemispheric transfer of recoded visual information, as in HAMILTON's experiments, be able to perform a visual-tactual match? Answers to questions such as these ought to shed more light on the extent to which neurally recoded information is functionally available to other brain systems.

Lateralized Lobular Function: MILNER (1963) has elegantly shown striking dysfunctions following left and right frontal lobe lesions. Specifically, lesions of the right and left produce perseveration revealed by the inability to easily shift conceptual hypotheses on the Wisconsin Card Sorting Test. Moreover, left frontals, as opposed to right frontals, have marked deficits in word fluency and spontaneous speech.

We have administered the Card Sorting Test to one patient with anterior callosal and anterior commissure disconnection in two forms - the normal approach and one where the stimuli were lateralized and quickly flashed onto the left or right visual field. The patient showed absolutely no hesitancy in responding to either test and performed well within the normal range. Another patient, however, where it is believed some splenial fibers remain showed a deficit on the Card Sorting Task. In addition defects were observed on the word fluency test suggesting the presence of an overall general frontal decrement. Still another patient, completely split but suffering from cerebral palsy since the age of five, showed no deficit.

These data suggest that the proper synchronous function of the frontal lobes is not disrupted following the interhemispheric disconnection of the frontal callosal projections. This contrasts markedly, of course, with the basic sensory systems of vision, touch, and possibly also olfaction, where the appropriate callosal section does block interhemispheric transfer. The model that can

be entertained here, of course, is that the superordinate regulating mechanisms in behavior, such as those involving the frontal lobes, diffusely influence many brain systems that extend way beyond the boundaries of frontal callosal projections. It would seem most of the cerebral mantle has access and makes use of the processed output of the frontal lobes and as such can communicate it to the opposite half brain in a meaningful way, through a variety of callosal channels.

A similar point could be made on another observation of ours where we again followed up a study carried out by Dr. MILNER. We recently administered to the WILSON series the tactual-spatial match-to-sample test which was devised by MILNER and TAYLOR (1973) for the BOGEN (BOGEN et al., 1965) patients. They found a dramatic right hemisphere superiority on this task with the left being essentially unable to perform the task. In our test on the partially sectioned patients, the left was found to perform the task easily - even in the case where only splenial fibers remained intact but with the interhemispheric somatosensory communication system disconnected. Here again, the data suggests a superordinate function specialized to one hemisphere can be contributed to the other over almost any callosal channel.

Other Tasks: In several other mental assessment tests that are supposedly carried out with the aid of right cerebral processes, such as the McGill Picture Anomaly Series (MILNER, 1958), the Kohs Blocks (CRITCHLEY, 1953), and the Benton-Spreen Sound Recognition test (BENTON, 1961), the three WILSON patients proved able to perform all the tasks and probably for different reasons. Case J. K. T., with the anterior commissure and anterior callosum section most likely performed the task because there was no disconnection of the interhemispheric temporal and parietal and occipital lobe fibers. In case T. O., with a complete section following early brain damage, these functions have most likely been assumed by the left hemisphere. In the third case (J. K. P.), with the splenial fibers remaining, it could well be this fiber system can subserve the interhemispheric transfer of information of the kind used in these tests.

Lastly, in the fully commissure sectioned patient, it has been shown that olfactory stimulation of one hemisphere leaves the other largely ignorant of the nature of the stimuli presented (GORDAN and SPERRY, 1968). In preliminary tests of ours on the extent of transfer possible with olfactory cues in the patient with the anterior callosum and anterior commissure section, there has been evidence which suggests that there is a marked disconnection of interhemispheric transfer of this kind of information. This would be predicted from the fact that the interhemispheric connection of the olfactory bulbs had been cut as a result of the sectioning of the anterior commissure. Since, however, there are a variety of interhemispheric fibers remaining that interconnect the speech and language areas of the brain, it is indeed striking that, as with vision and touch, an interhemispheric communication of this type of information is not seen.

Summary

The demonstration of the basic brain mechanism through studying the partially commissure-sectioned case appears to be a most promising enterprise. The work with animals of HAMILTON and others in elucidating psychological brain process heretofore not imagined are mere indications of what the potential seems to be. Study of the partially disconnected patient seems equally revealing and productive in showing how many high level cognitive activities are managed in the cerebral flow of information.

With respect to the issue of localization of function, it would seem clear that those cerebral areas clearly involved in the immediate processing of raw sensory information can be selectively and specifically isolated and disconnected. In other words, the informational products of the long axonal type cells of Golgi, which MARCUS JACOBSON claims are the brain cells under strict genetic control, can be isolated, whereas the products of more complex and integrative mental activities which are managed by the more mutable Golgi type II cells do not seem to be so specifically disposed. Thus, these data suggest the lateralized specialities of the various left and right brain areas can make their contribution to the cerebral activities of the opposite hemisphere through almost any callosal area regardless of its size and location. Indeed, this interpretation suggests to me that the long-standing issue of the extent of localization could be better understood by considering the dichotomy in genetic specification as offered by HIRSCH and JACOBSON (1974). Those central processes that develop because of the mutability potential of Golgi type II cells are hard to localize because of their ubiquitous nature whereas those tied to a specific genetically determined system are not.

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Discussion

Dr. GLEES: Do all layers of the cerebral cortex contribute to callosal fibers or do you think they come only from a particular layer?

Dr. CREUTZFELDT: According to some recent electrophysiological work of FADIGA et al. (Arch. ital. Biol. 110, 444 (1972)) and INNOCENTI et al. (Experim. Brain Res. 19, 447 (1974)) cells in the somato-sensory cortex which are somato-topically organized with small peripheral receptive fields, send axons through the corpus callosum. But the cells which receive transcallosal input have large receptive fields, are not somato-topically organized and do not seem to receive primary monosynaptic input from thalamic afferents. These cells do not seem to send axons through the corpus callosum.

A question I would like to ask Dr. MYERS: What is your opinion now about the lack of transcallosal connections between the projection areas of the distal parts of the limbs. In the cat, INNOCENTI and his colleagues also clearly showed transcallosal projection from the primary projection area of the digits of the forepaws.

Dr. MYERS: The most clear information available with respect to this question comes from work with raccoons and cats (EBNER and MYERS, 1965)³. In the raccoon, a special complex of gyri has been set aside for the reception of those somatic sensory stimulations which originate from the opposite forepaw. Studies with the Nauta technique have shown that this complex of gyri completely fails to receive commissural fibers as is true also of a much smaller homologic zone in the cruciate gyri of cats. Both of these species also show an absence of commissural fibers within the striate cortex.

The situation with respect to monkey is quite similar. The striate cortex of the monkey neither sends nor receives commissural fibers (MYERS, 1962)⁴. The hand sensory area of the postcentral cortex also fails to receive any fibers through the corpus callosum (MYERS, 1965)⁵. Thus, both in carnivores and in the primate, those areas of sensory receptive cortex which receive stimulations from those areas of the sensory surface which are highly specialized for sensory processing, e.g. the retina, the skin of the hands, etc., do not receive fibers through the commissures from the opposite hemisphere. It is as if, where a zone of sensory receptors is specialized for highly discriminant use in sensation, the sensory receptive areas corresponding to it are so set up as not to be subjected to interfering cross-chatter from the opposite hemisphere.

³ EBNER, F. F., MYERS, R. E.: Distribution of the corpus callosum and anterior commissure in cat and racoon. J. Comp. Neurol. 124, 353-365 (1965).

⁴ MYERS, R. E.: Commissural connections between occipital lobes of the monkey. J. Comp. Neurol. 118, 1-16 (1962).

⁵ MYERS, R. E.: Phylogenetic studies of commissural connections. In: ETTLINGER, E. G., DE REUCH, A. V. S. and PORTER, R.: "Functions of the Corpus Callosum". pp. 138-143. London: J. & A. Churchill 1965. (CIBA Foundation Study Group # 20).

Dr. CREUTZFELDT: And in the motor areas is there a good commissural interconnection?

Dr. MYERS: Yes, the same thing also applies there.

Dr. KUYPERS: The interesting thing is that these areas which are free, correspond to the areas which give the densest direct projections to the motor neurons of the hand and the feet.

Dr. MYERS: In a sense we have witnessed at a macro-level a counterpart to that described by Dr. CREUTZFELDT at the micro-level. I think the clearest documentation of this distinction between "distal versus proximal" is the work referred to above with the racoon.

Dr. YAKOVLEV: May I take liberty to discuss this very interesting point. I would like to draw attention to the differences in the relative densities of the commissural callosal interconnections between the "association" areas and between the "projection" areas of the two hemispheres on one hand and the differences in the relative densities of the thalamic afferents, respectively, to the association areas and to the projection cortical areas in each hemisphere on the other hand. There appears to be an inverse ratio of density of the bilateral commissural interconnection between the cortical zones of these two functionally and structurally different orders and the relative densities of the terminals of the thalamo-cortical afferents to these two different zones, particularly in the human brain. By simple dissection ("Auffaserung") it should be evident that the frontal and the temporoparietal association areas of homotypical cortex on the free convexities of the cerebral hemispheres (outermost or "ectocortex") have massive and dense commissural interconnections respectively through the knee and through the splenium of the corpus callosum, but receive relatively scant, widely dispersed ("diffuse"), (WALKER⁶, 1938) thalamic afferents, and the frontal association areas (areas 6, 9 and 10) in man may be wholly "athalamic" (YAKOVLEV, 1951)⁷. This is the inverse of the relatively scant commissural interconnections between the intimately thalamus-bound, special heterotypical cortex of the centroparietal, superior temporal and, apparently, wholly "a callosal" calcarine projection areas, receiving the most densely concentrated terminals of the so-called "specific" thalamic afferents. The point seems to have a considerable theoretical interest inasmuch as it points to the relative emancipation of the association areas from thalamic tutelage and, correspondingly, to a progressively increasing functional autonomy of the left and of the right hemispheres in the evolution of the human brain and behavior.

Dr. KUYPERS: I would like to ask Dr. GAZZANIGA about the role of the motivation in behavior as seen in the split-brain animals.

⁶ WALKER, A.: The Primate Thalamus. Univ. of Chicago Press 1938.

⁷ YAKOVLEV, P. I.: Anatomical Studies in Frontal Leucotomies II - Cortical origin of the Fronto-pontine tract and organization of Thalamo-frontal projections. Transact. Am. Neurol. Assoc. 1951, pp.53-56.

Dr. GAZZANIGA: The study was directed at looking at the question of whether one can establish motivational differences between the two hemispheres. If you take a basic response like eating, can you then change the probability of eating by unilateral damage to structures which are supposedly involved in that process? This is the thesis work of Dr. A. GIBSON. He discovered that unilateral damage in one hemisphere could clearly effect the probability of eating; the animal became hyperphagic when looking through to the world with one eye. He would eat much more than he would if he was viewing the world with the opposite eye.

The fact is that in several of the animals where there was an equivalent brain damage and where anterior portions of the callosum remained intact, there was no such contrasting motivational state.

Dr. MYERS: I want to add a few comments to those of Dr. YAKOVLEV's. Sometime ago, we surgically removed the thalamus on one side in two animals leaving the hemispheres entirely undisturbed. Studies with the Nauta technique showed that the sensory-receptive cortical areas (the striate cortex, the cortex of the postcentral gyrus, the auditory cortex, and, also, the precentral gyrus) were the areas which received the largest numbers of fibers from the thalamus. The rest of the cortex, received projections from the thalamus only sparsely. This was very surprising. The second thing was - and here I agree very much with Dr. YAKOVLEV's. generalization with respect to an opposition effect - the greater the reception of associational fibers from other cortical areas, the lesser the reception of fibers from the thalamus. Thus, the more associative an area of cortex, the fewer the fibers it receives from the thalamus. In some senses, it can also be said that the more associative the cortex the greater the component of commissural fibers, although exceptional cases do not conform with these generalizations. One very interesting area fails to fit any generalization; it is an area that we have already talked about today: the anterior temporal cortex. This area receives few fibers from the thalamus and almost none through the corpus callosum or anterior commissure. However, associational fibers between this zone and the prefrontal cortex have been identified passing through the uncinate fasciculus. Thus, the anterior temporal cortex appears to be the most strongly influenced by the prefrontal cortex.

Dr. YAKOVLEV: The general heterotypical cortex ("mesocortex") of the limbis of each hemisphere is intimately thalamus-bound by the abundant afferents from the limbic nuclei of the thalamus. This limbic cortex, even as the special heterotypical cortex of the supralimbic "projection" areas (which may be regarded as being the tectogenetic elaborations of the general heterotypical cortex, YAKOVLEV (1968)⁸ has no or only scant commissural interconnections through the corpus callosum (see discussion on p. 293). What is taken for the myelinated commissural fibers, say, between

⁸ YAKOVLEV, P. I.: Telencephalon "Impar", "Semipar" and "Totopar". Morphogenetic, Tectogenetic and Architectonic Definitions. Internat. J. of Neurol. 6, 245-265 (1968).

areas 24 of BRODMANN, are probably the collateral branches of the cingulum bundles, which, like the fibers of the fornix longus, permeate the corpus callosum. These are not "commissural" fibers, but are "projection" fibers (i.e. transcallosal collaterals of the axons of the pyramid of the area LA3 of V. ECONOMO and KOSKINAS' nomenclature) from the cingulate gyri of the two sides to the corpora striata and other subcortical formations of the forebrain (SHOWERS⁹, 1959; YAKOVLEV and LOCKE¹⁰, 1961; YAKOVLEV et al.¹¹, 1966). RAMON Y CAJAL¹² (1911) said that he has never succeeded in detecting commissural fibers in the corpus callosum between what he called "écorce interhémisphérique" in rodents.

Dr. GLEES: The Australian mammals have no corpus callosum, one ought therefore to investigate their hemispheric functions from a comparative point of view. What can they really do if they work quite independently?

Dr. OBRADOR: But they have an anterior commissure.

Dr. GLEES: Yes, but the anterior commissure is mainly olfactory; certainly they have no commissures corresponding to the corpus callosum.

⁹ SHOWERS, M. J. C.: The Cingulate Gyrus: Additional Motor Area and Cortical Autonomic Regulator. *J. Comp. Neurol.* 112, 231-301 (1959).

¹⁰ YAKOVLEV, P. I., LOCKE, S.: Limbic Nuclei of Thalamus and Connections of Limbic Cortex, III Cortico-Cortical Connections of the Anterior Cingulate Gyrus, The Cingulum and the Subcallosal Bundles in Monkey. *Arch. Neurol.* 5, 364-400 (1961).

¹¹ YAKOVLEV, P. I., LOCKE, S., ANGEVINE, J. B., Jr.: The limbus of the cerebral hemisphere, limbic nuclei of the Thalamus and the Cingulum bundle. In: *Thalamic Integration of Sensory and Motor Activities*. Columbia Symposium, D. P. PURPURA and M. D. YAHR, Eds. pp. 77-97, New York: Columbia Univ. Press 1966.

¹² CAJAL, Ramon y: *Histologie du Système Nerveux de l'Homme et des Vertébrés*, Vol. II, pp. 814, 815. Paris: Maloine 1911.

Visual Evoked Responses in Commissurotomy Patients¹

P. S. Gott, V. S. Rossiter, G. C. Galbraith², and R. E. Saul

Studies of patients who have undergone surgical section of the forebrain commissures indicate that the two hemispheres are specialized for different cognitive functions. The left hemisphere has been described as superior in speech, calculation, and related linguistic or analytic activities, while the right hemisphere is superior in configurational, spatial, and synthetic activities (SPERRY and GAZZANIGA, 1967; SPERRY, et al., 1969).

Subjects lacking direct interhemispheric communication offer a unique opportunity to study brain activity related to specific modes of information processing. In the present study we recorded visual evoked responses (VERs) in these subjects to investigate possible electrophysiological correlates of the "split-brain" phenomenon during the performance of tasks involving lateralized verbal and spatial stimuli.

Method

Tests were conducted on five subjects who had undergone surgical section of the forebrain commissures, including the corpus callosum, to help control intractable epilepsy (BOGEN et al., 1969). A control group consisted of five college students.

Monopolar VERs were recorded from left and right occipital (O_1 and O_2) and left and right parietal (P_3 and P_4) scalp areas, using the ear as a reference. The horizontal component of the electro-oculogram was also monitored to insure proper eye position during stimulus presentation. VERs were recorded to both verbal and spatial stimuli presented by means of a computer-graphics display. The stimuli were presented 5° lateral to a central fixation dot on the screen. While the subject fixated the dot, stimuli were flashed pseudo-randomly into the right, left, or both visual fields. Stimulus duration was 84 msec, which was brief enough to prevent eye movements that would have stimulated different portions of the visual field.

¹ This work was supported in part by U. S. Public Health Service Grant MH-03372; U. S. Public Health Service Fellowship 1F 02 NS 51207; Office of Naval Research under Contract N00014-70-C-0350 to the San Diego State College Foundation.

² The paper was presented by Dr. GALBRAITH.

In both tasks a response was indicated by pushing one of two buttons which were out of sight. In order to optimize set, the subject responded with the right hand during the verbal task and the left hand during the spatial task (the responding hand was thus under control of the hemisphere dominant for each task).

The verbal (rhyming) task required the subject to decide if a flashed word rhymed with another word constantly displayed below the fixation dot. Continuous presentation of the reference word facilitated performance in the patient group. Four different center words (KEY, MAT, EYE and SON) were used, each having ten rhyming and ten nonrhyming words that were flashed in each of the three stimulus combinations (left, right, or both fields). There were thus 80 stimulus presentations in each position.

The spatial (matching) task required a judgment as to whether a flashed geometric shape was the same as or different to another reference shape constantly displayed below the fixation dot. For each of four reference shapes ten shapes that were identical to the reference shape but rotated between $0^\circ - 270^\circ$, and ten entirely different shapes were presented. Stimuli were selected from a series of eight-point shapes reported by VANDERPLAS and GARVIN (1959) to have low association value.

VERs associated with correct behavioral responses were averaged; incorrect responses were not analyzed since the small number of errors committed by some subjects made averages too unreliable. In order to quantify patterns of VER waveform, correlation coefficients were computed between responses from within the same hemisphere, and between hemispheres. Correlations were then transformed to Z-scores, and an analysis of variance (ANOVA) for repeated measures was performed between the commissurotomy and control groups (WINER, 1962).

Results

The behavioral performance of each subject, and group means, are presented in Table 1. For a series of eighty stimuli, a performance above 61.2% is required to be statistically significant ($p < .05$) (HUNTSBERGER, 1961). All controls performed above chance in every condition, and there were no patterns of asymmetry according to the field of stimulus presentation. All patients were above chance during right-field and both-field verbal stimulation, and three were above chance during left-field stimulation. However, group means show a definite right-field (left hemisphere) superiority in the verbal task (80.3% for the right field as compared to 65.5% for left field). In the spatial task three patients performed above chance, two with either the right or left hemisphere and one with only the left. Thus, in the present experiment only the verbal task was successful in producing the lateralized effect typically found in commissurotomy patients.

Results of the ANOVA showed significant VER differences between patients and controls in the pattern of within- and between-hemisphere correlations. For both spatial and verbal stimuli, patients

Table 1
Performance

	Rhyming Test			Percent Correct			Matching Test		
	Left Field	Right Field	Both Fields	Left Field	Right Field	Both Fields	Left Field	Right Field	Both Fields
Patient:									
L. B.	75	82	78	94	94	97			
C. C.	62.5	76	71	87.5	79	94			
N. G.	91	87	82.5	50	58.8	47			
N. W.	47	72.5	82	56	62.5	51			
R. Y.	52.5	84	84	55	56	54			
Mean	65.5	80.3	79.5	68.5	70.1	68.6			
Control:									
1	75	73.8	81.3	68.8	62.5	73.8			
2	75	81.3	75	77.5	75	81.3			
3	68.8	67.5	61.3	75	75	77.5			
5	86.3	86.3	80	74.1 ^a	72.2 ^a	76.9 ^a			
6	81.3	81.3	88.8	75	76.3	75			
Mean	77.3	78.0	77.3	74.1	72.2	76.9			

^a Mean of other subjects to replace missing data.

showed overall higher correlations for within-hemisphere VERs ($p < .05$), while for verbal stimuli the between-hemisphere correlations were significantly ($p < .05$) lower, as compared with controls (Fig. 1).

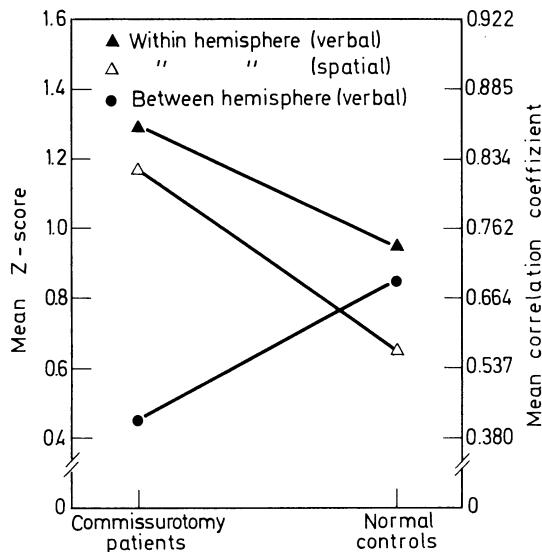


Fig. 1. Overall mean Z-score (left ordinate) and mean correlation coefficient transformed from Z-score (right ordinate) comparing commissurotomy patients and controls. Points plotted are the means for within- and between-hemisphere. Within-hemisphere data average correlations between O_1 and P_3 (during right-field stimulation) with correlations between O_2 and P_4 (during left-field stimulation). Between-hemisphere data average correlations between O_1 (right-field stimulation) and O_2 (left-field stimulation) with correlations between P_3 (right-field stimulation) and P_4 (left-field stimulation)

In addition to significant main effects, a significant ($P < .01$) interaction occurred for the left and right within-hemisphere VERs to verbal stimulation (Fig. 2). Thus, right-field inputs to the left hemisphere resulted in identical correlations for both groups, while left-field inputs to the right hemisphere resulted in widely divergent correlations. Commissurotomy patients showed an increase in right-hemisphere correlations, and controls showed a decrease.

Discussion

A basic assumption underlying the quantitative analysis used in the present study is that cross-correlations between VER waveforms reflect important properties of central nervous system coding. Previous research (BUSCHBAUM and FEDIO, 1969; JOHN, 1972; BARTLETT and JOHN, 1973) lends support to this assumption. In the present experiment high correlations (similar waveforms) are as-

sumed to indicate dependent or interrelated functioning, while low correlations (dissimilar waveforms) are assumed to indicate independent functioning.

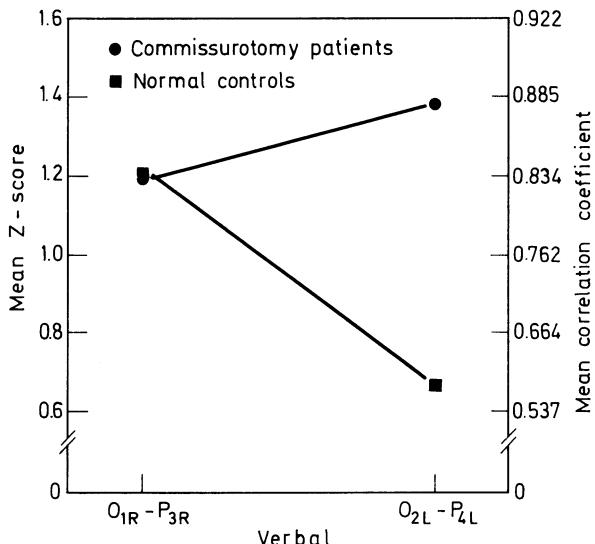


Fig. 2. Graph of within-hemisphere interaction to verbal stimulation for left- and right-hemispheres

The results of Fig. 1 show that commissurotomy patients have highly dependent within-hemisphere functioning, but independent between-hemisphere functioning. Presumably, the decrease in between-hemisphere coupling reflected in dissimilar VERs is due to the anatomical decoupling following surgical sectioning of the major forebrain commissures. The significantly higher within-hemisphere correlations, on the other hand, suggest increased similarity in functioning within the isolated hemisphere. This might result from the removal of regionally specific patterns of inhibition and excitation normally mediated via the corpus callosum.

Data presented in Fig. 2 show within-hemisphere correlations to verbal stimuli. Note that when a right field stimulus is presented, the left hemisphere correlations are identical for patients and controls. Since hemispheric functioning is obviously independent in the patient group, it is as if the left hemisphere of normal individuals is also independent in processing verbal information. However, when a left-field verbal stimulus is delivered to the right hemisphere (a task more difficult for the commissurotomy patients) there is wide diversion between patients and controls, the former showing an increase and the latter a sizable decrease. The high patient correlations suggest an autonomous right hemisphere attempting to process the verbal material (the mean performance of 65.6% was above chance). The reduced correlations for controls, however, is consistent with ev-

idence that the normal right hemisphere usually does not process verbal information independently. Rather, information is most likely transmitted via the corpus callosum to the left hemisphere.

From the present results it would appear that certain clearly lateralized functions in the commissurotomy subject can be identified in the sensory evoked response. Moreover, the data also suggest that lateralized information processing can be detected in the evoked responses of normal subjects. Although the present study is by no means definitive on this issue, it does appear that questions concerning the localization of function can be dealt with meaningfully by the evoked-response technique.

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Transcallosal Potentials in the Corpus-Callosum Cat

K.-A. Hossmann¹

The functional role of the corpus callosum for interhemispheric communication is a well-established fact which has been demonstrated convincingly in both experimental animals and humans (2, 9, 17). When the corpus callosum is sectioned (split-brain preparation), information which is fed into one single hemisphere is lateralized in this hemisphere and not available for processing in the opposite side (10, 11, 18). Transcallosal potentials (i.e. cortical potentials evoked by activation of callosal nerve fibers), therefore, have been considered to be the neurophysiological correlation of interhemispheric transfer of information (3, 4).

The anatomical organization of the corpus callosum is a relatively simple one. The callosal fibers mainly connect homotopic fields of both hemispheres (20, 21). In the primate the fibers originate and terminate in the granular and infra-granular layers (15, 19); in lower species the cells of origin are situated in the deeper layers (15), and the terminations of the fibers in the superficial ones (12, 15). The physiological demonstration of pure orthodromic transcallosal potentials nevertheless is quite problematic. The direct electrical stimulation of the callosal fibers evokes both anti- and orthodromic potentials because the callosal fibers run in equal numbers in both directions (4-7, 16). Efforts have been made to calculate the orthodromic transcallosal potential by simply subtracting the antidromic component from the mixed ortho- and antidromic response (5), but the validity of such an approach remains doubtful.

A more physiological method of obtaining transcallosal potentials is to evoke a primary cortical potential in one hemisphere and to record the corresponding transcallosal potential from the homotopic field of the opposite hemisphere (1, 3, 8, 14). In such an experimental set-up, however, precautions must be taken to avoid a contamination of the transcallosal potential by extra-callosal volleys (8). A radical but efficient way to solve this problem is the so-called corpus-callosum preparation in which all connections between the two hemispheres with only the exception of the corpus callosum have been interrupted. In the cat this preparation is produced in the following way (13): 1) the brainstem is transversely dissected rostral to the trigeminal nucleus, and 2) the forebrain is dissected in the midline below the corpus callosum using a small spatula which is introduced horizontally from behind the tentorium (Fig. 1).

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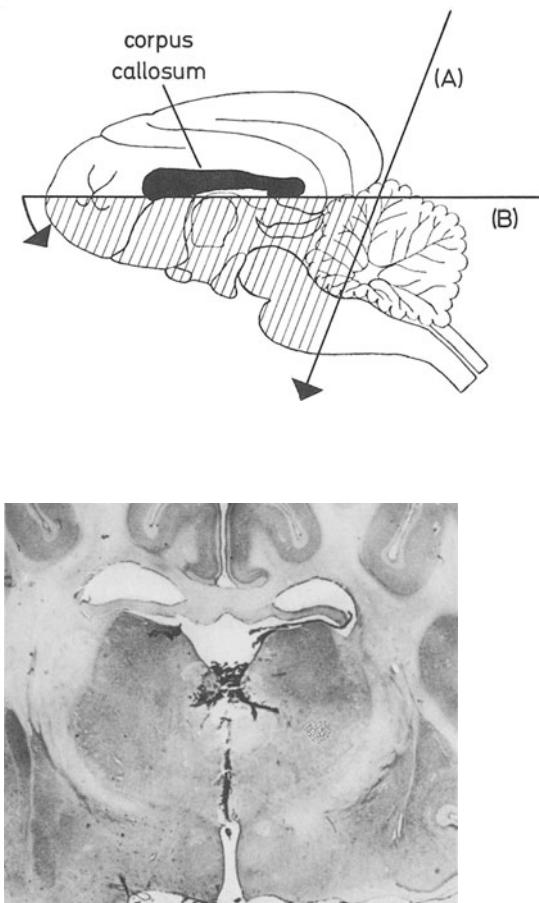


Fig. 1. Surgical procedure for the corpus-callosum preparation. First, the brain stem is transversely dissected rostral to the sensory trigeminal nucleus, followed by a section of the midline below the corpus callosum. The integrity of the corpus callosum is confirmed by histological examination (below)

Following this operation anaesthesia may be discontinued because the animal remains in a state of sleep after all sensorial input has been interrupted. This is confirmed by recording the encephalogram which shows a typical sleep pattern (Fig. 2). It is possible to evoke an arousal by electrical stimulation of the mesencephalic reticular formation rostral to the bulbar section. The arousal lasts as long as the reticular stimulation continues; a few seconds after termination of the stimulation a sleep pattern reappears (Fig. 2). Interestingly, the arousal effect is strictly confined to the side of the stimulation; only at very high stimulation intensities (above 1 mA) the arousal may spread to the contralateral side, particularly to the frontal regions. When two electrodes are placed bilaterally into the reticular formation each hemisphere can be kept individually in a state of sleep or alertness. Thus, cortical potentials can be easily studied under different conditions of vigilance (see below).

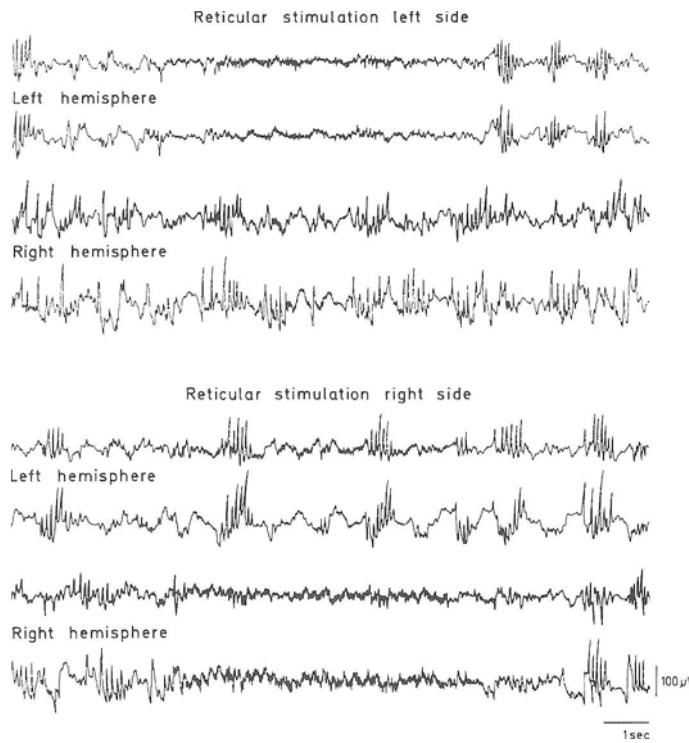


Fig. 2. Unilateral arousal effect in the electroencephalogram of the corpus callosum cat after electrical stimulation of the ipsilateral mesencephalic reticular formation. Above: stimulation of the left side; below stimulation of the right side

In the corpus-callosum cat orthodromic transcallosal potentials are evoked in the following way (Fig. 3): 1) a stimulation electrode is inserted into a thalamic projection nucleus and the primary cortical evoked potential is recorded on the side of the stimulation. 2) The cortical field in which a primary evoked potential of maximum amplitude is obtained is stimulated in turn and the homotopic area of the contralateral hemisphere is determined by recording the corresponding evoked potential. 3) By stimulating the thalamic nucleus again, primary and orthodromic transcallosal potentials can be recorded simultaneously from the so-defined cortical areas. 4) When a second stimulation electrode is inserted into the contralateral thalamus, primary and transcallosal potentials may be obtained from the same cortical field; this is particularly useful for microelectrode recording from single cells (see below).

In the corpus-callosum cat, transcallosal potentials have been recorded from the visual, the somatosensory, and the suprasylvian gyrus following stimulation of the contralateral geniculate body,

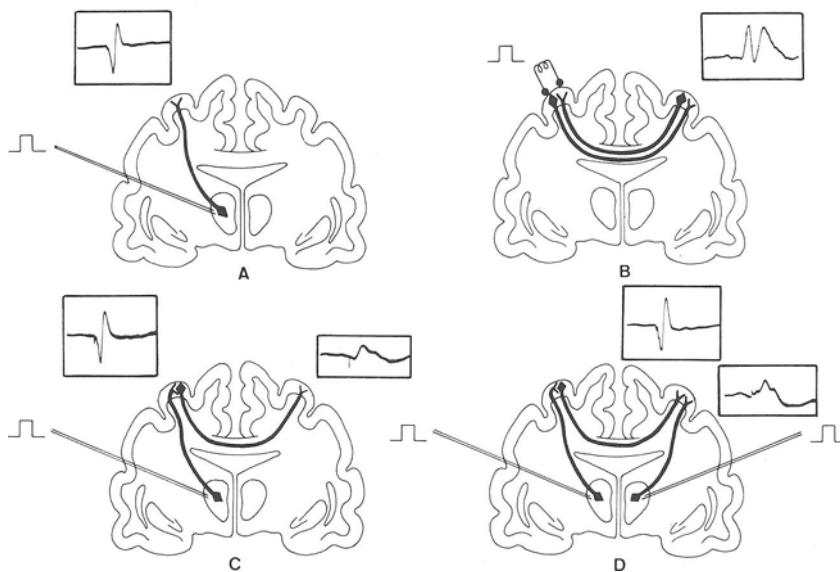


Fig. 3. Schematic representation of the recording of orthodromic transcallosal potentials in the corpus callosum cat. (A) Recording of a primary cortical potential after thalamic stimulation. (B) Determination of the callosal projection by electrical stimulation of the cortex. (C) Recording of the primary evoked potential in one hemisphere and of the corresponding orthodromic transcallosal potential in the homotopic field of the opposite hemisphere. (D) Recording of a primary evoked potential and of a transcallosal potential in the same cortical field by stimulation of the ipsi- and contralateral thalamus respectively

the ventral postero-lateral, and the lateral posterior nucleus of the thalamus respectively (14). Although very similar to each other, the transcallosal potentials differ considerably from the corresponding primary evoked potentials (Fig. 4). They consist of a monophasic surface negative wave which is occasionally followed by a second monophasic negative or biphasic positive-negative wave. At maximum stimulation intensity, the latency ranges from 2 to 5 msec, the duration of the initial monophasic wave is 10 to 15 msec, and the amplitude up to 500 μ V. Both the primary and the transcallosal volley may evoke a cortical 8 to 10/sec spindle of 1 sec duration after an interval of 50 to 100 msec. These spin-dles are sometimes but not regularly synchronous with each other.

The transcallosal potentials depend on the corresponding primary potentials in so far as their amplitudes increase with increasing stimulus intensities in parallel to those of the primary potentials. When the size or amplitude of the primary evoked potentials is changed by external interference, the transcallosal potentials are affected very little (Fig. 4). For example, the modifications of the primary evoked potentials by topical application of potassium chloride, strychnine, and anodal or cathodal polarisation are not reflected by parallel changes of the corresponding trans-

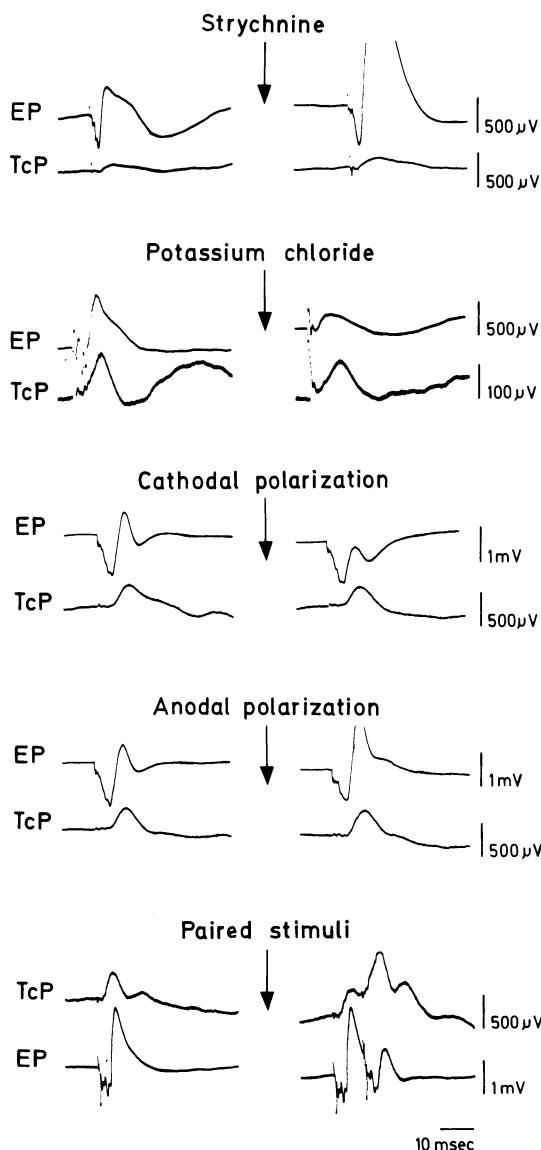


Fig. 4. Recording of the primary evoked potential (EP) and the corresponding transcallosal potential of the opposite hemisphere (TcP) after stimulation of the ventral postero-lateral nucleus of the thalamus in the corpus-callosum cat. The topical application of strychnine, potassium chloride and anodal or cathodal polarisation of the ipsilateral somatosensory cortex causes typical changes of the primary evoked potential, but does not influence significantly the corresponding transcallosal potential. Paired stimulation of the thalamus causes an occlusion of the primary and a facilitation of the transcallosal potential

callosal potentials. Occlusion of the primary evoked potentials by paired stimuli at short intervals even has a reverse effect on the transcallosal potentials, which instead are clearly facil-

itated (Fig. 4). Finally, the transcallosal potentials are not modified by a cortical arousal, regardless of whether this has been induced in the same, the opposite, or both hemispheres.

These observations suggest that the dipoles which generate the primary evoked potentials are not identical with those which give rise to the transcallosal volley. Consequently, the findings in the corpus-callosum cat contrast with observations in intact animals, in which the similarity between primary evoked and transcallosal potentials has been explicitly stressed (3).

The difference between the primary and the transcallosal potentials is further corroborated by unitary recording. With the experimental set-up which has been described above (Fig. 3), the effects of primary and transcallosal volleys can be compared in the same cell by simply changing the side of stimulation. About 50% of the cortical cells which are activated by a primary afferent volley also respond to a transcallosal impulse, but the firing pattern differs from the primary activation in a very typical way. The primary volley evokes a short latency (1 to 5 msec) activation, followed by an inhibition of spontaneous cell discharges for about 100 msec, and frequently by a rebound-like activation during the induced cortical spindle. The orthodromic transcallosal volley on the other hand, very rarely evokes a short latency response (in less than 10%). There is, however, the same pattern of delayed events, i.e. an inhibition of spontaneous cell activity, and a secondary activation during the cortical spindle (Fig. 5).

The interrelationship between spindle and cell activity is stressed by the following observation. When the animals are kept in a sleep state, spontaneous cortical spindles occur at irregular intervals. During such a spindle, 64% of the cortical cells change their discharge pattern: 13% are inhibited and 51% activated. When a spindle is evoked by primary or transcallosal afferent volleys, the same discharge pattern is maintained, i.e. the cells always respond in the same way, regardless of where or how the spindles originate.

Comparing the micro- and macrophysiological observations in the corpus-callosum cat, one gets the impression that interhemispheric transfer of information must be a complex process which cannot be reduced to the transcallosal potential *sensu stricto*, i.e. the monophasic surface negative wave which is the transcallosal counterpart of the primary cortical potential. Of particular interest is the inhibitory phase following the transcallosal potential, and the delayed cortical spindle which is triggered by the transcallosal potential. This pattern is evoked at the same interval and at the same threshold as by the primary potential although the thalamus on the side of the transcallosal potential is not directly activated. It is, of course, doubtful whether a process such as transfer of information can be described in terms of cortical potentials; however, if this is possible at all, then the delayed phenomena following the transcallosal potential should be the main target of future research.

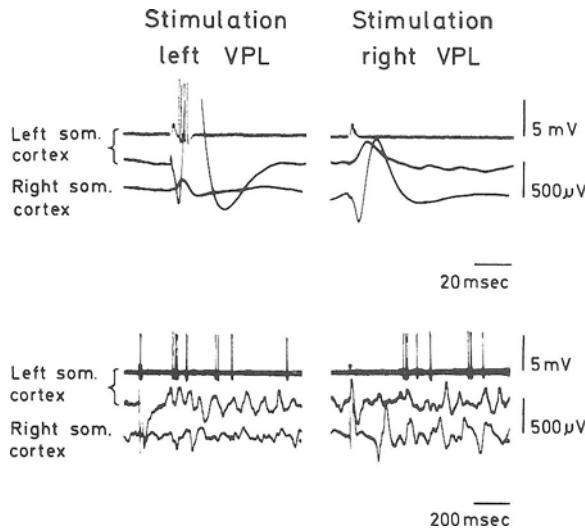


Fig. 5. Extracellular recording from an unidentified neuron of the somatosensory cortex following stimulation of the ipsilateral (left) and contralateral (right) ventral postero-lateral nucleus of the thalamus (VPL). Simultaneous recording of the primary and transcallosal potentials from the ipsi- and contralateral somatosensory cortex, respectively (above: fast sweep; below: slow sweep). Note the absence of a short latency activation of the neuron by the transcallosal volley, but the similarity of the delayed phenomena after primary and transcallosal volleys

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III. Social Behavior

Neurology of Social Behavior and Affect in Primates: A Study of Prefrontal and Anterior Temporal Cortex

R. E. Myers¹

The rhesus monkey is a generalized primate widely distributed and abundant in Asia. For these reasons, it has long been used for laboratory studies. More recently, the free-ranging behavior and population dynamics of the rhesus monkey has also been examined both in India and the United States, where a prime population has been maintained since the 1930s on Cayo Santiago, an island offshore of Puerto Rico. These studies have afforded a detailed description of the social behavior of this species.

Rhesus monkeys form social groups whose size varies from 8 to over 200 animals. The larger group sizes are attained only under circumstances of a favorable food supply. Under free-ranging circumstances, this species breeds seasonally, mating over a 3- to 4-month period each year and bearing its young 5 months later. Matings and births do not appear outside of the two respective distinct seasons. Social groups which live in proximity are mutually antagonistic, animals from one group failing to associate with animals from the other. Aggressive interactions occur between individuals or small groups when social bands meet during travel or at feeding stations.

A masculine hierarchy exists in every group and the most dominant male can be readily identified. The dominant males appear to maintain order within the group by breaking up fights and are the ultimate defenders of the band against outside threat. Consort relationships exist only during the breeding season, and, at other times of the year, mature males and females are not found in close relationship although the members of a group remain together as they move from place to place. Small subgroups consisting of members of a family are matriarchal in organization, mature females being surrounded by their immature offspring. Thus, an adult female may suckle its newborn at the breast and be surrounded by a yearling, a two-year-old, and a subadult daughter. The female's sister may be nearby with her own offspring. Thus, the physical closeness exhibited by two individuals within a social group and their frequencies of grooming reflect their degrees of blood-relatedness.

The male offspring leave the mother's side by the third or fourth year and take positions on the periphery of the social group, or

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they may leave the group entirely to join another. During their first years, the male offspring of dominant females win at games since their mothers, who oversee their play activities, enter in to protect them against adversities that arise. Correspondingly, these males later are seen to assume roles of greater importance within the group, perhaps because of the early effective support of their mothers during play and their conditioning in the process to be winners. The fact of being born within a stable social order and of growing up with the others in the band with its defined patterns of dominance and submissiveness lends an enormous subtlety and complexity to the derived behaviors of individual animals. Family ties are of major importance in defining who associates with whom and the qualities of the interrelationships.

This complex and highly structured social hierarchy of the rhesus monkey affords an opportunity for the study of the neurology of social behavior. Such studies have a major relevance for our understanding of the brain-basis for the behavior of the human species as it participates in a still more complex order. At a time when enemy lists and intergroup enmities still play a prominent role in our lives, attempts to study the biological foundations for human social behavior seem particularly relevant.

Most studies of the neural control of social behavior and emotion have emphasized the role of forebrain limbic structures. However, despite a long-term interest, little progress has been made toward clarifying the role played by the cerebral cortex. For reasons described earlier (MYERS, 1967), the prefrontal and anterior temporal cortex together have been suggested as contributing importantly to the regulation of social behavior. In pursuing this hypothesis, studies were carried out with free-ranging rhesus monkey social groups on Cayo Santiago (MYERS and SWETT, 1970; MYERS et al., 1973). The behavior of individual animals was carefully defined before and after ablation of the prefrontal, the anterior temporal, or the cingulate cortex (see Fig. 1). The greater number of the animals with large bilateral lesions of the cingulate cortex returned to their social group and to their families and showed little alteration in their patterns of behavior. The same was true for still other animals with control lesions elsewhere in their brains. In contrast to this, the animals with either prefrontal or anterior temporal cortex removals, when again released in the midst of their social group, fled to the surrounding underbrush leaving their group behind. They remained as isolates thereafter until no longer sighted (for as long as several weeks). Thus, animals with bilateral prefrontal or anterior temporal lesions showed the maximal disturbance possible of social behavior, i.e. they failed to return to their social group and avoided further participation in the family life. These lesions put in abeyance those profound instincts which cause rhesus monkeys to band together to form social groups.

However, these studies with free-ranging animals did not permit a refined analysis of the social behavioral deficits produced by the lesions since the prefrontally and anterior temporally operated animals failed to rejoin their social group. Thus, another series of studies were carried out on small social groups of rhe-

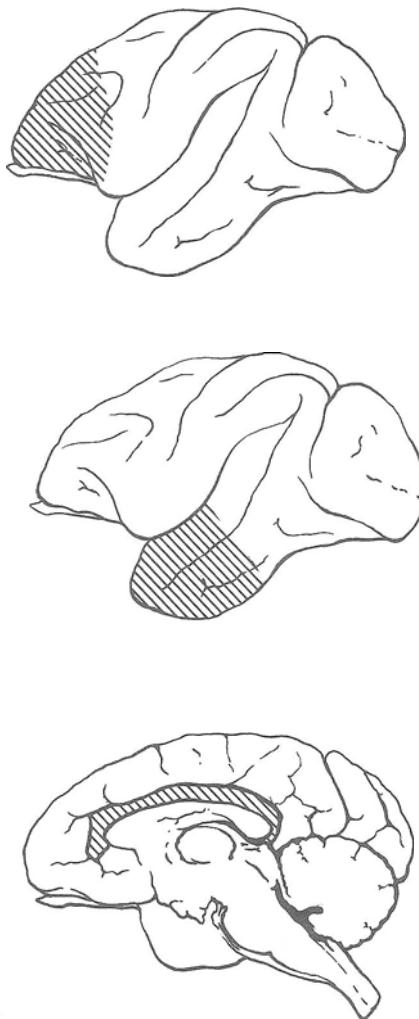


Fig. 1. Extents of cortical lesions: prefrontal (above), anterior temporal neocortical removal (middle), and cingulate cortex removal (below). These lesions were carried out bilaterally and symmetrically and were closely similar from animal to animal throughout the study

sus monkeys which were constituted and maintained in large enclosures (FRANZEN and MYERS, 1973a). On restoration to these enclosures following production of brain lesions, these animals were forced to remain in relation to or within their social groups.

The number of animals within these gang cage social groups varied from 6 to 12 and were selected so the groups exhibited relatively normal age and sex compositions. Again, bilateral cortical ablations were carried out including prefrontal lobotomies, anterior temporal cortical removals, and cingulate gyrus removals. Large bilateral visual association cortex lesions were also made as an additional control on the effects of cerebral ablation (see Fig. 2). The behavior of the animals within these groups was studied before and following the surgical ablations.

The prefrontal lesions produced the most dramatic changes. The alterations were global in character and affected every aspect of

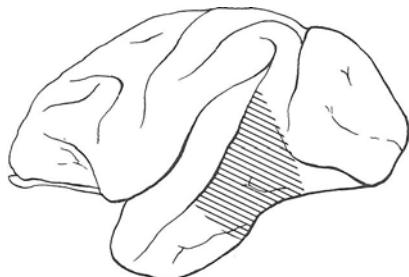


Fig. 2. Extents of lesions of visual associational cortex (areas 20 and 21). These lesions were bilaterally symmetrical and closely similar from animal to animal

social and emotional behavior. Thus, adult females caring for their infants completely lost their usual solicitude and protectiveness of them. They no longer defended them against threat or abuse by other animals or from outside humans. Instead, these mothers permitted their infants to wander about in a distressed state, emitting frightened, "I am lost" vocalizations. Nonetheless, most of the infants managed to continue to nurse at intervals at the breasts of their mothers, but all approaches and body contacts were initiated by the infants. The lesioned mothers failed to show the usual cradling or cuddling of the infants during such nursing intervals. Beyond these infrequent contacts, the infants were cared for or protected by other animals in the group (in two instances, by the dominant male).

The prefrontally operated animals showed their deficiencies in social interactions with other animals in a multitude of other ways. Facial expressions and vocalizations -- which normally play a prominent role in the social communication of the rhesus monkey (*vide infra*) -- were largely lost. These latter deficits left the prefrontal animals strangely mute and poker-faced. The frequent, complex, and usually rapidly unfolding patterns of interaction which take place many times throughout each day between individuals within a group were largely deleted from the repertoire of the lesioned animals. The prefrontally deficient animals no longer functioned at their previous levels within the dominance hierarchy and fell to a low regard within the group. They could be and usually were displaced by all other animals including the lowest. As a consequence of this altered status, a heightened frequency of attack of the lesioned animals by others within the group appeared and led to their increased submissiveness and flight. Apart from such evoked defensive responses, the demeanor and appearance of the prefrontally operated animals was largely that of automatons.

As already noted, the proximity displayed by any two animals within a group tends to relate to their closeness of blood relation. Also, during the mating season, the average distances exhibited between adult males and females are affected by consort relations. Again, the proximity scores of prefrontally operated animals with respect to other animals were greatly altered. During the initial postoperative period, the prefrontally operated animals were frequently approached by other animals within the group. Soon, however, the other animals, including their own family members, no

longer associated with the lesioned animals. Likewise, the close ties which appear during consort relationships again failed to appear and, in other respects, the lesioned animals (females) showed inappropriate sexual responses. Other changes in social behavior produced by the prefrontal lesions included decreased aggressiveness, decreased grooming of other animals, loss of play behavior, and inappropriate approach to other animals.

A second study of the effects of bilateral prefrontal cortex removals was carried out with infants, juveniles, and adults (FRANZEN and MYERS, 1973b). Pre- and postoperative observation of these animals showed that the above-described social behavioral deficits failed to appear following lesions in infants or one-year-olds. The first traces of such deficits appeared in animals operated on in the second year of life and were even more severe in operated three-year-olds. The full social behavioral deficits appeared only following lesions in still older juveniles or adults. These results show that the prefrontal cortical regions are late in maturing in the rhesus monkey and imply some inadequacy in the control of social behavior as a normal circumstance among animals of earlier age groups (up to three years of age) as compared to adults.

The prefrontal cortex lesions, in addition to producing the social behavioral changes already described, also caused a pattern of hyperactivity. This consisted of an aimless pacing activity which appeared in animals held both in the free-ranging state and in gang cages. This hyperactive pacing activity differed from the hyperactivity described in earlier reports in that the periods of pacing were interrupted by periods of marked motor stillness. During such periods, the animals would sit and stare straight ahead, not responding in any definite way to environmental stimulation.

Bilateral removal of anterior temporal cortex led to social and emotional behavioral deficits similar to those which followed prefrontal lesions. However, the severity of these deficits was less, and, unlike the prefrontal animals, those with anterior temporal lesions evidenced some recovery of their patterns of behavior as they survived beyond the first weeks. The animals with temporal lobe lesions also did not show any signs of the bizarre pacing behavior, but, instead, they exhibited a prominent sniffing of objects. This seemed part of a tendency toward an exaggerated olfactory exploration of the environment. Thus, the symptomatology of lesions of the prefrontal and of the anterior temporal cortical areas showed large areas of overlap but some dissimilarities.

The extensive bilateral removals of cingulate or visual association cortex failed to produce clear-cut or reproducible deficits in social behavior. This relative slightness of behavioral deficits following cingulate lesion is surprising inasmuch as lesions of this cortex zone have been described as producing clear-cut defects in motivation or affect in humans. Even more of interest was the absence of social or emotional behavioral deficits following the large bilateral lesions within the visual association

cortex. It might have been anticipated that such large lesions might have led to severe perceptual or mnemonic deficits associated with impaired recognition of other animals within the group or with disturbed interpretation of the significances of patterns of social activity. The absence of social behavioral deficits following the lesions of the posterior associational and interpretive cortex indicates this zone of cortex must play a role of lesser importance in defining the patterns of social and emotional response of the animals. The absence of social behavioral deficits following the visual association cortex removals also serves to emphasize the specificity and uniqueness of the global social behavioral deficits produced by the lesions of the anteriorly placed prefrontal and anterior temporal cortical areas.

Observations of monkeys in the field emphasize the intimate role played by facial expressions and vocalizations in social communication functions. That is, facial expressions and vocalizations, usually acting in concert, serve to express threat or attack, to communicate submissiveness, to give warning calls to others, etc. They may also serve to express inner feelings or affect as they may occur apart from any social setting as, for example, those vocalizations which express hunger, being lost, etc.

To further clarify the role of vocalization in the rhesus monkey, an investigation was carried out attempting to bring rhesus monkey vocalizations under instrumental control (YAMAGUCHI and MYERS, 1972). However, despite prolonged and diverse attempts at the instrumental conditioning of vocalization, no success was achieved. The difficulty encountered suggests that rhesus monkey vocalizations may be poorly under volitional control. In addition to fitting the facts of our prolonged and unsuccessful efforts at conditioning, this conclusion supports the supposition that rhesus monkey vocalizations and facial expressions are largely tied up with social behavior and affect - functions which themselves are largely outside of volitional control.

After failing to condition the vocal response of the rhesus monkey, a series of animals were nonetheless examined with respect to the patterning and frequency of their spontaneous vocalizations as they appeared within a standard setting. Those areas of the cerebral cortex presumed to be homologous to speech areas in the human were then ablated bilaterally (YAMAGUCHI and MYERS, unpublished studies). These lesions separately or in various combinations failed to produce significant alterations in spontaneous vocal output. This result suggested that vocalization in the rhesus monkey differs from speech in the human in that it is not primarily regulated by posteriorly located associative and integrative zones of cortex.

As it became clear that the prefrontal and anterior temporal cortex are involved in the control and regulation of social behavior and affect in the rhesus monkey and as it became clear that vocalizations and facial expressions in this species have meaning primarily in relation to social communication or the expression of affect, it was asked whether facial expressions and vocalizations also may be controlled by the selfsame cortex zones which regulate social behavior and affect. That is, is it possible that

the prefrontal and anterior temporal cortical areas regulate vocalization and facial expression in the rhesus monkey?

Subsequent studies have indeed demonstrated that lesions either of prefrontal or of anterior temporal cortex produce major deficits in vocal response (MYERS and YAMAGUCHI, unpublished study). That is to say, bilateral prefrontal cortex lesions regularly produced a near-total muteness of the animals and this vocal deficit tended to be permanent. Anterior temporal cortical lesions also caused major but not so severe decreases in the frequencies with which rhesus monkeys spontaneously vocalize. However, the severity of these deficits following temporal lobe lesions decreased to some extent over a several-week period. Bilateral lesions of the cingulate cortex produced variable and not so prominent effects on vocalization. Thus, it was concluded that the prefrontal and the anterior temporal cortex are both concerned not only with regulating and controlling social and emotional behavior but they also determine the patterns of facial and vocal activity.

Earlier studies showed that unilateral removals of the entire parietal or occipital lobe did not alter patterns of rhesus monkey facial movement. On the other hand, total frontal or temporal lobe removals both produced varying degrees of weakness of the opposite side of the face (MYERS, unpublished studies). Paradoxically, unilateral removal of the prefrontal cortex alone led to as severe a contralateral facial deficit as did removal of the entire frontal lobe, and, also, unexpectedly, restricted precentral gyrus removals occasionally failed to cause opposite-sided facial weakness. Thus, some cortex zone within the temporal lobe and, independently, the cortex in the prefrontal region both show evidence of controlling facial movements. These results now can be understood in the context of a prefrontal and anterior temporal lobe involvement in the regulation of social behavior and affect and of the associated facial and vocal patterns of activity.

Neurologists have long recognized two distinct types of facial expression in the human: the one expresses the actual inner feelings of the individual and is described as "emotional" facial expression while the second appears under the control of volition and enables the individual to recreate various expressions of the face at will but without feeling the appropriate affect. The forced smile or the baring of the teeth on command are examples of such "volitional" uses of the face. Corresponding to these two types of face use in the human, there exist two distinct neural mechanisms involved in their regulation (see also page 34). That is, lesions of the brain (usually located around its base or centrally within its substance) may produce paralysis of the "emotional" use of the face but leave its volitional use intact. This emotional control of the face in the human must be considered as similar to all uses of the face for expression in the rhesus monkey. Brain lesions in other zones (usually in the paracentral cortical region) lead to paralysis of the "volitional" use of the face and may leave facial expressions of an emotional nature intact. The present studies suggest that the emotional use of the face in the human closely corresponds to that use of the face which predominates in the monkey.

The human has also developed a volitional control over the vocal apparatus and, not mysteriously, the neural mechanisms involved in this volitional control are located in the posterior interpretive or associative zones of the cerebral cortex (as opposed to the anteriorly located zones of cortex which regulate emotional or social behavior). Since the volitional control over the vocal apparatus is brought about by mechanisms located within the posterior cortical zones, it is not surprising that this volitional control includes the capability of symbolic representations of the interpretive and mnemonic processes which are carried on in these zones. Thus, the volitional use of the voice is characterized by capabilities for communication between individuals of the species which go far beyond the primitive, primarily emotional modes of communication which characterize the social communications between subhuman primates. It is readily seen that symbolic speech in the human cannot be considered as an exaggerated development of the vocal responses of lower animals but as an entirely new development within the posteriorly lying zones of cortex, a development unique to humans among primates.

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Discussion

Dr. PLOOG: Is it correct that if you ablate the lateral surface of the prefrontal cortex, the monkeys are left mute?

Dr. MYERS: That is correct. The lesions included not only the convexity of the prefrontal cortex but also the orbitofrontal cortex and the cortex of the medial surface. In making this lesion we avoided the anterior cingulate area on the medial surface and all deep-lying ganglionic masses.

Dr. PLOOG: In a pilot experiment, we made a convexity lesion versus one of the medial surface and versus all the frontal cortex. We could not detect any appreciable effect on vocalization. There seem to be species differences as far as I can see at the moment. In some cases we cut off the whole prefrontal cortex, in others we ablated only the convexity and the medial surface. In neither case was there an affect on vocalization. Meanwhile substantial work on this subject has been published by SUTTON et al.². The second question is whether you have made stimulation studies in Rhesus monkeys and whether you found vocalization by stimulating the very areas that have been ablated.

Dr. MYERS: Yes. You are quite right. You also know the work of BRIAN ROBINSON, who, like you, failed to provoke vocal responses in rhesus monkeys when the cortex was stimulated. However, it is interesting to contemplate that both ROBINSON and you could elicit vocalizations when those brain tracts in the white matter where stimulated which originate from the prefrontal and the orbito-frontal regions of the cortex. However, we do not view the absence of vocal responses when the cortex is stimulated as negating our present interpretation of the role of the prefrontal cortex in the biology of vocalization in the monkey. I could point out that PENFIELD has continued to emphasize that speech cannot be produced by stimulating the cortex of man and yet we do not doubt that speech in the human depends on mechanisms in the cortex.

Dr. GLEES: I wonder how we could exclude what you find specifically in the brain from the general traumatization of the animal. One often sees animals being rejected by the community if there is some sort of general disability which is not necessarily a cerebral disability. Animals seem to exclude traumatically fellows in a general way.

Dr. MYERS: Two animals in the cingulate series did show some hemiparesis presumably due to damage to the motor cortex because of its retraction to reach the cingulate cortex or to vascular damage extending from the primary lesion to the underlying white matter. One of these animals was still hemiparetic 3 weeks after operation. However, these animals, despite their motor impairments, acted quite normally with respect to their social behavior and they were well accepted on their re-entry into their social group.

We also used control animals where lesions were placed in other areas of the cortex. The most interesting of these groups was that where areas 20 and 21 of both hemispheres were removed bilaterally. This represented a resection of a sizeable block of the visual association cortex. In evaluating these animals we were asking whether it was possible that the severe deficit of social behavior in the prefrontal or the anterior temporal animals may be due to some sort of a visual agnosia or an apraxia.

² SUTTON, D., LARSON, C., LINDEMAN, R.,: Neocortical and limbic lesion effects on primate phonation. *Brain Res.* 71, 61-75 (1974).

Beforehand, I suspected that these animals with the areas 20 and 21 removed would, indeed, show some sort of deficit. However, to our surprise, these animals showed no perceptible change in social behavior and returned to their social group. They interacted with the other animals in the usual way and showed no change in social rank. Thus, we concluded that the widespread changes in social behavior which we had observed in the animals with pre-frontal or anterior temporal lesions could not likely be explained as some sort of change in their visual perceptual or cognitive processes, but, rather, represented a deficit specific to the affective sphere.

Dr. ZÜLCH: I was interested in your distinction of the two types of facial expression, which corresponds exactly to our experience in the human after circumscribed lesions and hemispherectomy³, namely the emotional and the willingly directed facial movements, which have quite different anatomical substrata.

³ ZÜLCH, K. J.: Neurologische Befunde bei Patienten mit Hemisphärektomie wegen frühkindlicher Hirnschäden. *Zbl. Neurochir.* 14, 48-63 (1954).

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Emotional Areas of the Human Brain and its Programmed Stimulation for Therapeutic Purposes

S. Obrador, J. M. R. Delgado, and J. G. Martin-Rodriguez¹

The knowledge about the areas of the brain related to emotional feeling and its display took place much later than that of the motor and sensory systems.

However, the classical neurophysiologic experiments beginning with GOLTZ's decorticated dogs, followed by the pseudoaffective responses of SHERRINGTON's decerebrated preparation until the more precise studies of BARD and his group about "sham rage" in cats and dogs with removal of the cerebral cortex and different basal regions, opened the interest about the integration of these emotional responses.

Besides, various diseases, like encephalitis, tumours, etc., sometimes induced severe emotional disturbances in man due to different subcortical lesions. The early work in this field was reviewed by GAGEL (1936) in the classical Handbuch der Neurologie, edited by BUMKE and FOERSTER. GAGEL was a co-worker of FOERSTER in Breslau and one of us (S. O.) had the privilege of spending a few months in FOERSTER's Clinic during the last year of his medical studies (1932-1933).

In the course of his neurological activity OTFRID FOERSTER observed that during tumour removal the surgical manipulation around the anterior portion of the hypothalamus and the floor of the third ventricle produced states of maniac agitation and excitation in some patients. On other occasions sleep and loss of consciousness followed manipulation in more posterior structures from the caudal hypothalamus to the aqueduct and medulla oblongata.

These observations of FOERSTER were published in the thirties (GAGEL, 1936; ZÜLCH, 1969) and they have since been confirmed by many neurosurgeons who observed emotional changes during and after operations in the basal regions of the human brain. Some of our early personal observations have already been reported (OBRADOR, 1955).

Other lines of research also increased the anatomo-physiologic knowledge about emotional integration. We could just recall the classical and extensive work of HESS starting in the thirties and demonstrating a great variety of affective and autonomic responses induced by stimulation of various parts of the brain through fine

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implanted electrodes in awake cats. RANSON, MAGOUN and many others have continued these studies which have also been developed in primates by one of us (J. M. R. D.) during the course of many years (DELGADO, 1969).

Another important line of research was started by the experiments of FULTON and JACOBSEN (1935) and KLÜVER and BUCY (1939) demonstrating profound changes in the emotional reactions of primates following the removal of some areas of the frontal and temporal lobes.

Psychosurgery by EGAS MONIZ was, in fact, partly based on some of these experimental findings and opened, since 1936 when the first frontal leucotomy was performed by ALMEIDA LIMA, a wide clinical field for the treatment of patients suffering from affective disturbances and pain. A tremendous amount of work has been carried out in this field by many authors as can be found in the classical book of FREEMAN and WATTS (1950) and in the books of the three International Conferences and Congresses of Psychosurgery of LISBON (1948), COPENHAGEN (1970), and CAMBRIDGE (1972).

Different general conceptions have been elaborated about complex anatomo-physiologic circuits relating to different areas of the brain which take part in the feeling and display of emotions. We may mention the classical PAPEZ'S circuit and the description of limbic brain or visceral brain by MC LEAN and others. YAKOLEV considered that the emotions (internal motions) are related to the mesopallium, formed by the cingulate, retrosplenial and hippocampal gyri, orbito-mesial frontal cortex, and the island of Reil. According to PRIBRAM (1971) symbols are constructed when the actions or motivations operate on feelings (out or apart from action, de-motions, to be possessed, passion) and in this basic emotional behaviour the closed loops of the limbic formations closely connected with hypothalamic and mesencephalic structures have a great importance.

A further expansion in this knowledge about emotional integration started in the fifties with the application of well-established neurophysiologic techniques for deep electrical recording and stimulation of the human brain affected by some diseases, like epilepsy, mental disorders, etc. DELGADO and HAMLIN, HEATH and co-workers, SEM-JACOBSEN, SWEET, MARK and others pioneered these studies and a review of the early results may be found in the books edited by RAMEY and O'DOHERTY (1960) and HEATH (1964).

A very important finding in animals, in 1954, was the induction of positive (reward) or negative (punishment) reinforcement by stimulation of various deep cerebral areas. OLDS and MILNER observed the positive reinforcement in rats and DELGADO, ROBERTS and MILLER the negative reinforcement. These reactions have been considered by OLDS (1964) and others as the two basic and opposing directions of behaviour.

Reward Pleasure or Inhibitory Areas in the Human Brain

After these general introductory remarks we shall now review the emotional reactions of the human brain to electrical stimulation within this basic concept of two opposite interacting systems of positive reinforcement, reward and pleasure, as opposed to negative reinforcement, aversive, punishment and stop mechanisms. Also we cannot forget the functional changes and modifications caused by the disease with the development of abnormal and fixed activity which may lead to changes in the interaction and dynamic equilibrium of the emotional areas. This concept is especially important for therapeutic purposes when we try to overcome a fixed functional activity induced by pain, obsessive thinking or aggressive behaviour, by creating, through long and programmed stimulation using implanted electrodes, other pleasures or rewarding areas that will compete or diminish such negative reinforcing foci already established within the brain of these patients.

Therefore, our main consideration has been directed towards these pleasure rewarding or inhibition areas. On the other hand, according to different authors and various studies, the negative reinforcing, aversive or punishing areas of the human brain inducing tension, anxiety, fear, and rage by electrical stimulation have also a wide distribution in the diencephalon, mesencephalon, amygdaloid region, and hippocampus. The possible therapeutic action on these aversive areas is the stereotactic destruction of such damaged and usually hyperactive structures, in epileptics and other patients with behaviour disturbances as has been demonstrated by many neurosurgeons placing stereotactic lesions at these different levels (NARABAYASHI, SWEET and MARK, SANO, UMBACH, HEIMBURGER, VAERNET, HITCHCOCK, SIEGFRIED, etc.).

Regarding the pleasure areas, HEATH (1964) summarized the results of his studies using multiple electrodes in 54 patients, since 1950, and stated that the areas of reward mapped by electrical stimulation were similar in the human brain to those found in animals. According to this author the septal region and its main outflow pathway through the medial forebrain bundle into the interpeduncular nuclei of the mesencephalic tegmentum is the main reward system. Very close to the reward points and similarly scattered through the deep midline structures of the diencephalon and mesencephalon are the aversive sites inducing fear, rage, and other negative reinforcing effects. Also the stimulation of the amygdaloid nucleus and hippocampus induced uncomfortable emotional reactions and anxiety (HEATH).

With septal stimulation HEATH (1964) observed that the patient became more alert and attentive. In three cases with intractable physical pain there was a striking and immediate relief. However, of six patients treated by GOL (1967) with septal stimulation only one observed a satisfactory relief.

Throughout the human reward system outlined by HEATH, the positive reinforcing or reward effects are more easily obtained with smaller current than the aversive ones (BISHOP et al., 1964). These authors made a comparative study of the current intensities nec-

essary to produce reward or aversive responses and to obtain these last ones a general increased range of the stimulation of about 25% was necessary.

From the septal areas only reward effects were obtained and from the caudate nucleus, amygdala, and intralaminar nuclei of the thalamus reward effects were obtained with smaller current intensity than aversive effects requiring higher current intensities. Lower threshold points were found in mid and posterior hypothalamus with similar difference in current intensity for the reward and the aversive responses (BISHOP et al., 1964). Finally from the mesencephalic tegmentum only aversive effects were elicited according to these authors.

The technique of self-stimulation demonstrated several interesting facts in the experience of HEATH and his group. Drowsiness and sleep was frequently noticed with stimulation of the caudate nucleus and when the level of consciousness decreased by stimulation the tendency to self-stimulation increased and some patients would stimulate themselves into grand mal seizures (BISHOP et al., 1964).

In other patients with multiple electrodes and self-stimulation devices the areas mainly chosen were the septal region and centro-median thalamus which could be considered as reward or pleasure areas (HEATH, 1964). Sexual sensations were sometimes obtained from the septal region but rarely objective evidence of sexual arousal could be observed (HEATH).

SEM-JACOBSEN (1968) has also gathered a large experience about human brain stimulation with implanted electrodes before producing stereotaxic lesions in patients. In a summary of his results positive emotional responses of relaxation, "well being", euphoria, laughing, etc. were obtained from scattered points mainly in the ventro-medial frontal lobes but also in the temporal lobes and around the third ventricle, diencephalon, and mesencephalon. Together with these positive points there are also negative ones inducing states of restlessness, anxiety, sadness, etc. or even more rarely ambivalent points (SEM-JACOBSEN, 1968).

LAITINEN and other neurosurgeons have also obtained reward or pleasant sensations stimulating the anterior-inferior cingular region, and the white matter around the knee of the corpus callosum.

Other levels of the human brain and especially the thalamus may be used for therapeutic positive rewarding effects. BECHTEREVA and her group (1972) have started electrical stimulation of the deep structures of the brain with therapeutical purposes. Out of their 4 patients with multiple and deep implanted electrodes one presented a painful phantom arm after amputation already treated by different peripheral operations without result, being finally relieved after 13 periods of stimulation in the pulvinar nucleus of the thalamus and its pathway. There was also a definite psychic improvement.

We have the same encouraging observations regarding the therapeutic application of selective intracerebral stimulation in some patients but undoubtedly we need further knowledge and experience of the critical cerebral areas that may be approached.

Recently one of us (J. M. R. D.) has extended his previous studies mapping the inhibitory areas in primates. No clear anatomical distribution was found and out of all the areas explored around the striatum (caudate nucleus, capsula interna, putamen) inhibitory responses were obtained from a very small extension corresponding to only 7% of the studied surface. No behaviour responses were obtained in 64% of the surface explored and motor effects were elicited from only 29% of this surface. Thus, the inhibitory areas occupied a rather discrete extension of only 1 to 4 mm in depth and the effect could be lost when the tip of the electrode was moved 1 mm away (DELGADO, 1973).

This small extension of the inhibitory or rewarding responses in the primates brain as has been found by DELGADO (1973) no doubt will make the attempts for the therapeutic application to the human brain more difficult.

Behaviour inhibition evoked by stimulation of septum, caudate and putamen always has a "quick fatigue" and the effect usually disappears within 60 sec. In order to prolong the duration of the behavioural inhibition a programmed stimulation is necessary. After testing different programs, DELGADO (1973) considers that the most effective one is 5 sec "on" and 5 sec "off" during one hour. In this way the responses can be reproduced during this time without signs of fatigue. All these physiological findings are very important for the possible therapeutic application to patients.

Clinical Material and Methods

During the last two years a clinical research project has started in Madrid between the Department of Physiology of the Faculty of Medicine of the Autonomous University and the National Department of Neurological Surgery of the Spanish Social Security. The general aim of this project is the neurophysiologic study and application of techniques of cerebral stimulation, which have been tested and carefully proved in the laboratory, to selected patients suffering from some intractable disease of the nervous system.

We have started with cases affected by intractable chronic "central" pain not relieved by conventional neurosurgical methods, such as painful phantom limb after brachial plexus avulsion or arm amputation and atypical facial pain or after trigeminal denervation. We have also treated patients with terminal pain due to advanced cancer.

All the patients are carefully selected and studied before, during and after different medical and surgical treatments by a psychiatric team under the direction of Dr. J. SANTODOMINGO and with the collaboration of the psychologist Miss ADELA ALONSO. A very

elaborated program of interviews with a large battery of tests is applied to each patient over a long time. These studies will be reported in due course by Dr. SANTODOMINGO, Miss ALONSO, and their co-workers.

The neurophysiologic techniques of stimoceiver and transdermal brain stimulator developed in primates in the course of many years by one of us (J. M. R. D.) have already been described (DELGADO, 1969).

Both methods have been used in our patients and fine multiple electrodes have been implanted with the Leksell stereotactic apparatus. The selected targets were the septal region, the medial part of the head of the caudate nucleus, the centro-median and pulvinar nuclei of the thalamus (Figs. 1 and 2).

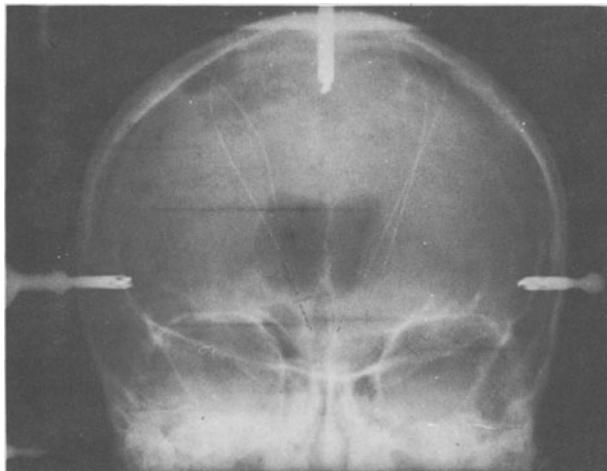


Fig. 1. A.P. X-ray view taken during surgery showing the multilead electrodes in position

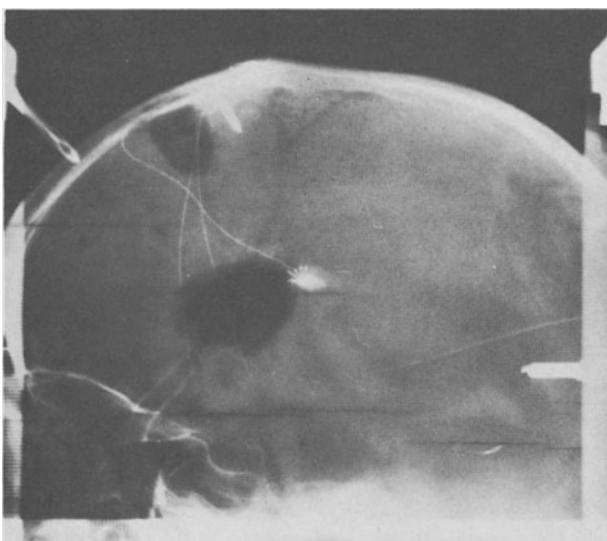


Fig. 2. Lateral X-ray view taken during surgery showing the multilead electrodes in place

Several days after implantation of the electrodes and once the deep electrical activity returned to a normal condition after the recovery of possible injury discharges the stimulation was started. In the first stage the mapping of different areas reached by the electrodes was carried out in sessions lasting one hour each day while the patient was subjected to the established psychological study that was tape-recorded for later analysis.

Programmed stimulation of the selected points was then systematically started. Usually the pattern of 5 sec "on" and 5 sec "off" during one hour as has been described in primates (DELGADO, 1973) was followed. The stimulation intensities usually varied between 0.3 to 0.6 mA. but in some cases with cancer pain a progressive increase in current intensity reaching 3 mA was required to obtain a positive rewarding effect. The frequency of stimulation was maintained at 100 Hz.

During the programmed stimulation sessions the patients were interviewed by the psychologist in a special sound-proof room with tape-recording facilities and a one-way glass window allowing observation from the adjacent room where all the stimulation equipment and recording was installed. The periods of stimulation were unknown to both the patient and the psychologist.

Preliminary Results

We shall only present here some preliminary results as some of the patients are still being treated and others are under observation.

The first case reported in the literature of the therapeutic use of the transdermal brain stimulator was presented in 1972 to the IIIrd International Congress of Psychosurgery held in Cambridge (DELGADO et al., 1973).

He is a young man suffering from intractable phantom limb pain following a traumatic avulsion of the left brachial plexus. The brain stimulator has been implanted for more than one and a half years and the patient has no discomfort, so much so that he wishes to keep the apparatus in place.

Different periods of programmed stimulation of the septal region were repeated 3 to 5 times weekly in one hour sessions and with intensities of 0.3 to 0.6 mA. The timing of stimulation followed the pattern of 5 sec "on" and 5 sec "off" during one minute and a total of 10 stimulation periods were applied in each session. A marked improvement of the pain was rapidly observed and also his preoperative hostile reaction towards the nurses and other patients disappeared. However, because of partial relapses of his discomfort the patient received a total of three therapeutic periods of programmed stimulation in seven months. Since then he has been at home for one year with no complaints, back to his work and socially adapted.

In other patients we observed different positive rewarding and pleasure responses that could be constantly reproduced in the course of the programmed stimulation.

A middle-aged man suffering from a post-traumatic atypical facial pain resistant to different treatments and to the injection of the Gasserian ganglion was also included in the project. Stimulation of the contralateral centro-median-parafascicularis complex induced very short lasting pain relief while stimulation of the pulvinar nucleus in its ventro-oral aspect was followed by marked diminution of pain lasting for several hours. Septal region stimulation induced emotional changes of well-being and relaxation. Programmed (5 sec "on"/5 sec "off") stimulation of this area at current intensities ranging from 0.3 to 0.8 mA. gave pain relief for periods of up to 18 hours. With combined septum and pulvinar stimulation, relief would sometimes last two days. This patient is still under treatment with programmed electrical stimulation.

In one patient with advanced cancer and widespread pain requiring daily several morphine injections the stimulation of the septal region induced a feeling of well-being and relaxation that sometimes lasted several hours. Stimulation of the centro-median thalamic nucleus produced a short lasting abolition of the pain and a feeling of emptiness of a pleasant nature together with a tendency to sleep. Combining the stimulation of the centro-median nucleus and septal region the pain could be controlled sometimes for periods of one or two days. During the three months of treatment until her death the intensity of the stimulation had to be increased from 0.25 to 3 mA as the beneficial effects were not so clear. However, she only needed some mild analgesics to control the pain, together with the sessions of cerebral stimulation in the last stages of her disease.

It seems that this type of progressive pain associated with cancer presents some important differences with other modalities of chronic pain, as in our phantom limb patient described above and in the similar one reported by BECHTEREVA et al. (1972) successfully treated by several periods of thalamic stimulation in the pulvinar nucleus.

In these two cases of chronic phantom limb pain (BECHTEREVA's and ours) periodic brain stimulation in the course of several months not only abolished the pain but also definitely improved the emotional changes of the patients. It may perhaps be postulated that the unbalanced predominance of fixed brain mechanisms related to the chronic pain may be regulated by the sustained stimulation during sometime of positive rewarding areas through the implanted electrodes. Once this unbalance is broken the normal self-regulatory mechanisms for emotional control could be restored. Thus, it seems possible in cases of chronic "central" pain to induce functional cerebral pacemakers with the aim to antagonize some of these forms of intractable pain avoiding the destruction of cerebral tissue.

According to our experience and that of other authors already mentioned the more conspicuous and accessible positive rewarding or pleasure areas are spread throughout the septal region, head of the caudate nucleus, ventro-medial portion of the frontal lobes, antero-inferior cingular region and white matter around the knee of the corpus callosum. Also the centro-median, pulvinar, and

other intralaminar nuclei of the thalamus may be included in this system of positive rewarding inhibitory areas which no doubt has a much larger extension (Fig. 3). From all these areas relaxation, pleasant feelings, decrease or abolition of pain with an inhibitory effect and tendency to sleep have been obtained at some points.

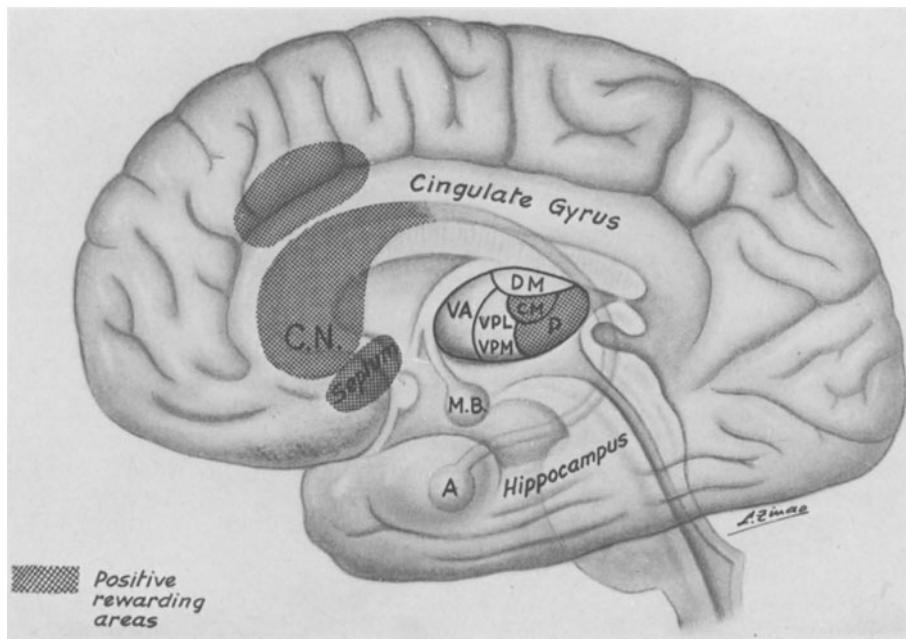


Fig. 3

However, we cannot forget the small extension of the areas inducing inhibitory and positive rewarding responses as has been found in primates (DELGADO, 1973) and also the mixture and neighborhood of the positive reinforcing points with the negative and aversive ones and their close interconnection. Other factors related to current intensity and fatigue of the responses have already been discussed and may be solved by an adequate physiologic technology.

Summary

In spite of their complexity, the emotional reactions may be approached through a very simple and basic concept of two inter-acting systems, one of negative aversive reinforcement and punishment opposed and balanced by another of positive rewarding reinforcement and pleasure. Both systems maintain a dynamic equilibrium through normal self-regulatory mechanisms.

It may be postulated that some pathologic conditions may break such a dynamic balance and sustain a fixed functional abnormal

state that eventually may dominate the normal brain activity. This occurs in some patients suffering from the so-called "central" and chronic pain.

In patients with intractable pain we have stereotactically implanted multiple electrodes in some positive rewarding or pleasure areas (septal region, caudate nucleus, centro-median and pulvinar thalamic nuclei) in order to antagonize and compete by their periodic programmed stimulation with the unbalanced predominance of the fixed brain mechanisms responsible for the chronic pain that may be considered of negative reinforcing or aversive nature.

The techniques and preliminary results are briefly presented, as well as the follow-up of our first case successfully treated by a transdermal brain stimulator more than one and a half years ago. All patients are very carefully selected and submitted to an extensive psychological and psychiatric study. Different medical and surgical treatments have been tried before the implantation of the electrodes.

Combining the application of well proved and tested neurophysiologic techniques with sound clinical and neurosurgical selection and good psychiatric evaluation we believe there is an indication in some patients with intractable pain to use this method and set up pleasure cerebral pacemakers by localized periodic and programmed stimulation of positive rewarding areas. Destruction of cerebral tissue which is a common feature of other therapeutic approaches is also avoided.

The aim and purpose of our working project in Madrid during the last two years has been precisely based on such collaboration to apply all the refined neurophysiologic techniques for the study and treatment of such patients suffering from intractable pain.

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Discussion

Dr. ZÜLCH: Were there any other disturbances of the autonomic nervous system?

Dr. OBRADOR: Not very obviously.

Dr. ZÜLCH: I had a patient in the war with a shell fragment exactly in the preseptal region who had a bladder disturbance; it is assumed by some experimentalists that this is the site of one of the centers for bladder function.

In three of our own cases at autopsy the lesions were found in the infundibular region and the caudal hypothalamus and seem to be produced partly by direct local action (contusion) and partly by tearing of the nourishing vessels at the base with resulting necrosis and cystic transformation.

The majority of the symptoms disappear after some months, probably because the disturbed autonomic functions are compensated by the several "levels" of regulating centers. This is easily understood for the symptom of hypertension with impairment in diencephalic control.

On the other hand, other forms of impairment of vasomotor control and other autonomic dysfunctions such as disorders of bladder function, diabetes insipidus, and disturbances of fat metabolism, may be of long duration or permanent. Symptoms of impaired temperature regulation with profuse sweating may be of long duration. The psychological disorders form a characteristic syndrome consisting of intermittent but antagonistic symptoms such as sleep and arousal, aggression and stupor, excitation and suppression. Such "posttraumatic hypothalamic permanent syndromes" seem to be particularly characteristic and consist of alterations of the fat metabolism, of the regulation of temperature and respiration, of the sexual sphere (impotence, amenorrhea), and finally, of behavior (rhythmic changes of agitation and apathy).¹

Dr. OBRADOR: We have never seen any obvious bladder disturbance by stimulation.

Dr. HASSLER: I am somewhat afraid about the long-term results, because if you introduce stimulating electrodes into the cerebral substance, there always will be a cell loss around the electrode. We have stimulated some thalamic nuclei and had autopsy findings with this result. Therefore you always need a higher current during stimulation. This may not be the case if a stimulus electrode is in one of the posterior columns, but in this central nuclear substance of the brain there will be limitation for long-term stimulations.

¹ For details see HESSELMANN, J., ZÜLCH, K. J.: Vegetative und endokrine Symptome nach traumatischer Hypothalamusschädigung. Acta Neuroveg. 30, 251-260 (1967).

Dr. OBRADOR: According to our clinical experience the only patient where we had to increase the stimulus had a progressive cancer. The experiments of DELGADO in primates demonstrate that there is not any variation of the threshold responses up to a period of 3 years.

Dr. MARTIN-RODRIGUEZ: In cancer the intensity of the current has increased, while the pain continues. Apparently cancer pain and the chronic pain, as for example in phantom limbs, are not the same. It is well known that cancer patients need higher and higher doses of drugs. We saw the same in the patient with the electrical stimulation; we needed more and more intensive currents, but up to the death this patient's pain was still being controlled by the electrical stimulation. In the other patients we never needed to go above 0.6 mA.

The Localization of Sex in the Brain

A. E. Walker¹ and D. Blumer²

Introduction

The hypothalamo-hypophyseal-gonadal axis has been generally looked upon as the neuroendocrine basis of sexual behavior and many animal studies support this view. Higher neuronal circuits must be involved in sexuality, at least in man, but there has been little curiosity and little knowledge concerning these mechanisms.

The fact that many patients with certain forms of focal epilepsy have both ictal* and interictal alterations of sexual behavior has been long overlooked. Two reasons for this failure are enumerated. For one, the future physician learns in medical school that he needs to undress his patient for full examination and soon overcomes a sense of shame; but he is not taught to explore the sex life of his patients. Second, there has been a stifling trend in research to investigate only what can be measured by objective methods. As a result, the systematic study of very private events in man, which to be valid requires a personal relationship of physician to patient, has been sorely neglected.

Evidence from Animal Studies

Hypothalamic centers. Impressive evidence from animal studies supports the importance of the hypothalamus for overt expression of sexual behavior (LISK, 1966, 1967a, 1967b). A hormone-dependent neuronal system initiating copulation has been localized in the preoptic hypothalamic region, in almost all species studied. Implants of estrogen or testosterone propionate and electrical stimulation in this area elicit the copulatory response, while lesions decrease or eliminate sexual behavior, which is not restored by exogenous hormone treatment. A second center exists in the median eminence region which regulates gonadotropin release. Exogenous hormone replacement restores the mating ability in animals deprived by lesions in this second area.

LISK (1966) suggests that an inhibitory system regulating the level of sex drive is located in the region of the ventral border of diencephalon and mesencephalon. This is based on his findings

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of increased copulation following lesions involving the posterior hypothalamus and mamillary bodies in the male rat. The overt sexual behavior of both male and female therefore would depend upon the balance of activity between a hormone-dependent integrative and facilitory system, likely localized in the preoptic region and a regulatory, inhibitory system located in the region of the mamillary bodies. MICHAEL (1965) showed specific uptake in certain regions of the brain, using systematically administered hexoestrol-H₃. In the cat, localization of hormone in the brain was confined to a bilaterally symmetrical system involving the septal region, preoptic area, and hypothalamus. The primate showed an additional localization in the caudate nucleus.

Higher Centers and Pathways. In rhesus monkeys and cats, hypersexuality has been described as a result of the removal of both temporal lobes (KLÜVER and BUCY, 1937), amygdala and overlying piriform cortex (SCHREINER and KLING, 1954), or of small lesions in the piriform cortex (GREEN et al., 1957). Excitatory (YAMADA and GREER, 1960; VELASCO, 1972) as well as inhibitory (ELWERS and CRITCHLOW, 1960; BAR-SELA and CRITCHLOW, 1966) influences on the gonadotropin secretion are ascribed to the amygdala.

MACLEAN (1957) found that electrical stimulation of the septum or caudal hippocampus in male cats induced after-discharges which resulted in enhanced pleasure and grooming reactions and sometimes penile erection. Similar effects were seen following local cholinergic stimulation of these structures.

MACLEAN's painstaking stereotoxic explorations for sexual responses in the squirrel monkey disclosed in the brain stem above the level of the hypothalamus two nodal regions which when stimulated elicited full penile erection (MACLEAN and PLOOG, 1962). One of these regions was located in the core of the medial dorsal nucleus of the thalamus from whence the major pathway followed the inferior thalamic peduncle, then joined the medial forebrain bundle. The other region was co-extensive with the medial septopreoptic area whose major efferent pathway was also traced to the medial forebrain bundle. Stimulation along the course of this bundle through the hypothalamus effectively elicited erection. At the level of the midbrain the pathway was followed laterally into the substantia nigra, from which it descended through the ventrolateral pons and entered the medulla just lateral to the exit of the sixth nerve (MACLEAN et al., 1963a). Stimulations at positive loci in the septum, anterior thalamus (MACLEAN et al., 1962; MACLEAN and PLOOG, 1962) and the medial frontal cortex (DUA and MACLEAN, 1964) recruited potentials in the hippocampus, leading in some instances to hippocampal after-discharges. During these after-discharges the erection might throb, but despite this orgastic appearance, ejaculation was never observed. Seminal discharge, sometimes preceding erection, occurred only when stimulation involved loci that lie along the course of the spinothalamic pathway and its medial ramifications into the caudal intralaminar region of the thalamus (MACLEAN et al., 1963b).

The significance of MACLEAN's findings for localization of sex in the brain is somewhat compromised by the squirrel monkey's

habit of utilizing aggressively genital display in an attempt to dominate other males, or as a form of social greeting (MACLEAN, 1973). Analogous stereotaxic explorations in the female elicited no sexual responses whatsoever.

Role of the Cortex: Sex Differences. The cerebral cortex is judged to be relatively unimportant in the maintenance of mating behavior in most female mammals. BARD (1939) removed increasingly larger portions of the cortex in the cat until all of the neocortex, most of the rhinencephalon, and a large part of the striatum and thalamus was destroyed, without eliminating estrous behavior in response to estrogen. Findings that removal of the whole neocortex in the rat does not interfere with estrous cycle, mating, pregnancy, or delivery have been repeatedly confirmed. In contrast, the cortex was found to be essential for the initiation of mating behavior in most male mammals. BEACH (1940) showed that while removal of 20% of the cortex in male rats did not reduce the percentage showing copulatory behavior, no male mated if more than 60% of its cortex had been destroyed. Similarly, mounting behavior was lost in female rats after decortication while their female patterns of activity were retained (BEACH, 1943). In these studies the location of the cortical area removed was considered less important than the quantity, a conclusion which has since been clearly disproved (LARSSON, 1962, 1964). The male mammal has a very complicated neuromuscular pattern to assume for a sexual response in contrast to the simple passive postural adjustment made by the female (in the form of so-called lordosis). The male response must include elements of recognition, orientation, mounting, pelvic thrusting, intromission and ejaculation. It is obvious that many regions of the neural system must be involved in the performance of the complete copulatory response in the male. The observation that the cortex may be superfluous for the maintenance of sexual behavior in female animals illustrates the vast gap between animal findings and the human condition.

Human Evidence

The continual sexuality of man contrasts sharply with the intermittent or seasonal sexuality of animals (JENSEN, 1973). The male is constantly ready to engage in sexual behavior (PHOENIX, et al., 1967), but sexual arousal in male animals tends to occur only in response to the cyclic female sexual behavior. The human female's sexual behavior is not locked to the estrous cycle, and man therefore is able to enjoy sex continually. In man, sexuality is intricately related to personality and general behavior, so that obviously the human cerebral cortex has a high degree of influence over sexual arousal and response.

Sexual Activity and Hormones. Sexual arousal in man is sometimes instantaneous and occurs independent of any change in the level of sex hormone levels in the circulating blood. MIGEON (personal communication) has shown that during sexual intercourse the androgen level does not change, although an increase in cortico-steroid levels can be documented. However, threshold complements of androgen do need to be present for normal sexual behavior in

man. Castration, the application of antiandrogenic compounds such as progestogens (e.g. medroxy-progesterone acetate, used for certain otherwise intractable sex deviations (MONEY, 1970; BLUMER and MIGEON, 1975)), or sectioning of the hypophyseal stalk (as practiced in cases of diabetic retinopathy) can abolish male sexual arousal by abnormally lowering the androgen level. Otherwise, sexual behavior in man is rather independent of hormonal mechanisms and depends largely on higher cerebral controls.

Effects of Lesions and Stimulation. A number of clinical observations tend to confirm the importance for sexual behavior of those areas which were found involved in animal experiments.

1. BAUER (1959) reviewed the findings in 60 autopsied cases of hypothalamic disease reported in the literature. Gonadal depression was associated predominantly with lesions in the inferior and more anterior region of the hypothalamus, whereas precocious puberty was associated frequently with disease in the posterior hypothalamus and often with disease in the mammillary bodies.
2. HEATH (1964) noted penile erection in three patients during electrical stimulation and orgasmic response in one female following chemical stimulation of the septal region. Conversely, MEYERS (1963) described loss of potency following lesions in the septo-fornico-hypothalamic region.
3. POECK and PILLERI (1965) described the case of a young woman who developed a gross hypersexuality following lethargic encephalitis. The autopsy showed lesions mainly in the mesodiencephalic border area.
4. Hypersexuality has been documented in cases with deep frontotemporal tumors (BENTE and KLUGE, 1953; ANASTASOPOULOS, 1958; TORELLI and BOSNA, 1958; VAN REETH et al., 1958; LECHNER, 1959). Rabies, a disease of the limbic system, reportedly has also resulted in hypersexual states (GASTAUT and MILETO, 1955).

The role of the frontal lobes in human sexual conduct may be understood according to KLEIST (1934). He pointed out that orbital lesions may lead to the loss of moral-ethical restraints and gross sexual misconduct (without a hypersexuality proper, i.e. without increased frequency of sexual arousal). Lesions of the frontal convexity, on the other hand, are associated with a loss of general initiative, including sexuality, but the patient can still perform sexually if he is led step-by-step (BLUMER and BENSON, 1975).

MEYER (1955), WALKER (1961) and others have shown a decrease of sexual arousal and response after head injuries which tends to be global, affecting both libido and genital arousal. This emphasizes the significant vulnerability of sexual functions to cerebral injuries.

Sexuality and Epilepsy. The most significant evidence of the neural basis for sexual behavior in man stems from observations in patients with focal epilepsy. The ancient Romans had an approp-

riate saying: "Coitus brevis epilepsia est." The mood of sexual desire is likened to the prodrome of an epileptic attack, the premonition of the orgasm to the aura, and the sexual climax to the epileptic paroxysm. A refractory period, sleep and tension reduction tend to follow both the sex act and the epileptic attack (TAYLOR, 1971). We must, however, go beyond such loose analogies to a closer look at the relationship between sexual arousal and epilepsy.

Table 1. Changes of Sexual Behavior in 50 Temporal Lobe Epileptics (42 operated)

Chronic global hyposexuality	29
Postoperative hypersexuality	2 ^a
Hypersexuality induced by medication	1
Postictal sexual arousal	4 ^b
Ictal sexual arousal	1
Homosexual behavior	2
	35 (70%)

^a both patients were hyposexual, preoperatively

^b one patient also with homosexual behavior;
another patient also with hypersexuality
induced by medication (Mysoline).

Interictal sexuality: Of all forms of epilepsy, it is clearly temporal lobe epilepsy that is associated with abnormal sexual behavior. Table 1 lists the changes observed in fifty temporal lobe epileptics whose sexual behavior was carefully explored (BLUMER, 1971). It is evident that sexual normality is the exception and a chronic disorder in the form of *global hyposexuality* is predominant. Hyposexuality in patients with minor seizures was first observed a century ago by GRIESINGER (1868-69; see PETERS, 1971), then rediscovered and well documented by GASTAUT and COLLOMB (1954). The finding of a marked decrease of libido as well as genital sexual arousal is confirmed by a number of investigators. HIERONS (1971) and HIERONS and SAUNDERS (1966) described the deficit as impotence for they were impressed by a continuing desire to perform sexually but the inability to do so in late-onset temporal lobe epileptics. In contrast, TAYLOR (1969, 1971) refers to a lack of appetite with continuing ability to perform sexually, which he calls a cerebral "fault of integration." Our own investigations (BLUMER and WALKER, 1967; BLUMER, 1971) convince us that GASTAUT's concept of a *global hyposexuality* is indeed correct. Patients with late onset of temporal lobe epilepsy who have been married may complain of insufficiency, but

upon close inquiry they do not show any significant amount of libido which cannot be satisfied. While complete sexual arousal can take place in a majority of temporal lobe epileptics, it is the frequency of this arousal which is often drastically reduced. It is not unusual to find sexual arousal as rarely as once a year in temporal lobe epileptics. There are temporal lobe epileptics, with onset of the illness prior to or at time of puberty, who may never have had any sexual arousal or only on very rare occasions during their lifetime.

The global hyposexuality is not irreversible. Contrary to some suspicions, anticonvulsants may re-establish sexual arousal if they suppress the seizure activity (GASTAUT and COLLOMB, 1954; PETERS, 1971). The relationship of mesial temporal seizure discharges and sexual arousal is dramatically confirmed by findings in patients who were previously hyposexual but are completely free from any seizure activity after unilateral lobectomy: normalization of sexual desire and ability is commonly observed in such cases. Occasionally hypersexuality may present itself in the second post-operative month (BLUMER and WALKER, 1967; BLUMER, 1970). The hypersexuality is usually reversed soon by the recurrence of temporal lobe seizures. In one case, we observed a hypersexual behavior lasting for two years following unilateral temporal lobectomy in a previously hyposexual woman. The hypersexuality gradually subsided without recurrence of seizures.

Ictal and postictal sexual arousal: The hyposexuality of a majority of temporal lobe epileptics contrasts to the reputation of epileptics as suffering from deviant and excessive sexual arousal. KRAFFT-EBBING (1898) had already pointed out this paradox. The excessive sexual excitement so vividly described in old psychiatric textbooks stems from striking abnormal sexual arousal in a few epileptics at the time of their seizures. Global hyposexuality, on the other hand, being a very silent condition, was easily overlooked, in spite of its frequent occurrence. Our own observations indicate that sexual arousal may take place as a direct result of seizure discharges (*ictal sexual arousal*) or may follow the clinical seizure (*postictal sexual arousal*).

For an understanding of the relationship between ictal events and sexual arousal in temporal lobe epilepsy, a clear understanding of the seizure pattern is required. Table 2 lists, partly following JANZ' classification (1969), the ictal and postictal phenomena in temporal lobe epilepsy. In most cases, an experienced observer can distinguish the ictal from the postictal phase of the attack; therefore, it is usually possible to identify a sexual arousal as ictal or postictal. Table 3 notes the types of ictal experiences which either precede or accompany the *ictal sexual arousal*. We note that fear is particularly often described and is noted as a pre-pubertal phenomenon in seizures which assume a frankly sexual character after puberty. The aura associated with sexual seizures is frequently of the oro-alimentary kind. Often sexual seizures are easily triggered by sexual arousal in the form of intercourse or masturbation. By the same token, "non-sexual" seizures have been noted as a form of reflex epilepsy upon sexual intercourse (HOENIG, 1960). We believe that seizure

Table 2. Symptomatology of Temporal Lobe Seizures

A. Ictal Phenomena.

Stereotyped sequence of events: expressionless stare, passive experience, not related to environment. Duration, a few seconds to $1\frac{1}{2}$ minute.

I. Primictal Events (aura) - recalled

- | | |
|------------------------|--|
| "Dreamy state": | déjà-vu, jamais-vu, illusions, hallucinations, mood changes, fear |
| "Oral-digestive type": | visceral sensations, olfactory-gustatory sensations |
| "Adversive type": | dizziness, crescendo sensations, auditory or visual hallucinations |

II. Ictal Events - not recalled

- | | |
|------------------------|---|
| "Oral-digestive type": | oral-alimentary and respiratory automatisms |
| "Adversive type": | supple turning of eyes, head or trunk |
| "Speech utterances": | euphasic or dysphasic |
| Other phenomena: | repetitive motions, autonomic changes, tonic-clonic alterations |

B. Postictal Phenomena

Increasingly more variable and more complex events: looking about, more active, more related to environment. Duration often prolonged (up to 1 hour).

I. Simple Repetitive Motions

II. Scenic Behavior

III. Attempts at Re-orientation

phenomena may follow sexual stimulation more often than is generally assumed.

Personal Case: A clear example of the ictal attack was presented by a 24-year-old head-injured veteran of World War II who consulted one of us (A. E. W.) ten years ago. He was having frequent spells and behavioral disturbances. In the course of the examination he had an attack. He stopped talking and stared into space, a few twitchings occurred at the right corner of the mouth and he smacked his lips. At the same time, his hands began to move over his chest and abdomen, his right hand eventually moving about his pubis. For some minutes he mumbled incoherently and was unable to follow even simple commands. He gradually regained consciousness and was then able to reply coherently regarding his attack. He admitted that with the onset of the attack he always remembered experiencing a pleasant erotic sensation as if he were about to have an orgasm. Apparently, he would lose consciousness before it occurred.

Table 3. Symptomatology Associated with Psychomotor Ictal Sexual Arousal

Precipitating or triggering mechanisms

Sexual intercourse or masturbation
Erotically charged objects or events
Hypnosis or suggestion
Self-stimulation

Primictal

Epigastric sensation
Chest or anal sensation
Abdominal pain
Olfactory sensation

Ictal equivalents

Fear (prepubertal!)
Paradoxical painful experience
Urinary incontinence

Of particular interest is the case reported by BANCAUD et al. (1970): A girl, aged 20, had suffered from seizures since age 4, which initially consisted of a feeling of fear that prompted her to run to her mother. At age 8, the seizures changed; she would sit on the floor with her hands under her and turn around uttering incomprehensible words. Then she would lift her skirt, bite her cheeks, look around in a confused manner and urinate. She said these seizures were initiated by an epigastric pressure and undefinable fear. At age 11, she had her first spectacular and frankly sexual seizure: She called her mother, fell down with an expression of fear on her face and screamed loud and louder; then she made complex movements of her body and limbs while rubbing herself with closed fists in the pubic area and demanding silence. Abundant vaginal discharge took place with urination. She had a sensation of diffuse oppression, then a contraction of thigh and pelvic muscles accompanied by a pleasurable feeling identical with the one she experienced with masturbation. The sexual pleasure replaced the fear she had experienced prior to age 11. Since that time, the seizures, usually provoked by masturbation but once brought on by heterosexual petting, remained about the same.

On examination the girl was mildly mentally retarded. She had a left superior temporal visual field defect. Neuroradiological studies showed a right inferior temporal mass without displacement of structures. An EEG showed sporadic right temporal spikes. During depth EEG's induced and spontaneous attacks were observed. The EEG analysis showed that participation of the right hippocampus was essential to the elaboration of the paroxysmal sexual manifestations. The amygdala, gyrus parahippocampi, and isocortex of the temporal lobe were secondarily involved while the contralateral limbic system was not implicated at all during the attacks. An astrocytoma, invading the amygdala as well as the anterior hippocampus, was found at operation and removed.

Although FREEMON and NEVIS (1969) reported what they thought was the first case of sexual seizures, BANCAUD and co-workers (1970) from the literature summarized 26 cases of temporal lobe sexual

seizures and 10 cases of seizures with sexual manifestations due to involvement of the paracentral lobule. The French authors point out that *seizures due to lesions of the paracentral lobule consist chiefly of lateralized genital paresthesias at the level of the penis, rectum, anus, abdomen and sometimes the chest, which are experienced without sexual resonance; while with temporal lobe sexual seizures the entire pattern is integrated into the instinctive-affective content of dominating lust.* This is in contrast to the impression given by ERICKSON's (1945) well-known case with a hemangioma of the paracentral lobule, where his female patient's episodic genital sensation is misnamed "eromania" or "nymphomania". Fig. 1 is a sketch of the medial aspect of the brain, depicting the involved structures: the paracentral lobule and hippocampus as well as the connection through the cingulate gyrus to the hippocampus. The role of the cingulate gyrus, however, is unclear.

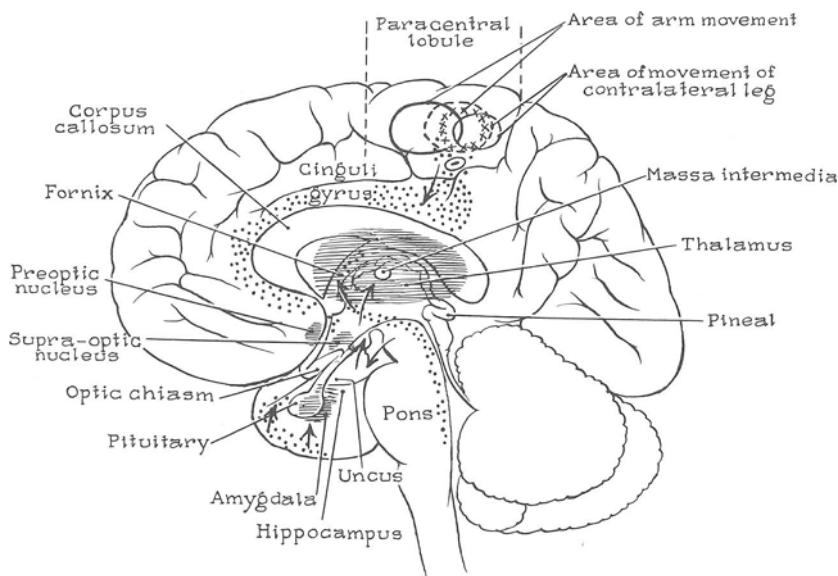


Fig. 1. Midsagittal section of the brain with the sexual pathways and centers indicated by dotted lines or areas. The brain-stem tract passes to the base of the thalamus from which fibers (not indicated in the sketch) project, via the internal capsule, to the paracentral lobule and also via the inferior thalamic peduncle to the amygdala. Fibers from the medial temporal structures pass to the cingulate gyrus and by the fornix to the hypothalamus which modulates the activity of the hypophysis. The paracentral area indicated by a dot in a circle is where BATES (1953) obtained anal retraction upon electrical stimulation. The zones just above this area are the sites from which he elicited movements of the extremities (second motor area)

The listing of sexual seizures by BANCAUD and co-workers³ needs to be enlarged (see HALLEN, 1954; JANZ, 1955; NIEDERMEYER, 1957; CURRIER et al., 1971; BLUMER, 1970) on the one hand, and is somewhat uncertain on the other hand, because some of the authors quoted may have confused postictal sexual arousal with ictal sexual arousal.

The postictal sexual arousal is described by BLUMER (1970). It usually takes place in an appropriate setting with full recollection on the part of the patient and rarely seems engulfed in the phase of postictal amnesia. Reported cases of exhibitionism (HOOSHMAND and BRAWLEY, 1969) may represent only confused undressing by a patient following a temporal lobe seizure, with or without sexual arousal. Postictal sexual arousal is not part of the immediate postictal phase and may be interpreted as a release phenomenon after excessive mesial temporal seizure discharges have terminated, not unlike the sexual arousal observed following successful temporal lobectomy. We have noted that it occurs in individuals who are not markedly hyposexual, while the belated sexual arousal manifested several weeks following unilateral temporal lobectomy typically occurs in patients who have been very markedly hyposexual. We have never observed excessive sexual arousal in patients who were not hyposexual prior to operation.

Sexual deviations and epilepsy: Homosexual, and in particular, transvestite and fetishistic deviations have been noted in a small number of temporal lobe epileptics (BLUMER, 1969). A close relationship between perversion and temporal lobe abnormality is strongly suggested by two cases in the literature where the perversion was completely abolished following cure of the temporal lobe epilepsy by unilateral temporal lobectomy (MITCHELL et al., 1954; HUNTER et al., 1963). Unlike the exhibitionism which is most probably postictal, these sexual deviations seem to be present during the interictal phase in temporal lobe epileptics. Two patients in our own series had homosexual behavior which disappeared following unilateral temporal lobectomy, despite the fact that the seizures were not completely abolished.

Comments

This discussion has emphasized the presence of centers in the hypothalamus, temporal lobe, and paracentral cortex which seem to modulate sexual activity in man and animals. To some extent, the influence is hormonal dependent, and, in fact, feedback mechanisms may determine the hormone level.

The neural mechanisms involved are similar to other sensory systems. The paracentral representation seems to be the cortical representation of the perineal genital system akin to other somato-motor cortical receptor areas. The thalamic locus of this

³ BENTE and KLUGE, 1953; FREEMON and NEVIS, 1969; GASTAUT and COLLOMB, 1954; MITCHELL et al., 1954; NOGARA, 1966; PATARNELLO, 1963; VAN REETH et al., 1958; VAN REETH, 1959.

mechanism has not been defined. According to the charts of thalamic topography, it should lie in the basal lateral part of the ventral thalamic nucleus, but stimulation of this area has not induced perineal or sexual hallucinations. Perhaps future thalamic mappings may uncover the relay mechanisms. Theoretically, projections should be to the hypothalamus both anteriorly and posteriorly, and to the paracentral cortex. From the latter, fibers pass to the cingular gyrus and hence to the amygdala and hippocampus and adjacent cortex. The efferent pathways probably involve direct fibers to the hypothalamus via the stria terminalis, anterior thalamic peduncle, or anterior commissure. The neuronal basis for sexuality would seem to be related in part, at least, to the medial temporal structures. The presence of both facilitory and inhibitory mechanisms makes it possible for a more delicate balance and control of the hormone level.

The complex changes resulting from interruption of one or more of these control systems is not easily understood. Not only are there secondary pathways which tend to restore function, but the primary neuronal systems may undergo a hypersensitivity which modulates the activity of the complex system.

Let us assume that the chronic firing of an anterior temporal epileptic focus modifies the activity of diencephalic nuclei. Excision of these structures not only eliminates the facilitory or inhibitory input to the hypothalamic neurons but by reason of denervation hypersensitivity makes them more susceptible to incoming impulses from other sources, especially frontal, which are likely to be excitatory. Multiple inputs from one or both sides of the brain to hypothalamic centers may account for the varied results of lobectomy. The delay in the onset of sexuality after anterior temporal lobectomy may be related to the gradual recovery of chronically depressed neurons, or to their slow development of hypersensitivity (WALKER, 1973).

There is then a growing body of evidence implicating a system - which is in fact somewhat complex - of medial temporal and hypothalamic structures which regulate sexual arousal and response. The hippocampus, the area in the entire brain with the lowest seizure threshold may be most significantly involved in sexual climax. However, the precise role played by the hippocampus, amygdala, hypothalamus, and connecting fiber bands is not clear; but, perhaps this is not too important, for MAYANAGI and WALKER (1974) have shown that the medial temporal structures often act as a unit and that in epileptic discharge the functional limits of these structures are blurred. Probably the same is true for the regulation of sexual behavior especially during sexual climax.

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Discussion

Dr. POECK: It always strikes me when I observe patients in the intensive care unit recovering from midbrain or diencephalic lesions or from encephalitis that an aggressive behavior to an extent which you can almost call sham rage, is observed much more frequently than a release of sexual behavior. Do you think this has a functional reason, for instance, that aggressive behavior perhaps is more important than sexual behavior for the individual or has it an anatomical reason that the lesions are perhaps more widespread?

Dr. BLUMER: I think it may have a functional reason. The importance of sex tends to be overrated at times of peace and leisure. We know that, like in man, sexual arousal is much more frequent in domesticated animals who are well cared for than in wild animals who must be constantly preoccupied with problems of survival. The ability to respond with aggressive arousal is of greater vital significance. It is also a fact that not only in temporal lobe epilepsy, but with most forms of brain damage, hyposexuality tends to be rather common, and hypersexuality rare.

Dr. PLOOG: In your collection of cases of temporal lobe epilepsy, how many were aggressive in association with the fits, and how many had sexual phenomena accompanying the temporal lobe attacks?

Dr. BLUMER: As far as sexual phenomena are concerned I gave the percentage for ictal and postictal sexual arousal in our series. As far as the angry-aggressive arousal is concerned, a majority of temporal lobe epileptics may be very good-natured but episodically tend to react with excessive anger upon little provocation during the *interictal* phase; in some this tendency is accentuated in the *preictal* phase. Only one of our patients presented a problem with his *postictal* rage; his family had the habit of restraining him whenever he had an attack. Aggressiveness as the direct manifestation of a clinical seizure in all probability does not exist.

Dr. PLOOG: If you read the literature, for instance the reports by MARK and ERVIN,⁴ you always get the impression that you have either temporal lobe epilepsy without sexual phenomena or you actually have either the aggressive type or the sexual type as a concomitant response.

⁴ MARK, V. H., ERVIN, F. R.: Violence and the brain. New York, Evanston, London: Harper and Row 1970.

IV. Plasticity and Dominance

Plastic Brain Mechanisms in Sensory Substitution¹

P. Bach-y-Rita²

Introduction

In recent years considerable success has been achieved in the development and utilization of apparatus designed to provide the blind with a substitute visual input. Several groups of investigators have used the skin to relay the output of a camera to the central nervous system, one of the best known results being the Bliss-Linvill Optacon, to enable the blind to read printed matter (7). Our own endeavors at the Smith-Kettlewell Institute of Visual Sciences have been directed toward development of a tactile vision substitution system (TVSS) to present pictorial information to the blind (3, 4, 5, 12, 30). Briefly, with the TVSS, optical images picked up through a television camera are presented as a two-dimensional pattern of pulses to a mosaic of stimulators arranged on the skin of the trunk. Information of the patterned stimuli is then transmitted via the ascending somatosensory system to cortical areas for analysis and interpretation. Several factors indicate that the pictorial information can be interpreted as "visual". For example, after sufficient training with the TVSS apparatus, including learning the motor control needed to direct the camera toward the visual field, our blind subjects report experiencing the picture as located in space in front of them rather than on their skin. They rapidly acquire the ability to make perceptual judgments and discriminations, using monocular cues of depth, perspective, parallax, subjective spatial localization, and relative size of objects as an aid to relative distance. Although the resolution is limited and the TVSS is still in the early stages of development, practical application for education of the blind, and vocational applications (such as providing access to oscilloscopic information and to microcircuity, by means of a microscope adaptor for a blind electronic engineer) are being actively evaluated (4).

Our studies have revealed that information normally received through one sensory system, the visual, can be received through another, the somatosensory. This demonstrable fact is dependent on plastic neural mechanisms, the existence of which formed the

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Fig. 1. A blind subject is shown walking down a corridor using the portable system shown in Fig. 6. The batteries are held in pouches on a vest; the power supply is mounted on the right side of his vest, while the stimulus circuitry is on the left side of the vest. He is holding a control board on which are located video level, pulse-width, and pulse-amplitude controls. The stimulus matrix is under his shirt, held against his abdomen. (Reprinted from *Brain Mechanisms in Sensory Substitution*, P. BACH-Y-RITA, 1972, with permission from Academic Press.)

basis for our original conception of the development of a TVSS (2, 3). It would appear that the responsible plastic mechanisms are predominately central rather than peripheral, inasmuch as perception of pictorial inputs is readily transferred by our trained blind subjects when the stimulus matrix is moved to a new area of skin, or when the type of stimulus is changed from mechanical vibrations to electrical pulses. Moreover, a tilting of the camera does not disturb the recognition of an object even though the pattern on the skin is distorted.

It should be noted that the successful use of a TVSS by a blind subject depends on several factors. Among these are: recognition of the apparatus as a supplementary sensory input rather than a complete substitute; a carefully designed program of training, and sufficient motivation and involvement. Relative to the latter, for example, when one of our blind subjects seemed uninterested in the experiments, it was found that she had recently married and was absorbed in housekeeping; various kitchen utensils were then utilized as display objects and the subject's interest was renewed.

In the following section I will discuss some of the physiological mechanisms known to contribute to the plasticity of the CNS, and some experimental and clinical data providing further evidence of plasticity (a more extensive discussion appears in a recent monograph (3)). Finally, a few of our current studies, designed to determine specific neural mechanisms of plasticity, will be described.

I. Plastic Neuronal Mechanisms

There are undoubtedly many factors and mechanisms contributing to the variability and plasticity of the CNS, at least some of which must underlie the ability of the blind subject to perceive as "visual" an input received through his skin. The present section will be limited to three general types of mechanisms: a) those modifying the sensory input; b) those relating to the distribution of information at cortical levels; and c) those whose effects can be demonstrated at the individual cellular level in the cortex.

A. A number of physiological mechanisms are available for the modification of the sensory input itself. Among these are afferent or sensory inhibition, and the centrifugal control of input.

For adequate perception of both visual and cutaneous sensation, small differences in space must be distinguished. There are several known types of sensory inhibition which contribute to this function by enhancing contrast at boundaries and sharpening contours of image reception. One type is lateral inhibition, evidenced by inhibition of receptors adjacent to a single activated receptor in a mosaic, e.g. in skin or retina. Lateral inhibition results in suppression of weaker stimulus effects, and collection of stronger ones into a common pathway. The effects of afferent inhibition can be demonstrated at each level of the ascending somatosensory system including the cortex itself.

All major sensory systems include descending or centrifugal components, in addition to the ascending components which carry information centrally from the receptors. These centrifugal components are predominantly inhibitory, tending to filter out excess or extraneous information. As a result the "useful" or "significant" data is preserved or even enhanced. When operant, the centrifugal mechanisms reduce the quantity of signals from the receptors which reach the higher cerebral mechanisms. With-

out these filtering mechanisms the higher centers would be overloaded. Thus MELZAK and BURNS (21), who raised dogs in a sensory-deprived environment, noted that the inability to ignore stimuli was the principal result of the deprivation. The inappropriate behavior exhibited by the dogs was considered to be due to the lack of development of the centrifugal control mechanisms. In a normally developed sensory system, centrifugal control may be extended all the way from the cortex to the receptors themselves.

B. The processing of information received through an artificial input must depend to some extent on how this information is distributed to the cortex, and in part on the cortical interconnections which provide a substrate for the integration of sensory inputs.

Information on cutaneous sensation, transmitted centrally, is projected to the contralateral primary somatosensory receiving area of the cortex S I, with a high degree of somatotopic and modality-specific localization. Such information is also transmitted to the secondary somatic area, S II, although with less detailed representation and with some convergence of modalities; S II also receives information from the ipsilateral body surface. Several additional cortical areas are known to receive somatosensory input with a lesser degree of somatotopy, including the primary visual cortex (e.g. see 22). Information from the other major sensory systems, visual and auditory, is also distributed to several cortical regions in addition to the primary receiving areas.

The multiple cortical distribution of sensory inputs affords a variety of interactions between the several sensory modalities, providing substrates for the polysensory nature of integrated functions. A number of investigators have traced connections between the somatic, visual, and auditory systems both anatomically and by evoked potential studies. Recently JONES and POWELL (16) have traced some of the ipsilateral interconnections of the main cortical sensory areas in rhesus monkeys. These authors found that each primary field projects to an adjacent field in the parietotemporal cortex, and also to a different part of the premotor cortex. There is an orderly sequence of projections within each of three intracortical sensory pathways in both the parietotemporal and frontal lobes, with reciprocal connections. The evidence of JONES and POWELL indicates that convergence of topographic subdivisions within any one system precedes convergence between the three systems; further, all regions of convergence appear to be interconnected with one another as well as with the orbital surface of the frontal lobe and with the temporal pole. These and related studies suggest cortical mechanisms which may be related to the processing of sensory information received through an artificial receptor as in sensory substitution systems.

A number of studies, some mentioned above, have demonstrated the role of inhibition in learned brain mechanisms. The clinical importance of inhibition had been recognized many years ago. For example FOERSTER (32, pg. 65-66) noted its role in several func-

tions, including the prevention of associated movements. Further, even the concept of "synaptic facilitation" as a basis for learned responses has been seriously challenged by evidence that synaptic use may result in inhibition rather than facilitation. BLISS, BURNS, and UTTLEY (9), in conditioning experiments in isolated cat cortical slabs, have concluded that the great majority of pathways examined must have contained synaptic functions that were less likely to transmit excitation the more often the pathway was used (although some pathways with facilitated synapses were also observed). The majority of cortical synapses displaying plasticity between two cells, X and Y (so arranged so that X can excite Y) showed long-lasting changes of conductivity which were negatively correlated with both the firing rate of X and the use of the XY junction, but were positively correlated with the discharge frequency of Y. However, it should be pointed out that in other cases, synaptic facilitation may play a role in learning.

C. Modification of individual cortical neurons has been demonstrated under a variety of experimental conditions relative to both long-term and short-term changes.

In studies comparing animals reared in sensory-rich and sensory-deprived environments, use and disuse of neurons has been correlated with biochemical alterations such as changes in ACh levels (7) and with morphological alterations such as in the number of dendrites (25), dendritic spines (26), and cortical cell junctions (c.f. 3).

The elimination of one afferent input to a central structure can lead (even in the mature animal) to morphological reorganization. In rats, RAISMAN (24) showed that neurons in the septal nuclear complex in the forebrain receive afferent synaptic terminals from two sources. When one of these sources is selectively eliminated, it appears that afferents from the other source occupy the vacated synaptic terminals.

Physiological studies with microstimulation and evoked potential recordings also demonstrate the plasticity of cortical neurons. For example, WOODY and ENGEL (31) showed that the responses of individual motor cortical neurons can be modified during learning; further, microstimulation experiments revealed that plastic, persistent changes occur as a function of learning.

CHOW and STEWART (10) have provided convincing evidence that, in cats, "...recovery due to forced usage..." of a deprived and behaviorally blind eye can occur. Further, cellular changes in the lateral geniculate nucleus and visual cortex accompany the behavioral recovery from visual deprivation.

These and other studies indicate that individual cells may participate in many functions, and may be recruited for particular (learned) tasks. One consequence is that the cortical area representing a particular part of the body is not static, but changes in response to current demands. The extent to which such changes are utilized in sensory substitution is not as yet known.

II. Functional Recovery and Cerebral Reorganization Following Experimental Lesions

Experimentally produced brain lesions have been studied intensively in an effort to provide evidence of conditions under which functional recovery may occur. Results following controlled lesions have indicated a reorganization of cerebral tissue, demonstrated by the assumption of new functions by those parts of the brain remaining intact following extirpation of an area whose removal produces an initial functional deficit.

In 1842, FLOURENS (cited in 11) noted that destruction of isolated areas of the cerebral hemispheres in birds produced behavioral defects, but a short time after the injury normal behaviour returned. GOLTZ (cited in 11) in the last quarter of the 19th century, extirpated several cortical areas in dogs, producing defects, but noted that with the passage of time marked restoration of function occurred.

In work spanning the end of the last century and the beginning of this century, BETHE (7), a student of GOLTZ, developed concepts of CNS plasticity that have influenced many other workers. One of his demonstrations involved the assessment of functional reorganization following removal of one, two or three limbs of an amphibian. The animal continued to move about by recoordinating in a new manner. BETHE'S work on plasticity has led to the conclusion that the high degree of plasticity in man and higher vertebrates is due to dynamic reorganization and adaptation to new circumstances and not to regeneration.

Early in this century LEYTON and SHERRINGTON (18) showed that extirpation of cortical motor areas in monkeys produced marked paresis, but over a period of time recovery occurred. They further showed that ablation of the arm area produced marked motor deficits from which the primate recovered completely in one month. Re-operation, extending the lesion, did not increase the motor deficit. Two-stage operations removing the arm area of each cortex, revealed that recovery from the first lesion was not due to take-over by the corresponding area of the opposite cortex.

LASHLEY (17) confirmed these conclusions, and further demonstrated that recovery was more rapid following simultaneous bilateral ablation than if either side alone was destroyed. He attributed the increased rate of recovery to the forced use imposed by both limbs being paralyzed.

OGDEN and FRANZ (23) demonstrated the importance of training in functional recovery: they destroyed the precentral gyrus unilaterally in three rhesus monkeys. One was left untreated, the second received passive massage, and the third received training of the hemiplegic forelimb. The contralateral motor area was extirpated following recovery from the effects of the first operation. They noted little spontaneous recovery in the untreated monkey, but compulsory use was followed by nearly complete recovery within a few weeks.

In a more recent study, TRAVIS and WOOLSEY (28) have analyzed the effects of bilateral decortication in monkeys. The motor deficits were more severe when the cortex was removed in only two stages than when there were a number of stages. Further, the extent of recovery was increased when the animals were given passive exercise and assistance in moving actively. Along these lines, STEIN et al. (27) demonstrated in adult rats that successive removal of approximately equal amounts of brain does not produce the same deficits as single stage removal. Thus following sequential removal (30 days between operations with no intervening training) of cortical and subcortical associative areas, the operated animals could not be distinguished from normal controls with respect to performance on a variety of tasks. In contrast, rats with one-stage lesions at the same loci showed marked and long-standing deficits on these tests of learning and performance.

Thus, the degree of functional recovery after experimental brain lesions has been shown to be dependent on several factors. Among these are forced use, training, and abruptness of onset of a total lesion, compared with gradual or sequential removal of tissue. Of these at least the first two may contribute to the functional reorganization of cerebral mechanisms which must underlie the ability of the blind to utilize a TVSS.

III. Clinical Evidence for Plasticity

Some of the strongest evidence for cerebral plasticity is to be found in an evaluation of clinical data, particularly with reference to the extent of recovery of function following extensive lesions.

In the second quarter of this century, several clinical studies on muscle relocation demonstrated the CNS capacity to reorganize complex reflexes and motor functions. For example, WEISS and BROWN (29) transposed the biceps femoris muscle (a flexor) to the extensor side of a knee joint to substitute for the weakened or lost action of a paralyzed quadriceps muscle. Initially the muscle contracted only in the flexor phase, but "...surprisingly few trials were required to make the transplant suddenly contract in the extensor phase, too." After further trials, the muscle operated only in the extensor phase. WEISS and BROWN supported the view that the adjusted use of the transplant was due to the development in higher centers of a new type of action which could override the innate coordinative associations without abolishing them.

FOERSTER commented forty years ago on the compensation for neuronal lesions in terms of reorganization of the remaining parts of the nervous system due to an "...admirable plasticity of amazingly far-reaching adaptability" (32, p. 38). "Often the degree of such restitution makes us bow low in amazement and admiration..." (32, p. 64). It is appropriate to mention here the contribution of FOERSTER to the field of physical therapy, both in providing a neurological basis for therapy and in stressing a course of gymnastic therapy tailored to each individual's needs. The variable degrees of restoration of function in patients suf-

fering from comparable neurological illnesses appear dependent on such factors as physical therapy and training, and, to a great extent, involvement and motivation. Indeed, FOERSTER suggested that physical therapy "...not infrequently initiates restitution while such powers are lying idle and are not unfolded by the organism, as in the so-called habitual paralyses or in some cerebral hemiplegias" (32, p. 38). In the same way, the successful adaptation of a blind subject to the TVSS depends on extensive training and strong motivation.

The extent of possible recovery from lesions in such highly differentiated structures as the primary projection areas of the cortex and the descending pyramidal tract has been shown to be greater than previously thought. Indeed, GUTTMANN (15) found that if paraplegics begin extensive treatment and training early, more than 70% can be returned to gainful activity, whereas in the past paraplegics were considered hopeless cripples.

One example of the importance of training and motivation in recovery from cerebral lesions is the remarkable restitution of motor function in a man (my father) who suffered a major stroke at the age of 65, resulting in severe right-sided hemiplegia and aphasia. This patient received prompt and extensive physiotherapy; he was highly motivated and exercised constantly. Several months after his attack, he could typewrite with one finger of the right hand, then two or three fingers, and finally all fingers. He ultimately regained normal speech, gait, and motor control including fine movements such as handwriting. Three years after the stroke he was able to return full time to his professional work. A neurological examination four years following the stroke revealed no residual defects except for slight clumsiness in using the right hand for such fine movements as buttoning his shirt or tying his shoelaces, although these were accurately performed. There was no difficulty with writing and speech was normal. Neuropathological examination following death seven years after the cerebral thrombosis revealed unilateral infarction of the basis pontis with marked atrophy, demyelinization and gliosis of the distal corticospinal tract in the left lower pons and medulla, extending into the cord (1). A few fibers remained intact and these may have formed the basis of the functional reorganization. Indeed, KUYPERS (personal communication) has found from his studies of pyramidal tract lesions in monkeys that if 5 - 10% of the fibers are preserved, fine movements of the extremities can return. Further, in experimental lesion studies, only 2% of the optic tract fibers or 2% of the visual cortex was found to be necessary for the restoration of functional vision (these studies were reviewed in (3)). A further factor in the recovery of this patient was the absence of "associative" cortical lesions. LURIA (19) has noted "The nearer the wound to the peripheral divisions of the cortex (its receptor or effector areas) and the more highly preserved its higher, secondary and tertiary divisions, the greater the residual possibilities of compensation of the ensuing defects by means of the reorganization of functional systems and the creation of new functional connections in the cortex." LURIA (19) considers preservation of the newest structures of the temporo-parieto-occipital cortex to be particularly important for the "conceptual reorganization" of the dis-



Fig. 2. Coronal section of the medulla oblongata of a 72-year-old patient who had marked recovery from a stroke. The atrophy and demyelinization of the left pyramid is shown. Luxol fast blue-periodic acid-Schiff stain. (Reprinted from *Amer. J. phys. Med.* with permission of Williams and Wilkins Company.)

turbed function. Thus, the neural substrate was preserved, adequate training was received and the motivation level remained high; all of these are factors that facilitated the functional recovery. However, the case is still particularly noteworthy because of the patient's advanced age, arteriosclerotic cerebral vessels, and because of the possibility to correlate the clinical and neuropathological results.

The degree of functional restitution in this case is unusual but not unique. Indeed FOERSTER (14) noted that arm and hand movements could be restored in adult human patients in spite of anatomically verified complete pyramidal tract degeneration, if adequate training was instituted and maintained.

RASMUSSEN (personal communication) discussed the unpublished case of a man who became paraplegic following an automobile accident, but gradually regained complete function and was able to enlist in the U.S. Navy. He served three enlistment periods with no physical limitations. He died in a second automobile accident. Autopsy revealed that a complete (approximately 1 cm) separation of the spinal cord at the level of T7 had resulted from the first accident. However, microscopic study revealed approximately 150 axon cylinders embedded in the fibrous tissue separating the two portions of the spinal cord. Thus, it is likely that recovery

was obtained by the functional reorganization of the input to the cell bodies of the 150 remaining fibers, as well as the possible redirection of the axon terminals.

An evaluation of the factors that lead to recovery following brain lesions in humans is particularly valuable for an understanding of the mechanisms underlying sensory substitution. Recovery of functional capacities implies the development of cerebral mechanisms to compensate for those lost or disrupted by the injury. These compensatory mechanisms may be similar to those that operate in the presence of a new form of sensory input, as in sensory substitution.

An analysis of the results of human brain lesions may offer other pertinent clues in the search for brain mechanisms underlying sensory substitution. For example, data, obtained from the study of humans with lesions of the precentral gyrus or internal capsule, strongly support the probability that some synapses and pathways exist as a "subliminal fringe" in these patients. The degree of paralysis of an affected limb varies from day to day. Indeed, the paralysis may partially or wholly disappear during an emotional disturbance, only to recur when the disturbance is over (17). The "subliminal fringe" suggests the presence of structures and pathways available to the central nervous system learning to adapt to the use of a substitute sensory system.

IV. Studies in Progress

Studies of cortical potentials evoked by tactile stimulation in blind and in sighted subjects are providing further evidence of the modifiability of the CNS and will hopefully provide further insight into the specific mechanisms of neural plasticity which make sensory substitution a practical reality.

We have recently demonstrated that the late components of somatosensory evoked responses (SERs) revealed several highly significant differences between normal sighted subjects and blind subjects with extensive tactile training (Braille, Optacon, Tactile Vision Substitution System). Whereas the early latency components (reflecting principally neural transmission) are similar in both groups, the later components appeared after shorter latencies in the blind group. This finding was interpreted to reflect a faster processing of the tactile information in the blind subjects. Since our blind subjects acquired their high tactile skills by intensive training, we suggested that the changes in their SERs may be an objective correlate of the learning process, and may thus serve as a useful tool for further investigations into the dynamics of the training process (13). In studies in progress, we have demonstrated that SERs produced by our sensory substitution systems resemble closely the visual evoked potentials, including similar ON - OFF components and after-activity. Our studies suggest that visual and somatosensory information may be processed in the brain according to a common pattern.

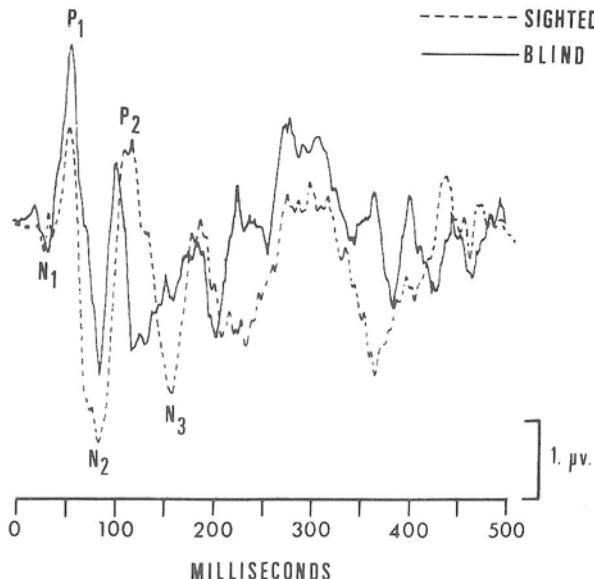


Fig. 3. Typical somatosensory evoked responses (SERs) to vibratory stimulation (one burst of pulses of 20 msec duration each 1.3 sec, produced by a 24 × 6 array of vibrators covering an area between the vertex and the left upper temporal region. 250 stimuli were averaged for each record. The dashed line is an SER from a sighted person, while the solid line is an SER from a blind person (note the shorter latencies, particularly of components N₃ and P₂)

Conclusions

Our sensory substitution studies were begun, in part, to test hypotheses regarding CNS plastic mechanisms. A congenitally blind person offers a "natural" experiment, in the tradition of HUGH-LINGS JACKSON, FOERSTER, LASHLEY, LURIA and TEUBER. Experiments with such persons using the TVSS have demonstrated that a brain which has never been exposed to visual information can quickly adapt to such information, can develop visual means of analysis, and can receive such information transmitted over nonvisual pathways. The extent to which these abilities are dependent on each of the known (and unknown) physiological mechanism of neuronal plasticity must await further investigation. However, training has been found crucial in adaptation to the TVSS, even as it is in obtaining functional recovery from experimental or clinical brain lesions. The cerebral reorganization revealed by such functional recovery may have features in common with the reorganization necessitated by processing information received through the skin in visual terms. For example, it is conceivable in both cases that latent or subliminal fringe pathways may be activated by the imposition of new demands on the CNS.

The identification of the mechanisms involved in recovery from brain lesions is complicated by factors that are difficult to control. For example, to what extent does recovery from edema play a role? Further, since autopsy findings are either not available or are obtained only years later in brain injury cases followed by marked functional recovery, what was the true extent of the damage? This contrasts to the more controlled conditions of our vision substitution studies, in which the extent of the sensory loss is known (total blindness, in many cases from early infancy), and in which the total training with a sensory substitution system can be controlled. Thus, the existence of plastic mechanisms underlying sensory substitution has been established, although to date the specific pathways and structures involved have not been identified.

By extrapolation, plastic mechanisms similar to those underlying sensory substitution can be considered when evaluating the factors underlying recovery from brain lesions. Thus, I consider that our results strongly support FOERSTER's views on the usefulness of physical (and mental) rehabilitation in the reorganization of brain structures and pathways following brain lesions.

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Discussion

Dr. GALBRAITH: NOTON and STARK³ have demonstrated some very interesting scan-paths in normal vision, and your scan-data look very similar to his. Do these patients repeat a very predictable scan-path as in normal vision?

Dr. BACH-Y-RITA: Well, it is not what I might call truly the same. You might call them predictable; there are some variations within it.

Dr. GALBRAITH: The interesting thing about the scan-path data is the suggestion that this is a sequential way in which elements are stored in the memory. Is there anything in your data that would relate to this?

Dr. BACH-Y-RITA: I would think in our cases it's more likely that the amount of information is picked up because their parallel input is reduced.

Dr. POECK: Is it possible, for instance, by the evoked potential technique to demonstrate where this information is processed?

Dr. BACH-Y-RITA: Well-controlled evoked potential studies matching blind and sighted persons have shown highly statistical significant differences in the time of the late components. The early ones didn't really show any difference.

Dr. CREUTZFELDT: If people blind from birth regain their vision by operation, one of the great difficulties is for them to develop a spatial concept. If they go past a shop window, they think that all objects are just in front of them and do not realize that they are distant.

Dr. BACH-Y-RITA: We had a comparable case: a case of restoration of vision in which we used similar techniques to train visual response. It is much more difficult to train a previously blind person to use his sight and it probably involves changes of the central nervous system and the development of eye movement control), than it is to train a blind person to use a tactile vision substitution system.

³ NOTON, D., STARK, L.: Scanpath in eye movement during pattern perception. Science 171, 308-311 (1971).

Some Problems of Cortical Organization in the Light of Ideas of the Classical "Hirnpathologie" and of Modern Neurophysiology. An Essay

O. Creutzfeldt¹

The scientific analysis of the functions of the cerebral cortex during the last 150 years appears to oscillate between the two extremes, localizationism and holism, and it is interesting to see how the two positions take on a new appearance in the light of new discoveries. Beginning with the crude method of macroscopic comparison of different brain or even skull areas in the beginning of the 19th century (GALL vs. BURDACH), the controversy arose again when the effects of localized extirpations, stimulations or clinical lesions became known 100 years ago (HITZIG vs. FLOURENS); and when anatomists discovered the different projection areas and cytoarchitectural differences between cortical fields at about the same time. The controversy became apparent at all levels: the psychological level (e.g. structuralism vs. Gestaltpsychology), the macroscopic level of lesion effects (e.g. WERNICKE'S subdivision of language disturbances vs. the more holistic views of "Sprachfelder" represented by S. FREUD, HEAD, MARIE and others; or the extreme subdivision of cortical functions by KLEIST, FOERSTER and PENFIELD against more holistic views of GOLDSTEIN, v. MONAKOW or LASHLEY); even in clinical psychiatry the controversy goes on between the biological psychiatrists who follow WERNICKE'S "Geisteskrankheiten sind (lokalisierte) Gehirnkrankheiten" against holistic views of the more psychodynamically oriented groups; or at the cellular level where already MEYNERT (1868) like some modern authors tended to localize specialized functions or memory traces into individual cells. In sensory physiology, we have the "classical" psycho-physical positivism (MACH and HELMHOLTZ) against the holistic views of LASHLEY and the Gestaltpsychologists (KÖHLER, WERTHEIMER, and METZGER). These arguments went on simultaneously as well as successively at the different levels, and during the long discussion of the last century most of the essential ideas related to the localization vs. holism problem have been expressed in some way or another.

It is fascinating to see that, if well expressed, both views are equally satisfactory and appear equally correct. One of the reasons for this situation may be that it is practically impossible to separate the introspective knowledge of our own cognitive and mental processes from our functional interpretation of experimental or clinical results in brain research. No wonder that KANT'S philosophy can be discovered again and again in the analysis of brain functions by neurologists, psychophysicists and neurophysiologists, as his analysis of pure reasoning has used

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introspective methods for the analysis of mental processes in an unsurpassed perfection. And no wonder that analytical, structuralistic explanations of brain functioning clash with the holistic views, like KANT'S analytical philosophy produced such a strong reaction reaching from idealism to vitalism. None of the views gives a fully satisfactory picture of how we really see ourselves, although the theory may be fully consistent in itself. We have simply not discovered the unifying model and we will possibly never find it. Maybe there are good arguments to suggest that the two alternative views represent only two different aspects of brain functioning: the brain as a sequential analyzer of signals from sensory inputs to the motor output and the brain as the indivisible representation of the universe and the self as the center of this universe.

Electrophysiological stimulation and recording techniques have enormously increased our knowledge of the functional as well as the anatomical organization of the cortex. Recording techniques have demonstrated the existence of secondary etc. projection areas, and have given us, with the microelectrodes, an insight into the actual working of the cortex. Of course, the initial enthusiasm reinforced by unexpected discoveries is now followed by some reflections as to where these discoveries have led us.

Structuralism in Modern Neurophysiology

The most important model developed from modern neurophysiology is that of hierarchical organization of perception processes. It goes back, of course, to concepts of association and structuralistic psychology and has its roots in common sense logic. In modern, psychological terms it is proposed again and represented in its purest and strongest form by the Hubel-Wiesel model of the visual cortex. In this model it is assumed that in the primary visual cortex several geniculate fibers whose receptive fields are lined up in a row, converge on one cortical neurone. This neurone therefore becomes most sensitive to a line at an orientation determined by the row of receptive fields of the converging geniculate fibers. Such "simple" cells, called "orientation" or "line" detectors, are supposed to extract the basic elements from our visual environment: lines of certain orientations and tangents to curvatures.

At the next level, it is supposed that several "simple" cortical cells with the same orientation sensitivity but different location in the visual field converge on a higher order, a "complex" cell, which is now assumed only to detect "orientation", more or less invariant of localization in the visual field. Several complex cells with different orientation sensitivity are then supposed to converge on "hypercomplex" cells, which thus are assumed to become "detectors" of complex visual stimuli like angles, crosses, etc. The philosophy behind this was well expressed by W. WUNDT, who argued against the rather global association law of association psychology (in *Grundzüge der Psychologie*, 1896): Jene zusammengesetzten Vorstellungen, welche die Assoziationspsychologie als unzerlegbare psychische Einheiten voraussetzt, entstehen selbst schon aus Verbindungsprozessen, die of-

fenbar mit den (gewöhnlich Assoziation genannten), komplexeren Verbindungen innig zusammenhängen.Daraus folgt, daß den gewöhnlich allein so genannten Assoziationen zusammengesetzter Vorstellungen elementare Assoziationsprozesse zwischen ihren Bestandteilen vorausgehen" (p. 273, 12. Aufl.). (The complex ideas, which association psychology presumes to be indivisible units, consist themselves of processes of combinations.This means that elementary associations between single elements are the predecessors of the so-called associations of complex ideas.) One recognizes here in the hierarchical concept of modern neurophysiology the classical epistemological error which one can trace through the whole history of "Hirnpathologie" and neuropsychology: psychological ideas (or, as we may add nowadays, terms borrowed from information theory) are used to describe the function of complex neuronal systems or even of individual neurones, like localizationists drew psychological schemes into the brain and thus assumed to have found a basis for further functional analysis of behavior in anatomical terms (H. WOLFF, 1904).

It should be pointed out here that the sequential "hierarchical" organization from simple to complex to hypercomplex cells in the visual system, due to excitatory convergence of several lower order onto higher order neurones is but a hypothesis with which a number of recent findings are not compatible. STONE and HOFFMANN (1973) found that complex cells may be excited monosynaptically by optic radiation afferents with faster conduction velocity (deriving from retinal y-cells) than simple cells (excited by x-cells). PETTIGREW et al. (1968) found that some complex cells show optimal responses to stimuli moving at such high speeds to which simple cells do not respond anymore. SAN-SEVERINO (1973) confirmed this for the complex cells in area 18. In fact, except for the "typical" cases, there are great difficulties in such a simple - complex classification and authors disagree quite a lot on that point (cf. BROOKS and JUNG, 1973; CREUTZFELDT et al., 1974). As useful and plausible as such a classification might have been for descriptive purposes in the beginning, so dangerous it is if it becomes part of a theory or dogma. The situation reminds one of that of aphasia research at the beginning of this century, where too rigorous classifications of different forms of aphasia obscured rather than enlightened the problems. We have therefore proposed to use a more descriptive terminology: visual cortical cells with small or large receptive fields which largely correspond to the simple and complex cell categories respectively (CREUTZFELDT et al., 1974). As impracticable as it will probably be to introduce such a new terminology against well established names, the purely classifying nature of the Hubel-Wiesel terminology should be kept in mind if it continues to be used. In fact, it mostly turns out to be much more difficult to find the right stimulus pattern for a "simple" than for a "complex" cell.

A further aspect of this "hierarchical" organization of feature-detecting systems is the *repetition of sensory projections in a somatotopic manner* in secondary etc. cortical areas, first discovered by ADRIAN and elaborated essentially by MARSHALL, TALBOT, WOOLSEY and his students. It is often believed that the degree of complexity of features, to which single neurones are specialized,

increases from one area to the next, so that finally cells highly specialized for complex stimuli are found in the subsequent areas. Consequently, GROSS searched for the trigger features of individual neurones in the inferotemporal gyrus of monkeys and discovered cells which could "best be driven by such stimuli as the shadow of a monkey's hand" etc. This may be so, but the implication that such cells actually are representing to the brain in a sort of all-or-none manner the presence of a monkey's hand is of course not proven by such a demonstration. The same can be said for the auditory system where cells in the auditory cortex responding to species specific sounds are thought to be specific feature detectors for such sounds. SUGA (1973) rightly argues that one necessary condition for calling a cell a "feature detector" for a certain sensory pattern is that this cell has a "rejection mode" for all signals which do not represent this feature. But this condition is not fulfilled by most of these cells, or has not been sufficiently tested. All that one can conclude from such observations is that the signals tested (the hand or the sound) still drive neurones at the structure from where these activities were recorded and that these signals are thus still influencing activities transmitted to other structures.

In fact, individual neurones in the visual cortex which respond best to lines of a certain orientation moving normally to this orientation would be, for the communication engineer, pretty bad line "detectors". If one tests them with contrasts of different curvature, one finds that by far the majority of cortical cells is very broadly tuned to different curvatures and that some respond stronger to convex, others to concave contours (HEGGELUND and HOHMANN, personal communication). But the large response variability to any shape excludes *per se* that signals from such neurones signal a certain curvature be it a straight line, a convex or concave shape. Furthermore, even the orientation sensitivity is not a strict functional description of a "simple" cortical cell: the tuning width may be as wide as 40° or more, and the optimal orientation may differ by up to 20 - 30° depending on whether the stimulus moves forward or backward, or on the reversal of contrast (CAMPBELL et al., 1968; ALBUS and HEGGELUND, personal communication).

The hypothesis of increasingly higher degrees of abstraction due to sequential projections from one area to the next is in its simple form also not tenable anymore on anatomical and physiological grounds. Historically this concept goes back to WERNICKE'S model of speech areas (1876). In the cat, areas 17 and 18 both get primary geniculate afferent input. Cytoarchitectonic analysis suggests that area 18 may be the phylogenetically older structure as compared to area 17, the latter being pushed in as a new structure (SANIDES, 1970). There is some anatomical evidence that this holds true also for other sensory areas. Electrophysiological findings indicate that fast conducting y-fibers of the geniculocortical radiation excite both area 17 and 18 neurones monosynaptically while the slower conducting x-fibers appear to project only into area 17 (STONE and DREHER, 1973; SINGER, personal communication). Furthermore, cells in area 18 maintain their "trigger features" even if area 17 is taken away (DREHER, personal communication). Anatomically, a bifurcating afferent projection

system to areas 17 and 18 as well as a direct projection system to area 17 has been known in the cat for some time. But besides this double thalamo-cortical projection, retino-topically organized intracortical connections between areas 17 and 18 do exist. In primates, no direct geniculate input to areas 18 and 19 has been demonstrated. Here only the mirror-like projection from 17 to 18, 19 and further retino-topic repetitions (up to five) (ZEKI, 1969, 1970; COWEY, 1973), but not yet the diencephalic afferents to the secondary etc. areas are known. The Clare-Bishop area in the cat receives visual cortex, geniculate as well as pulvinar input. In the somato-sensory system, recent findings have indicated different input areas for cutaneous and Ia-muscle afferents (ROSEN, 1972). Such findings emphasize the mechanisms of parallel processing of sensory inputs in the cortex in addition to serial analysis. Mechanisms of parallel rather than hierachic processing are also suggested by some neurophysiological findings in the visual brain. In the monkey, the peristriate area (area 18) appears to contain neurones which are highly sensitive to the binocular disparity of visual objects (HUBEL and WIESEL, 1971), while in the temporo-parietal area neurones show highly specific responses to color (ZEKI, 1973).

Serial analysis in a hierarchical or pedigree-like manner had much appeal to information engineers, who developed models of layers of filters each generalizing more abstract features (MARKO, 1969). And, curiously enough, such models turned out to be quite useful for the recognition of standardized letters and numbers. But recognition of more complex features which are really important for the behavior of animals and man, such as movements, recognition of species, prey, companions or enemies have even not been attempted and cannot be simulated by such models.

Mosaic Versus Network: Organization of the Cerebral Cortex. The classical antithesis between localizationism and holism, between KLEIST (1934) and V. v. WEIZSÄCKER (1940), if one wants two typical representatives of these positions, reappears again at the microscopical level. Is the cortex organized in a mosaic-like fashion or as a continuous network? In the somato-sensory cortex, MOUNTCASTLE (1957) described "columns" of neurones which were all excited by one type of cutaneous receptors and subsequently HUBEL and WIESEL (1963) found "columns" of neurones in the visual cortex which were all sensitive to the same orientation of a line. The orientation columns may be superimposed by columnar systems such as ocular dominance columns. Neurones within a column were not supposed to interact with neurones from other columns.

Firstly, it is clear that both columnar concepts are not directly comparable with each other. MOUNTCASTLE'S "columns" indicate that different types of receptors project into different spots of the somato-sensory cortex, whereas the HUBEL-WIESEL columns are more of a functional character (orientation), but with the different functional types of afferents (on- and off-center fibers and, as we now know, x- and y-cells) being mixed up in each "column".

But even the actual concept of a functional column in the visual cortex is questionable in the light of recent analysis: If one penetrates the visual cortex in a horizontal direction and deter-

mines the optimal orientation for each neurone, one finds that orientation "columns" as defined by the identical optimal orientations, are in fact not wider than about 50 - 100 μ , i.e. the width of one or two neurones and that no sharp boundaries exist (ALBUS, in preparation). Neurones lying near each other are more probable to have a similar optimal orientation than those lying further apart. But within a distance of about 300 to 500 μ around one neurone, all orientations are "represented". If, on the other hand, a vertical penetration is done, one finds that the optimal orientation of neurones within a column may vary up to 30, 60 and sometimes even 90°. Often groups of neurones are found which have identical or nearly similar optimal orientations, but such cell clusters are restricted and it is difficult to find neurones with exactly the same optimal orientation throughout a whole "columnar" penetration (HEGGELUND and CREUTZFELDT, in preparation). It is not rare that neurones picked up by the same microelectrode tip or within 100 μ distance have optimal orientations different by 90°. Furthermore, neurones within one penetration have variable preferred directions, some neurones being more sensitive to the forward, others to the backward movement of a line moving normal to its orientation (CREUTZFELDT et al., 1974). These findings indicate that the variability of optimal orientations and directions is similar in the vertical and the horizontal domain of the visual cortex. All that can be said is that there is a certain statistical coherence of similar orientations in the vertical and horizontal domain, but no well-defined functional column representing only one orientation.

The impact of "cellular pathology" (VIRCHOW) on brain research and MEYNERT'S demonstration of basically different cellular patterns in different cortical structures led to the discovery and elaboration of cytoarchitectonic differentiation of different cortical areas. Two of the most prominent exponents of cytoarchitectonics were mainly impressed by the individuality of the different cortical areas [v. ECONOMO (1927) speaks, in the tradition of MEYNERT, of different cortical organs] and they practically ignored the impressive new data on intracortical connectivity emerging from the application of Golgi's method to the microanatomy of the cerebral cortex (CAJAL).

The situation is, although on a different scale, in many respects similar to that of modern neurophysiology, where the "columnar concept" appears to dominate the thinking on cortical organization. This concept implies that the columns are separate functional units and horizontally not connected with each other. The cortex is thus assumed to be composed of a mosaic structure of columns, each representing a different quality or extracting a different information from the environment. The concept led anatomists to look for the anatomical structure of "columns", in vain.

Anatomically, the large amount of intracortical fibers has been known for a long time and Golgi-impregnations suggest some ideas about the intracortical circuitry (SZENTAGOTTHAI, 1974). But there are only little hints from anatomy as to the actual function of these intracortical connections. Intracellular recordings demonstrated that electrical stimulation of cortical afferents produces

excitatory as well as inhibitory post-synaptic effects on the cortical neurones. Because of their latency delay it was concluded that the inhibitory actions are of intracortical origin, i.e. mediated through intracortical interneurones (CREUTZFELDT et al., 1966; CREUTZFELDT, 1973). Such inhibitory effects can also be demonstrated if physiological stimulation is used, i.e. light stimulation for visual cortex neurones and skin or hair (whisker) stimulation for the somato-sensory cortex. This intracortical inhibition plays an essential if not the exclusive role for the elaboration of the peculiar response properties and "trigger features" of cortical neurones (CREUTZFELDT et al., 1974). If at all, excitatory convergence of thalamo-cortical afferent fibers does not exist to such an extent that it could explain the trigger features of cortical neurones by simple geometrical models such as suggested originally by HUBEL and WIESEL (1962) and still more recently by HENRY and BISHOP (1974).

One may suppose that, in addition to the simple afferent excitatory input, cortical cells receive a massive intracortical excitation through intracortical fibers. We therefore investigated the action of intracortical connections: we introduced two electrodes with their tips separated 50 to 500 μ from each other into the visual cortex. One electrode contained glutamate which excites only nerve cells but no fibers. If glutamate is injected by electrophoresis into the tissue 50 μ around the recording electrode, an initial excitation is always seen. But to our astonishment, at a distance between 100 - 300 μ glutamate injection always produces inhibition at the recording site. At a distance of 300 - 500 μ , effects are mostly difficult to see, but if at all, again only inhibition is seen (HESS et al., in preparation). Similar observations have recently been reported for the somato-sensory cortex (RENAUD and KELLY, 1974).

These findings indicate that over a distance of about 300 - 400 μ , each cortical neurone is inhibited by its neighbors and that the intracortical connections are essentially and dominantly inhibitory. The findings also indicate that cortical neurones are not isolated but embedded in a network of intracortical connections where each neurone is influenced by the activities of its neighbors. The cortical module would then be a cylinder of a diameter of about 500 up to 1000 μ and the individual neurones in the center of this cylinder would be inhibited by other neurones contained within that cylinder. This module is, however, not a column, as it is repeated continuously and each individual neurone is again the center of such a cylinder. This is the organization of a network of interconnected elements rather than of a mosaic of functionally independent pieces of neuronal tissue. It follows that such a network shows cooperativity, and the response of one individual member of this network will depend on the responses of its neighbors and vice versa. Asymmetric properties of any individual neurone in this cortical network would then be the consequence of asymmetries of the network itself and of asymmetries of its afferent input. In the visual cortex such a basic asymmetry is given already by the distorted projection of the visual field which is represented by a larger number of retinal ganglion cells in the central or foveal area than in the periphery.

Conclusions

Such a model of the cortex as a cooperative network onto which the body surface and environment is projected according to the dimensions of the receptor surfaces is essentially different from the concept where the cortex is supposed to be composed of different "organs" (MEYNERT, v. ECONOMO) or of a mosaic of individual functional columns. The mosaic model supposes that the results of the calculations within individual columns are combined to ideas (or associations) of higher order - like in the structuralistic psychology of W. WUNDT. In the network model the responses to stimuli are not invariant but depend on the context of a set of stimuli, and the picture of the environment transmitted by such a network to further stations of the brain is not simply the sum of the stimuli but a function of the combination of the elements in a whole pattern as picture. These may be simultaneous, i.e. spatial, or successive, i.e. temporal combinations. Such a model corresponds much closer to the original concepts of Gestaltpsychology so beautifully expressed by WOLFGANG KÖHLER who compared the situation of Structuralism vs. Gestalt-psychology to that of classical physics vs. quantal physics: "The dynamic structures of the physiological processes of the brain (concerned with the organization of visual perception)must be functional entities." (W. KÖHLER, 1969). Modern neurophysiology seems to support such concepts. But we are now in the position to propose different mechanisms for the interaction of stimuli in the cortical network from what KÖHLER could extract from neurophysiology of his days. He concluded from perception experiments, especially the figural after-effects, that inhibitory interactions must exist between stimuli but tried to find them in aneurotonic effects and after-effects. Since then, post-synaptic inhibition has been discovered and has been shown to be an essential mechanism which combines the individual neurones to a network and which enables us to perceive combinations of points and lines, or frequencies and intervals as that what they are, i.e. a visual or auditory environment.

Note Added after Finishing this Manuscript

The problem of "abrupt localization" (JACKSON) vs. overlapping localization and representation of function in the motor cortex has recently been discussed in a brilliant historical review by PHILLIPS (1973). Also here, on the output side, a columnar patch-like organization of the input and output functions does not exist.

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V. Cerebral Speech Mechanisms

Vocal Behavior and its “Localization” as a Prerequisite for Speech

D. Ploog ¹

In view of the long natural history of vocal behavior in vertebrates it is certainly not just a whim of nature that language is transmitted by sound. Therefore, I share the opinion of PHILIP LIEBERMAN (with CRELIN and KLATT) that the phonetic aspect of language may contribute substantially to the question of the evolution of language.

There is no doubt that language serves social communication, and there is evidence that phylogenetic steps in the evolution of social communication systems in mammals bear on mechanism which are involved in the emergence of human language. Hence it is legitimate to study social communication and especially vocal communication in subhuman primates in order to compare their vocal signaling system with the human speech mechanism and its ontogeny.

From ethology we know from very well-documented examples that there is a parallel evolution of the apparatus which emits a set of signals, and the apparatus which receives the signal and decodes it. If this were not so it would be difficult to understand how selective pressure could be forced on the behavior of the individuals which communicate. From the neurological point of view, a signaling system must consist of at least four parts. These are: (i) the peripheral apparatus (with its anatomical properties) which generates the species-specific signals; (ii) its cerebral motor control system which does the patterning of the signal; (iii) a sense organ which receives the species-specific signal (in terms of physical energy); and (iv) the cerebral decoding apparatus which transforms the signal into a message which may or may not produce a modification of behavior on the receiver's side. How the cerebral motor and decoding system is tied together is an open question and is probably the keystone for the understanding of communication processes in general. These four logical parts, functioning as an interdependent system in communication processes, form the framework for our studies on squirrel monkeys. Here, I will mainly dwell on the vocal system and its ontogeny.

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Brain Stimulation Studies

In 1962, in a paper on the cerebral representation of penile erection in the squirrel monkey (MacLEAN and PLOOG) it was noted that species-specific calls, such as chirping and cackling, were elicitable from certain brain structures, e.g. the septum, the preoptic area, and the periventricular structures.

In subsequent brain stimulation studies, these findings were substantiated (JÜRGENS et al., 1967), and in 1970 (JÜRGENS and PLOOG) an extensive and systematic study on the cerebral representation of vocalization revealed the following results which are given here briefly: The whole brain (including the neocortex and excluding the cerebellum) was explored. A large variety of calls, spectrographically and otherwise indistinguishable from natural calls, were electrically elicitable from extended and well-definable brain structures. According to the physical characteristics of the sound spectrograms of the reproducibly elicited calls all vocalizations were classified into eight types (Fig. 1):

Cackling calls are frequently heard and make up a substantial proportion of the total vocal output of a monkey group. This type of call has been found in situations characterized by general aggressiveness and excitement; it is usually uttered by several animals simultaneously. Growling has been interpreted as an expression of directed aggressiveness, for it often occurs in connection with specific dominance gestures of the vocalizing animal. Chirping calls, which are the most frequently heard calls under natural conditions, probably aid contact and group cohesion; furthermore, they seem to be performed particularly when the attention of the animal has been attracted by new events. Trilling has been interpreted as a call whose function is to maintain minimum distances between individuals; it probably also serves to focus the attention of other group members on the emitter. Moreover, trilling is strongly associated with all situations concerning feeding. Quacking is a typical call of irritation and expresses a state ranging between uneasiness and threatening behavior. Shrieking, finally, represents the highest degree of excitement. The remaining two types, groaning and yapping, do not show a clear correlation with brain structures and will therefore not be considered in the following.

Figure 2a shows schematically the anatomical substrate from which cackling is elicitable. It leads from the caudal end of the periaqueductal gray through the periventricular gray of the diencephalon. At the level of the inferior thalamic peduncle the system branches off into three components: the first follows the inferior peduncle dorsally towards the anteromedial thalamic nucleus; the second follows the inferior peduncle ventrolaterally into the amygdala and from there through the external capsule and uncinate fasciculus to the rostroventral temporal cortex; the third follows the anterior thalamic radiation along the ventromedial border of the internal capsule into the ventromedial orbital cortex and the precallosal cingulate gyrus.

Figure 2b shows the system for growling calls that partly overlaps the cackling system but also has its own extensions, e.g.

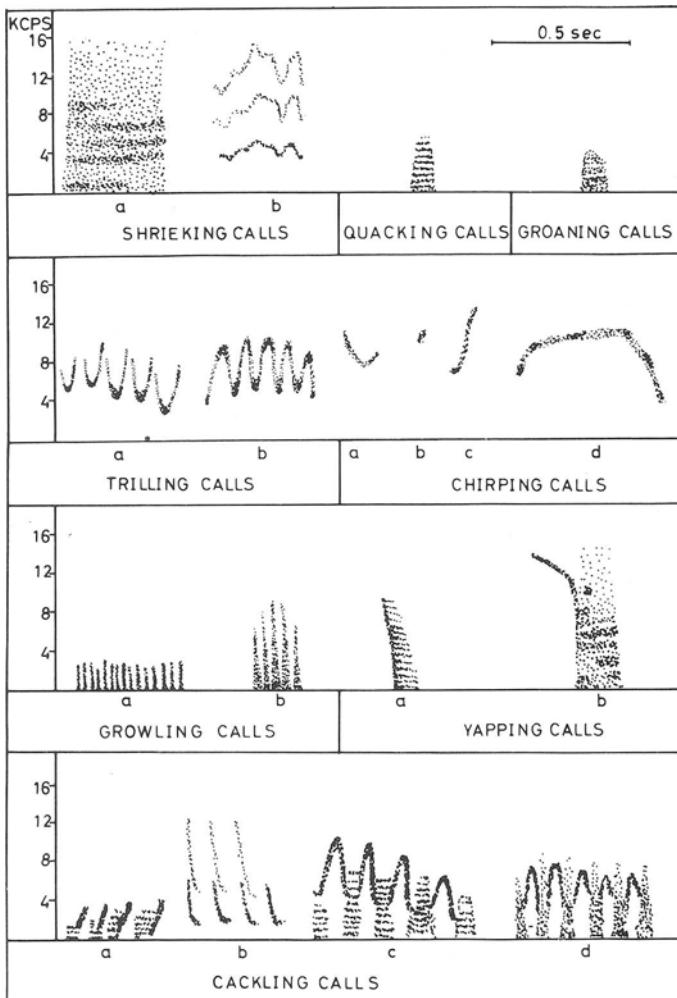


Fig. 1. Schematic representation of the eight fundamental vocalization types according to which all electrically elicited vocalizations were classified (JÜRGENS and PLOOG, 1970)

into the area ventralis segmenti of Tsai and via the medial forebrain bundle into the lateral hypothalamus. At the level of the inferior thalamic peduncle, another important deviation from the cackling system leads into the preoptic region just anterior to the anterior commissure, turns to the stria terminalis, and follows these fibers into the amygdala. The distribution of the growling calls is essentially identical with that of the hissing and growling of cats, with the amygdala, stria terminalis, perifornical hypothalamus, periaqueductal gray, and tegmentum as mediating structures.

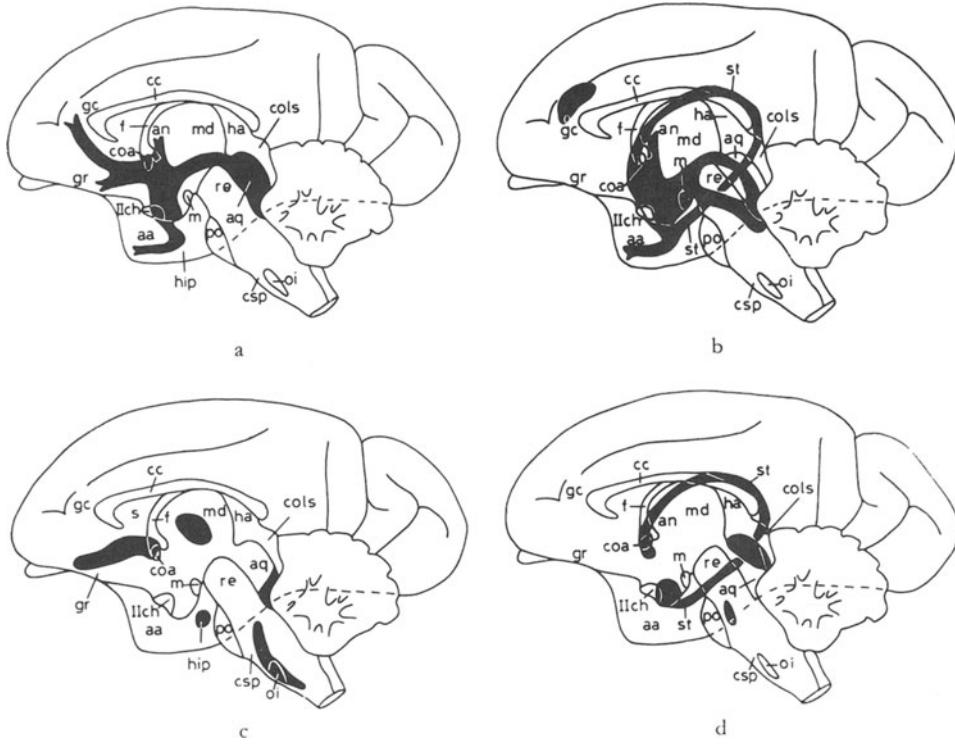


Fig. 2. General (sagittal) view of the cerebral system (in black) yielding vocalizations: (a) cackling calls, (b) growling calls, (c) chirping and trilling calls, (d) quacking and shrieking calls (JÜRGENS and PLOOG, 1970 and JÜRGENS, 1971).

Abbreviations: aa, area anterior amygdalae; an, nucleus anterior; aq, substantia nigra; cc, corpus callosum; coa, commisura anterior; cols, colliculus superior; csp, tractus corticospinalis; f, fornix; gc, gyrus cinguli; gr, gyrus rectus; ha, nucleus habenularis; hip, hippocampus; m, corpus mamillare; md, nucleus medialis dorsalis thalami; oi, nucleus olivaris inferior; po, griseum pontis, re, formatio reticularis tegmenti; st, stria terminalis; Il ch, chiasma nervi optici

Other groups of calls, such as chirping, trilling, quacking and shrieking, are represented not in continuous systems but in circumscribed areas only. For example, the chirping calls, which aid contact and group cohesion, are elicitable in the subcallosal gyrus and medioventral caudatum region, the midline thalamus, the rostral hippocampus, the caudal periaqueductal gray, and along the caudal spinothalamic tract (Fig. 2c). Shrieking calls which express a high degree of excitement, are elicitable in the stria terminalis and its bed nucleus, in the ventral hypothalamus and in a small section of the medial lemniscus (Fig. 2d).

Without going into further anatomical and any neurophysiological details, the cerebral substrates can be shown to give a general

impression of the specificity of the vocal system and its correlation with limbic structures and their thalamic, hypothalamic, and midbrain connections. This is not to say that the structures outlined above represent a pure vocalization system in the sense of excluding other, especially autonomic stimulus responses. The majority of elicited calls is accompanied by either penile erection, micturition, salivation, changes in respiration or any other type of autonomic response.

Ontogeny of Calls

When observing neonate squirrel monkeys one is surprised to hear a substantial part of the vocal repertoire already during the first days of life (PLOOG et al., 1967). It is obvious that the vocal apparatus and the cerebral system as outlined above is rather well developed at birth. The question then arises whether or not an auditory input of species-specific calls is needed for a full-fledged vocal signal production. If one deafens adult squirrel monkeys no apparent difference in the quality of the vocalizations can be detected even after several years (TALMAGE-RIGGS et al., 1972). From that one might conclude that the squirrel monkey is not in need of his own differential acoustical feedback for maintaining the proper species-specific vocalization. However, these deafening experiments do not settle the question as to whether an early species-specific input is necessary for establishing the proper calls. Recently the hypothesis of an innate vocal repertoire was put to a direct test by raising infants born of muted mothers in acoustic isolation (WINTER et al., 1966). The vocalizations were compared with neonates isolated with their intact (non-muted) mothers. The muting operation (removal of the vocal folds) was performed 1 - 2 months before delivery. Under these conditions all call types as defined by WINTER, PLOOG and LATTA except twitter/trill were recorded within the first day in both normal infants and the acoustic isolates. The first recordings of location trill were obtained on the third day. The latest call to develop was the twitter call in normals and isolates. The first occurrence of call types obviously depends on the appropriate conditions, i.e. the presence of releasing stimuli, and on maturational factors. Among the selectively isolated animals were one hand-raised infant and one that was deafened on its 5th day of life. Even under these conditions the infants displayed all aspects of normal vocalization. By the standards of our observational techniques, mutism of the mother does not interfere seriously with the mother - infant relation. On the basis of these experiments we can assert with a high degree of probability that the vocal repertoire of the squirrel monkey develops without species-specific auditory input. Moreover, the observations of the deafened infant and the supporting data on deafened adults indicate that even the auditory feedback of the animal's own voice is not necessary for the development of proper calls. The vocalizations of squirrel monkeys bear the characteristics of fixed (genetically determined) action patterns.

Voluntary Control over the Voice

The development of the vocal behavior and the brain structures from which vocalizations are electrically elicitable lead to the question of the voluntary control of the voice (RIKLAN and LEVITA, 1969). Although monkeys (and more so apes) are known to be skillful in imitating motor gestures they are quite inapt at imitating vocal gestures which do not belong to their repertoire. While the vocalization of cats, dogs, and dolphins can be shaped and trained, it was doubtful until very recently whether the voice of monkeys were conditionable at all. LEANDER et al. (1972) and SUTTON et al. (1973) have demonstrated quite convincingly that cebus monkeys and rhesus monkeys, respectively, can control their vocal behavior contingent upon conditional stimuli and reward. The latter authors have shown that rhesus monkeys can even control for the length and the intensity of a call (the "coo"). However, so far no one has shown that a monkey has voluntary control over a variety of his natural calls nor the modification of the sound patterns itself.

Contrary to man, neither in the squirrel monkey nor in the rhesus monkey (ROBINSON, 1967) and hardly ever in the chimpanzee, was it possible to elicit vocalizations from the cortical area where the face, the tongue and the larynx is represented. However, it was reported by HAST and MILOJEVIC (1966) that a small area just dorsal to the Sylvian fissure and anterior to the Rolandic fissure yields movements of the vocal folds. This finding has been confirmed recently in my laboratory by JÜRGENS (unpublished data). According to cytoarchitectonic studies of ROSABAL (1967) this field is homologous to Brodmann's area 44, and has also been identified in various New World and Old World monkeys and apes. Recently, SUTTON et al. (1973) employed their above-mentioned conditioning technique in ablation studies. They were able to demonstrate that bilateral ablation of frontal and motor cortex, Broca's area included, did not alter the control over the length and intensity of the rhesus monkey's "coo" call whereas the ablation of the anterior cingulate gyrus (area 24) abolished this training effect entirely.

Vocal behavior as means of social communication has a very old evolutionary history. The sound producing peripheral organs (larynx, pharynx, tongue) evolve together with cerebral structures which are involved in the patterning and decoding of the vocal signals. The sound production and the patterning of calls become increasingly refined with the cerebral evolution. Whereas auditory feedback of the voice is not necessary in monkeys (squirrel monkeys) this control is highly necessary for human speech development. The control of the voice is possible in monkeys as far as length and intensity of certain calls are concerned but impossible with respect to the voluntary control over the variety of their natural calls or the modification of the sound pattern itself.

Man appears to be the only primate in which the cerebral representation of vocalization has its cortical substrate in the motor area. It is thought that this arrangement serves in part as the

neuronal basis for the voluntary control of the human voice; i.e. herein lies the species-specific capability to imitate and learn phonemic combinations and sequences during ontogeny. However, in the light of the above-mentioned ablation studies it remains to be explained which control features are due to the motor cortex and Broca's area, and which to the limbic cortex (area 24) and possibly other subcortical structures.

Although man appears to gain an almost unlimited control over his voice (along with the developmental changes of the vocal tract) during the various phases of language development there seem to be limits to that after full maturation of the system, e.g. foreign accents cannot be overcome easily after puberty (LENNEBERG, 1967). The foreign accent phenomenon could have contributed "to the establishment of a highly adaptive population structure involving a degree of endogamy in sub-units of the total population, in which rapid and flexible adaptive response to selective pressures would then be possible" (HILL, 1972). This hypothesis seems especially plausible if one takes into account that selective processes of this kind seem to occur already in subhuman primates: "dialects" in closely related but physically distinguishable monkey populations can be demonstrated (WINTER, 1969).

Besides the many similarities among all primates, there are already very important differences between subhuman and human primates on the phonetic level of sound production which can be related to structures and functions as well. Various recent experiments on newborn human babies (EIMAS et al., 1971, 1973) have shown that they are able to distinguish phonemic sound patterns from non-phonemic ones which leads to the assumption of a special human decoding mechanism for certain phonemes represented universally in all human languages.

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Discussion

Dr. CREUTZFELDT: Did you try to interfere with the subcortically evoked phonation by stimulation of area 44, i.e. did you paralyse by stimulation like Rasmussen does? Did you stimulate limbic or other structures?

Dr. PLOOG: These experiments are in progress and, together with others, are concerned with the motivational value of these vocalisation areas, but I cannot give a definite answer yet.

Dr. GALBRAITH: In your introduction you commented about the importance of sensory and motor relationships and the coding relationship between them. Yet, your data relate only to the motor component. Would you expect the distribution of sensory evoked potentials to the various trills and calls to bear some similarity to the structures you find with motor elicitation?

Dr. PLOOG: No, I don't think I would find that because this vocal system is certainly not the place where the natural calls are decoded. Rather I think by stimulation you change the motivation of the animal, so that the animal generates the sound. The sur-

prising thing is that these areas are so well confined and even attributable to certain groups of calls. Now to your question: there is evidence by WINTER and FUNKENSTEIN² and subsequent workers like JOHN NEWMAN and WOLLBERG³ and others, that there are certain populations of cells which do not respond to physical sounds but they only respond to natural calls. Apparently there is a decoding system which is rather complicated and not well understood.

Dr. POECK: Imagine that infant monkeys brought up with muted mothers develop the same vocal repertoire as monkeys brought up with normal mothers. What happens if you keep them together with their muted mothers? Do they loose this repertoire or is there some change afterwards? Do they apply it in a different way afterwards?

Dr. PLOOG: No, they are vocalising in the appropriate context but if they live for a longer time with their muted mothers, let us say a year, the frequency of calling per day or per week decreases, as we have seen in our deafened adult monkeys. The "talking" decreases but the quality of the signal does not deteriorate even after a very long time.

Dr. POECK: Is it merely quantitative?

Dr. PLOOG: Merely the amount of vocal communication decreases.

Dr. KUYPERS: I don't know anything about linguistics but I wonder whether you cannot distinguish two components in the language: the actual purely intellectual components and the monkey-song. Perhaps the cortex only handles the intellectual aspects while the diencephalon handles the monkey-song in our language.

Dr. PLOOG: What you are referring to is the distinction between propositional and emotional speech. Anyway, I think that even under the condition that this is a pure expression of an emotional state, there should be a way in which this can be controlled. I don't see yet that the cortex controls this for the length and for the quality of the signal, but the cingulate gyrus does. I have again no explanation why the cortex controls the voice.

² WINTER, P., FUNKENSTEIN, H.H.: The effect of species-specific vocalization on the discharge of auditory cortical cells in the awake squirrel monkey. *Exp. Brain Res.* 18, 489-504 (1973).

³ NEWMAN, J.D., WOLLBERG, Z.: Multiple coding of species-specific vocalizations in the auditory cortex of squirrel monkeys. *Brain Res.* 54, 287-304 (1973). NEWMAN, J.D., WOLLBERG, Z.: Responses of single neurons in the auditory cortex of squirrel monkeys to variants of a single call type. *Exp. Neurol.* 40, 821-824 (1973).

Clinical and Surgical Studies of the Cerebral Speech Areas in Man

T. Rasmussen¹ and B. Milner¹

The continuing studies of localization of function in the human brain at the Montreal Neurological Institute stem directly from Dr. WILDER PENFIELD'S 1928 period of study in Breslau with OTFRID FOERSTER. This experience provided a major part of the background and stimulus for the program of surgical treatment of medically refractory focal epilepsy initiated by Dr. PENFIELD when he returned to North America and took up his new post at McGill University in Montreal (4, 6). This program and the associated studies of cerebral localization of function were steadily expanded through the years by Dr. PENFIELD, his associates and his successors (5, 8, 9, 10, 11, 13, 14). It is therefore particularly appropriate and with much pleasure that we submit this report in honor and in memory of OTFRID FOERSTER.

There are three sections to this report on studies of the cerebral speech mechanisms carried out at the MNI over the past 40 years in the course of the investigation and surgical treatment of medically refractory focal epilepsy. In the first section we will summarize briefly and update our data on the identification of the speech areas, carried out preparatory to cortical excision, by electrical stimulation of the cerebral cortex in patients under local anesthesia. In the second section, we will summarize the data obtained by studying the effects of cortical excisions adjacent to the speech areas, on the localization of the boundaries of these areas, and will comment on a few of the implications of these data. In the third section we will present and update our data on the lateralization of cerebral speech functions as determined by the intracarotid injection of sodium Amytal (amobarbital) in patients who were candidates for surgical therapy for seizures.

Cortical Stimulation Studies of the Speech Areas

The invariable effect of electrical stimulation of an area of cortex is to produce interference with the normal employment of the area affected by the electrical current. If this produces an after-discharge in the cortical electrogram the localizing value of the response is considerably reduced because of uncertainty as to the extent of the spread of the abnormal neuronal activity. In our cortical localization studies, therefore, we have disregarded all stimulation responses associated with electrical

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after-discharges in the cortical electrogram. These induced after-discharge, however, are of considerable importance in analyzing the patient's seizure problem.

In some cortical areas the electrical stimulus produces activation of neuronal systems as well as interference with normal function. Thus, vocalization is frequently produced by stimulation of the face area of the precentral gyrus and, somewhat less frequently, from the corresponding region of the postcentral gyrus (Fig. 1). This vocalization response occurs with equal ease

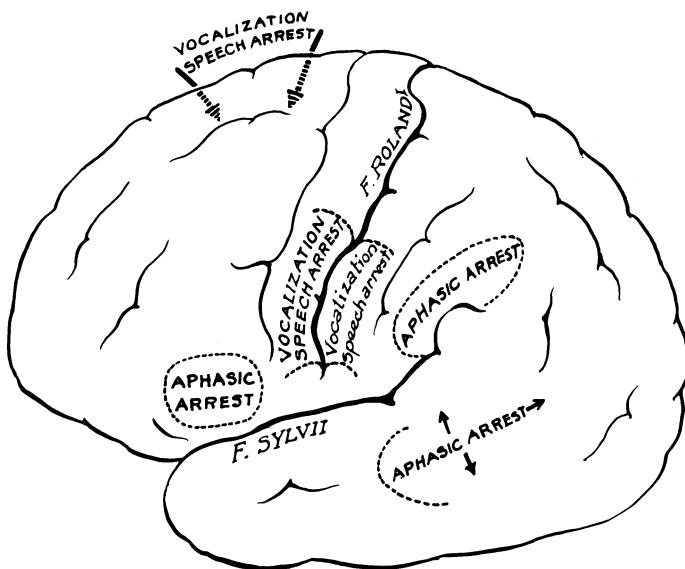


Fig. 1. Summary of areas in which stimulation may interfere with speech or produce vocalization in the dominant hemisphere (from PENFIELD and RASMUSSEN (7))

in the non-dominant and the dominant hemispheres. The same type of vocalization has been produced, but much less frequently, from the medial surface of the frontal lobe in front of the motor leg area and above the cingulate gyrus, the so-called supplementary motor area. These vocalization responses are likewise elicited equally from the non-dominant and dominant hemispheres. Vocalization, however, has never been produced from stimulation of the frontal, temporal or parietal speech zones themselves.

The negative effect of electrical stimulation of the speech mechanisms is more easily elicited and results in arrest or disturbance of speech of different types. In the lower central region and probably in the supplementary motor area the speech arrest of interference results from the preempting of the motor mechanisms of speech by the electrical current. When an effective stimulus is applied to the speech zones proper, however, arrest

or disturbance of speech is produced without interference with movement of the lips, tongue or larynx - aphasic interference with speech. If the stimulation is carried out while the patient is counting or talking, his speech is interfered with until the electrode is withdrawn. He is able to move his mouth and tongue on command during the time he is unable to talk normally. When asked why he stopped talking or had difficulty saying what he wanted to, he usually says, "My mind got mixed up" or "I couldn't think of the word".

If the speech interference produced by the stimulus is not complete, the words may be slurred or distorted, repeated or mixed up, or there may be inability to name with retained ability to speak. In the latter instance, the patient usually says "That is a, that is a" until the electrode is removed, when the object's name is correctly produced. Sometimes there is misnaming, with or without perseveration, or the patient describes or demonstrates the use of an object he is unable to name. Each of these various types of speech interference has been produced by stimulation of each of the three speech zones, frontal, temporal and parietal (Figs. 2, 3, 4, 5 and 6).

A. Stimulation Parameters

A variety of wave forms have been effective in producing aphasic speech arrest, (thyroton discharges, sine waves, rectified sine waves, saw toothed waves and square waves of 0.1 to 5 msec pulse duration), so that the wave form of the stimulating current is clearly not critical for effective stimulation of the speech areas. For a number of years now the standard wave form used at the MNI has been a 2 msec undirectional square wave.

The intensity required to produce aphasic speech interference is usually 1 - 2 volts greater than the threshold voltage required to elicit a response from the sensorimotor cortex. The voltage is ordinarily not raised to more than 3 volts above the sensorimotor threshold to avoid undue risk of producing a seizure.

The usual frequency employed has been 60 per second, but aphasic speech interference has been produced with frequencies ranging from 5 to 200 per second.

Bipolar and unipolar stimulating electrodes are equally effective, but in recent years the unipolar electrode has been used exclusively to facilitate stimulation of depth electrodes in addition to the surface exploration.

Review of our cortical stimulation data clearly indicates that while certain stimulation parameters are more effective than others in producing aphasic speech interference, the nature of the response is not dependent on any of the parameters tested to date.

B. Localization of Cortical Speech Areas by Electrical Stimulation

1. *Frontal speech area (Broca).* Dysphasic speech arrest or interference is elicited from the frontal lobe only in the dominant cerebral

hemisphere, and only from one or the other, or both of the two frontal opercular convolutions immediately anterior to the lower end of the precentral gyrus. The responses may be elicited only from the opercular convolution directly in front of the precentral gyrus (Figs. 2 and 3). In other patients, there is a silent convolution, not yielding aphasic speech interference (Fig. 4). In some patients, both of these opercular convolutions yield such responses (Fig. 5 and 6).

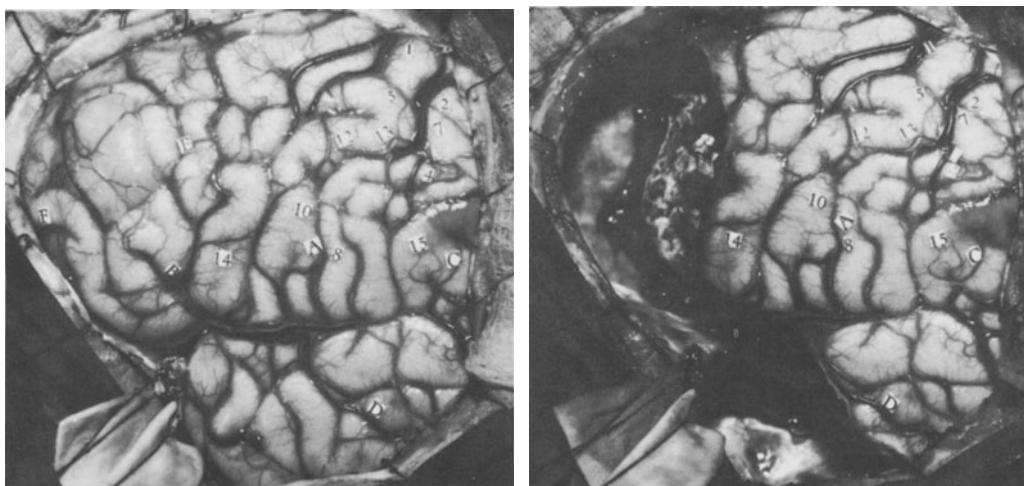


Fig. 2. Pt. G.Ha. - Left frontal lobe seizures due to discrete oligodendro-glioma. Letters indicate positions of electrodes recording maximum epileptiform abnormality. Numbers indicate responses to electrical stimulation. *Left* note tumor between letters E and F. *Right* left frontal and temporal lobectomy. 14 saying months of the year interrupted - "stopped to make sure I got them in the right order". 10, 12, 13, 5, 1 precentral gyrus responses. 8, 4, 3, 7, 2 postcentral gyrus responses. 15 mistake in saying days of the week forward, corrected after withdrawal of electrode

2. *Temporal speech area.* In the temporal lobe, dysphasic speech interference is elicited mainly from the second temporal gyrus behind the level of the postcentral sulcus and extending posteriorly for 2 - 3 cm and from the adjacent convolution above, behind the transverse gyri of Heschl. The first temporal gyrus proper ordinarily ends in a transverse sulcus which is usually at the level of the postcentral gyrus or sulcus and represents the outermost segment of the anterior gyrus of Heschl's region. The continuation, behind this transverse sulcus, of what seems to be the first temporal gyrus, anatomically seems to belong to the parieto-temporal opercular region. Dysphasic speech responses are elicited from this convolution in comparable numbers to the second temporal gyrus (Figs. 3, 4, 5 and 6). Occasionally, however, the first temporal gyrus extends backwards as a single convolution, uninterrupted, well behind the level of the postcentral gyrus. In these instances, aphasic speech interference responses are not elicited from this convolution just below the

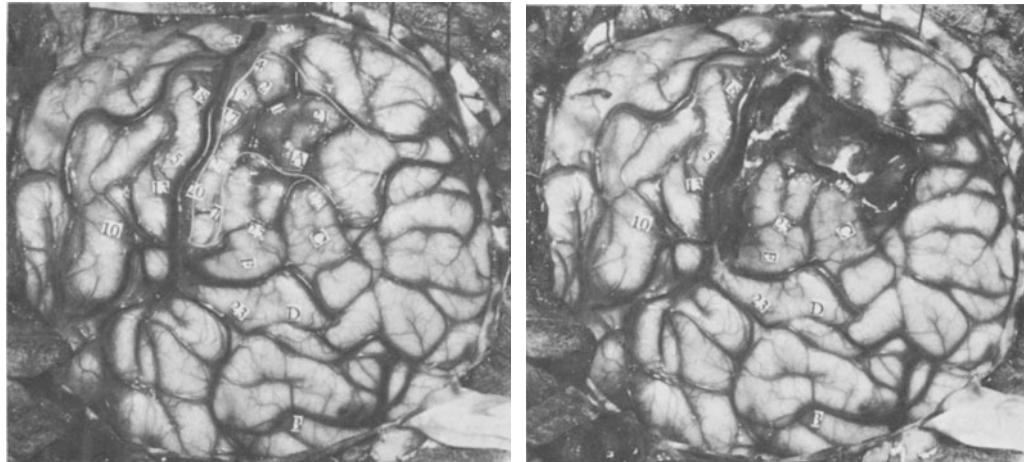


Fig. 3. Pt. C.Av. - Left somatosensori-motor seizures. *Left* slight subpial effusion of blood between points 1 and 21 and letter A from microelectrode recording. *Right* excision of postcentral gyrus and parietal cortex above angular and supramarginal gyri. 10 stopped saying days of the week, lips continued to move. 13, 5, 8, 18, 3 precentral gyrus responses. 7 tingling right leg, second somatosensory response. 20, 24, 17, 12, 2, 4, 14 postcentral gyrus responses. 1, 21, 22 sensory aura reproduced. 25 after-discharge at letter E. Patient did not answer. 23 slowness and hesitation in saying days of week forward

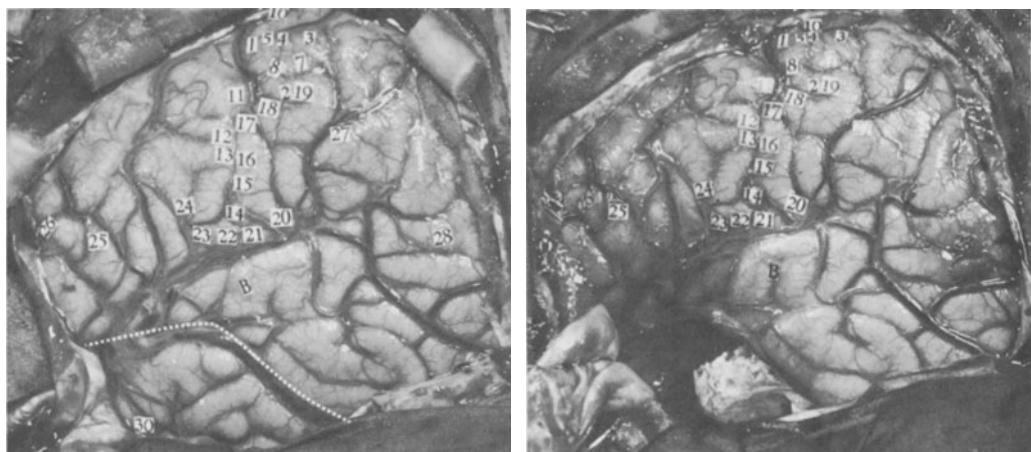


Fig. 4. Pt. C.Hu. - Left temporal lobe seizures. 26 "I know what that is - that is what you put in your shoes". After withdrawal of electrode, he said "foot". 25 Hesitated, then named butterfly. No interference with speech on stimulating adjacent convolutions in front and behind. 24, 23, 22, 21, 13, 12, 11 precentral gyrus responses. 20, 14, 15, 16, 17, 18 postcentral gyrus responses. 27 unable to name tree, said "I know what it is", after electrode was withdrawn, said "tree". 28 unable to name - after withdrawal of electrode he said "Now I can talk, butterfly;. 30 electrographic seizure

posterior aspect of the fissure of Sylvius and the parietotemporal speech zone curves around behind this unusually long first temporal gyrus.

Aphasic speech interference responses have never been elicited from the third temporal convolution either on its lateral or its inferior surface.

3. Parietal speech zone. In the parietal region, speech interference responses are elicited from the parietal opercular convolutions anteriorly up to the post-central sulcus. The superior and posterior boundaries, as determined by electrical stimulation, are more variable than the other speech zone boundaries. Superiorly, the responses extend upward 1 to 4 cm from the level of the Sylvian fissure. The posterior limit of the responsive area ranges from 2 to 4 cm behind the postcentral sulcus but the occasions demanding determination of this boundary occur much less frequently than for the anterior and superior boundaries (Fig. 3). Inferiorly, the parietal speech zone seems to be continuous with the posterior portion of the temporal speech zone, as far as can be determined from the cortical stimulation area.

While positive speech interference responses give valuable evidence that the cortex stimulated is involved in the process of speech, negative stimulation responses of adjacent cortical re-

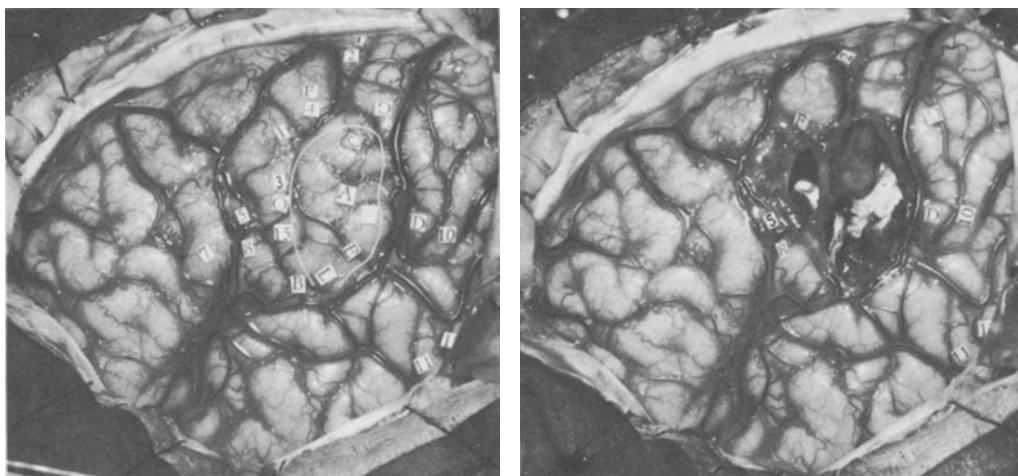


Fig. 5. Pt. J.Al. - Left somatomotor seizures. *Left* Initial cortical excision outlined by white thread. *Right* final excision, removal of face area of pre- and postcentral gyri (point 7 dislodged and lost). 7 hesitation in saying days of the week. 5 counting arrested. 8 saying days of the week arrested, movements of mouth continued. 15, 3, 4, 2, 1 precentral gyrus responses. L, E, N, A, C, G on postcentral gyrus - no responses elicited by stimulation. 10 errors in saying days of week forward and backward. 11 errors in saying days of the week forward. 12 (partly beneath bone edge posteriorly) - many speech errors

gions do not guarantee that these areas are dispensable as far as normal speech is concerned. More accurate information on the boundaries of the cortical speech zones is provided by analyses of the effects of discrete cortical excisions adjacent to the speech areas after the sensorimotor and speech areas have been mapped in appropriate detail by electrical stimulation.

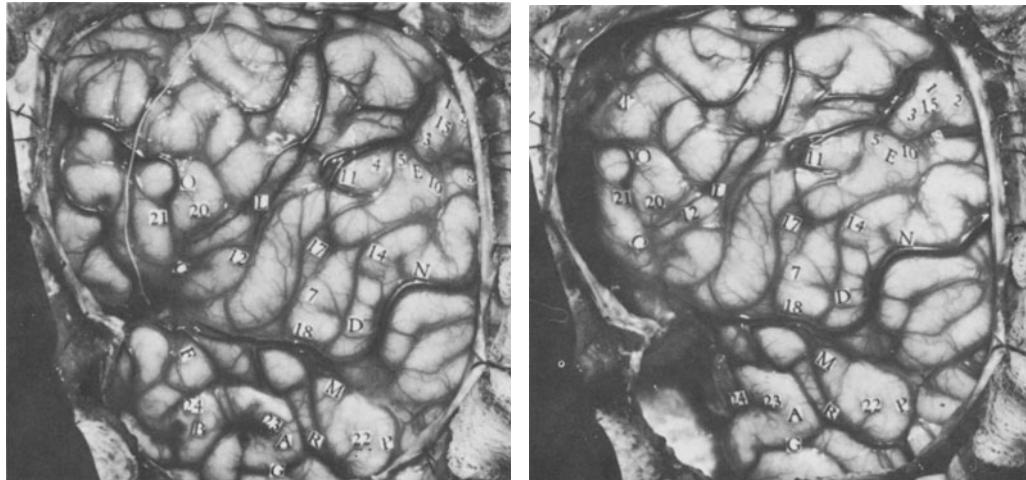


Fig. 6. Pt. R.Tr. - Left frontotemporal seizures. *Left* initial frontal excision outlined by white thread. *Right* anterior frontal and temporal lobectomy. 21 saying days of the week arrested, he then repeated the incomplete sequence - completed the sequence after withdrawal of electrode. 20 counting and saying the days of the week slowed, then stopped. 12 after-discharge at letter L without clinical manifestation. 17, 11, 4, 5, 3, 15, 1, 2 precentral gyrus responses. 18, 7, 14, 10, 8 postcentral gyrus responses. 22, 23 counting and saying the days of the week slowed, then stopped. 24 no speech interference (negative stimulation marked to facilitate determination of maximum safe extent of temporal lobectomy)

Cortical Ablation Studies

A. Frontal Cortical Excisions

In the effort to remove the epileptogenic area of cortex as completely as possible it has frequently been necessary to extend the area of the cortical excision close to the speech and motor areas. Thus, in the treatment of frontal lobe epilepsy it has frequently been necessary to remove the frontal opercular convolutions back to one gyrus in front of the gyrus yielding aphasic speech interference stimulation responses or, more rarely, completely back to this gyrus (Figs. 2 and 6). In addition, the intermediate frontal region has frequently been removed down to the sulcus outlining the toe of the opercular gyrus yielding the speech interference responses. Following any cortical excision in the vicinity of the speech zones there is nearly always a

temporary dysphasia of variable severity during the period of postoperative cerebral edema. In the case of frontal excisions, as long as the two frontal opercular gyri immediately in front of the lower end of the precentral gyrus are untraumatized and their vascularity not compromised, speech returns to normal after the postoperative cerebral edema recedes.

Removing the anterior part of the temporal lobe in addition to the cortex in front of and above Broca's area likewise does not result in persisting dysphasia (Figs. 2 and 6).

Thus, removing the cortex in front of, above and below the two frontal opercular gyri in front of the precentral gyrus (Broca's area) does not result in persisting dysphasia.

B. Central Excisions

Similarly, removal of the convolutions between the frontal and parietal speech zones does not result in persisting dysphasia, whether the postcentral face area, the precentral face area, or the lower portion of both the central gyri are removed (Fig. 5).

Prior to 1964, when it was thought that persistence of epileptiform activity from the surface of the insula might be responsible for continued seizures after temporal lobectomy (15), the cortex of the insula was sometimes removed, more or less completely, after temporal lobectomy, by aspirating the insular cortex from beneath the middle cerebral vessels using a small right angled suction tip. This cortical excision, which doubtless injured or interrupted the underlying capsula externa when carried out in the dominant cerebral hemisphere, likewise did not result in persisting dysphasia unless the rare complication of manipulation hemiplegia occurred (12). This complication, due to traction and manipulation of the middle cerebral arteries and resulting ischemia in the region of the internal capsule, resulted in hemiparesis, dysphasia and sometimes homonymous hemianopsia.

Since this removal of the insula cortex doubtless also interrupts the capsula externa and since removals of the face area of the pre- and postcentral gyri interrupt the cortico-cortical U fibers between the anterior and posterior speech zones, it seems clear that cortico-cortical connections between these areas are not essential in the coordination and integration of the speech mechanisms of these two areas. These integrative processes must therefore be carried out by means of cortical-subcortical pathways. Our data give no clues, however, as to the subcortical region of regions involved in these integrative mechanisms.

C. Temporal Excisions

The temporal lobe of the hemisphere dominant for speech can be removed with confidence back to the level of the Rolandic fissure at the Sylvian fissure without producing persisting dysphasia (Fig. 4). When temporal lobectomy must be carried out under general anesthesia, in children for example, or in adults whose ability to cooperate is questionable, the removal is never carried backward beyond this level. In a large number of dominant hemi-

sphere temporal lobectomies of this magnitude carried out since 1958, there has been no instance of dysphasia persisting after there was complete recovery from the effects of postoperative cerebral edema.

When the patient is alert, cooperative and answering questions promptly and accurately, however, it is often possible to remove the temporal lobe further posteriorly, in stages, if required by the persistence of epileptiform activity in the post-excision cortical EEG after a conservative standard removal has been done. In a considerable number of such patients cortical removals have been carried back to the level of the postcentral sulcus without producing persisting dysphasia. Cortical excision further posteriorly has not been carried out in the dominant hemisphere unless there has been definite evidence of old injury to this posterior temporal region. In a few such patients the temporal lobe of the dominant hemisphere has been removed still more posteriorly, but only with the patient talking constantly and after testing each convolution to be removed by having the patient carry out verbal tasks after a small 2 - 3 mm coagulation had been made on the surface of the gyrus to be removed. This tactic has provided satisfactory safeguards against persisting dysphasia in such patients.

The third temporal gyrus of the dominant hemisphere is clearly not essential for normal speech. We have frequently removed it in dominant hemisphere temporal lobectomies as far back as 8 to 9 cm from the anterior end of the middle fossa, without resulting dysphasia.

As mentioned in the section on electrical stimulation, the first temporal gyrus proper also seems to be relatively unimportant as far as speech is concerned. When this gyrus extends backwards behind the transverse gyri of Heschl as an uninterrupted convolution it can be removed as far back as 9 - 10 cm without producing persisting dysphasia (11). Extensive experience with temporal lobectomy has verified the fact that the first temporal gyrus is not essential for normal speech, but if this gyrus ends in a sulcus at or just behind the transverse gyri of Heschl, the cortex behind this sulcus and just below the fissure of Sylvius is important for speech and must be carefully preserved.

4. Parietal excisions. Our data on the superior and posterior boundaries of the parietal speech zone from parietal cortical excisions are limited because the majority of patients who have had excisions of the convexity of the left parietal lobe have had previous injury to this region and the parieto-temporal speech functions were in the right and not in the left hemisphere. Since the parietal speech area is the largest and apparently the most important of the speech areas, our relatively few dominant parietal lobe excisions have skirted the superior and posterior boundaries of the parietal speech area with a generous margin.

Further comment will be made in the following section, on parietal lobe excisions carried out in patients in whom the carotid Amytal speech test had demonstrated that there were some speech functions in each hemisphere.

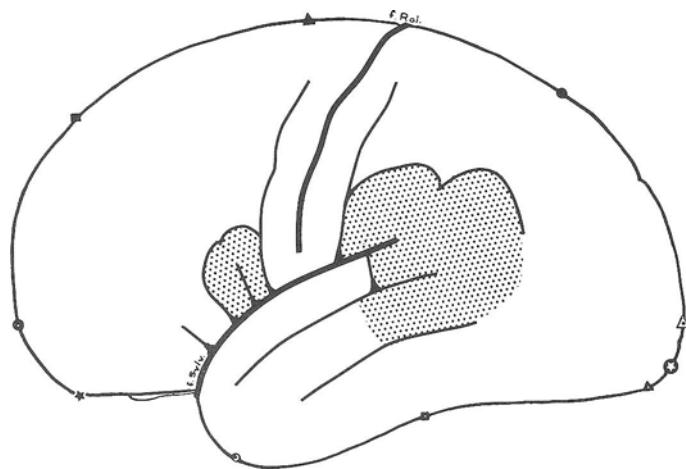


Fig. 7. Primary speech areas of the dominant hemisphere from stimulation and cortical ablation data

These cortical ablation data indicate that the cortical speech zones have relatively sharply defined boundaries, with the parieto-temporal speech area comprising several times as much cortex as the frontal speech area (Fig. 7). The dispensability of the cortex around and between these two speech areas indicates that the coordination and integration of these two areas must be carried out via cortical subcortical pathways rather than through cortico-cortical neuronal mechanisms. Our information as to the subcortical mechanisms and structures involved, however, is minimal.

Intracarotid Amytal Speech Studies

In 1956 Juhn WADA, then a Rockefeller Fellow at the MNI, introduced us to the use of the intracarotid injection of 10% sodium Amytal for the lateralization of cerebral speech functions, a test he had described in the Japanese literature in 1949 (16). During the past 17 years this test has proved to be of great value in enabling us to make maximal removals of epileptogenic cortex with safety in left-handed and ambidextrous patients, and in right handers when lateralization of cerebral speech functions was uncertain for one reason or another (17, 1).

In our present procedure, standardized speech testing including both naming and series repetition tasks and subsequent memory testing is carried out during a 2 - 6 minute period of hemiparesis induced by the injection of 200 mg of 10% sodium Amytal through a catheter placed well up in the internal carotid artery on one side. A 2 cc arteriogram is then done so that the symmetry of the arterial supply to the two cerebral hemispheres can be assessed. The right and left carotid arteries are injected on different

days so as to be certain no lingering generalized Amytal effect from the injection of one hemisphere can interfere with the interpretation of the effects of the injection of the opposite carotid artery.

This test has now been carried out in 371 patients. As in our earlier analyses it has been useful to divide the group into those with some clinical evidence of damage to the left cerebral hemisphere during the early years of life and those without.

In this series of 371 patients there were 262 who had no clinical evidence of early damage to the left cerebral hemisphere (Table 1). The test was carried out in the 140 right handed patients in this

Table 1. Speech lateralization as related to handedness in 262 patients without clinical evidence of early damage to the left cerebral hemisphere

Handedness	No. of cases	Speech representation		
		Left	Bilateral	Right
Right	140	134 96%	0 0%	6 4%
Left or mixed	122	86 70%	18 15%	18 15%

group either because some aspect of the patient's seizure pattern or psychological test profile raised the possibility that all of the patient's cerebral speech representation might *not* be localized to the left hemisphere, or in order to evaluate the risk the temporal lobectomy might produce a significant memory deficit in patients with some evidence of bitemporal damage or dysfunction. All patients not strongly right handed have been grouped together because previous analyses had shown little difference in the speech lateralization in left-handed and in ambidextrous patients (1, 2).

Ninety-six percent of the 140 right-handed patients had speech representation in the left cerebral hemisphere. In 6 (4%) speech representation was in the right hemisphere. None had evidence of bilateral speech representation.

In the 122 non-right handers 70% had speech in the left hemisphere, 18 (15%) had speech in the right hemisphere and another 18 (15%) had definite evidence of some speech function in each hemisphere (3).

In contrast, in those 109 patients who did have some evidence of early damage to the left cerebral hemisphere (Table 2), 23 (30%) of the 78 non-right handers had speech on the left, 40 (51%) had speech on the right and 15 (19%) had bilateral speech representation.

Table 2. Speech lateralization as related to handedness in 109 patients with definite clinical evidence of an early left-hemisphere lesion

Handedness	No. of cases	Speech representation		
		Left	Bilateral	Right
Right	31	25 81%	2 6%	4 13%
Left or mixed	78	23 30%	15 19%	40 51%

There were 31 patients who were right-handed despite evidence of early damage to the left cerebral hemisphere. Speech was on the left in 25 (81%), on the right in 4 (13%) and was bilateral in 2.

It is of interest that the evidence of bilateral speech representation was essentially the same in the non-right handers without evidence of early left hemisphere injury (15%) (Table 1) as in those with early injury to the left hemisphere (19%) (Table 2).

Analysis of the time course and quality of the dysphasia seen in right handers after left hemisphere injection reveals a remarkably constant pattern. Typically, the patient is unable to speak for about 2 minutes but will move the ipsilateral, left, extremities on request and will demonstrate the use of objects he cannot name. This is followed by a period of dysphasia characterized by mistakes in both object naming and series repetition, tasks such as saying the days of the week or the months of the year forward and backward. Speech usually returns to the pre-injection level in about 8 1/2 minutes, about 3 minutes after the hemiparesis has cleared. In these same right handed patients right carotid injection rarely interrupts speech for more than a few seconds and no mistakes in either naming or series repetition are seen.

In the patients with evidence of bilateral speech representation the speech defects were mild from both the right and left sided injection, although the mean duration of contralateral hemiparesis was the same as for the cases classed as unilateral. In a half of these patients with bilateral speech representation, speech was not arrested with either the right or left injection, but clear dysphasic responses were obtained with each. In the other half, in whom speech was temporarily arrested by the injection, the duration of the arrest was significantly shorter than the speech arrest resulting from injection of the dominant hemisphere of patients with unilateral speech representation.

Early in our acquaintance with this interesting group of patients with bilateral speech representation, it became clear that in nearly half of them, there was a qualitative difference in the nature of the dysphasia induced by the injections of the two

Table 3. Quality of dysphasia: Relation of errors of naming (N) to errors of serial order (S) in 40 consecutively tested right-handers with left hemisphere speech representation and 35 patients with bilateral speech representation

Group	No. of cases	N and S associated	N and S dissociated
Right-handers (speech left)	40	34 ^a	0
Bilateral speech cases	35	20	15

^aIn 6 right-handed patients tested early in the series no distinction was made in the record between errors of naming and errors of serial order.

hemispheres (Table 3). Fifteen (43%) of the 35 patients with bilateral speech representation show this dissociation to a greater or lesser degree. In these patients the intracarotid Amytal injection on one hemisphere produced errors of naming with little or no disturbance of verbal tasks of serial ordering such as counting, saying the days of the week, the months of the year, the alphabet, etc. Injection of the opposite hemisphere produced the reverse, errors or difficulty in verbal serial ordering tasks with little or no disturbance of naming.

Patient J. Du., a 15 year old, left-handed girl, provides a particularly striking example of this phenomenon. She was operated upon for seizures arising in the right parietal lobe, present since she was 7 years of age. Her birth was normal and the only abnormal event prior to the onset of seizures was measles at age 1 1/2 years associated with a temperature of 106° but without obvious evidence of any involvement of the central nervous system. Because she was left-handed, the carotid Amytal speech test was carried out to determine the lateralization of her speech mechanisms. When the left internal carotid was injected, she did not stop talking and carried out all serial ordering tasks, saying the days of the week correctly forward and backward, but she misnamed most objects shown to her. When the right internal carotid was injected, the side of the proposed operation, she had a little difficulty in naming the first few objects shown to her, then named all subsequent objects correctly, but she had difficulty in series repetition, for example, saying the days of the week forward and backward, which persisted for 2 minutes after the transient left hemiparesis had cleared up.

At operation, carried out under local anesthesia, it was necessary to remove, in stages, the right parietal parasagittal region, the parietal opercular region and the postcentral gyrus well up into the arm area before the epileptic activity in the cortical EEG disappeared (Fig. 8). Speech was tested constantly during the excision, both naming and serial ordering tasks, and remained unpaired until she was put to sleep for the closure.

Sixteen hours after operation her spontaneous speech seemed normal and she named 15 objects correctly and promptly. She was able to count forward correctly but on counting backwards she mixed up the numbers and mispronounced them.

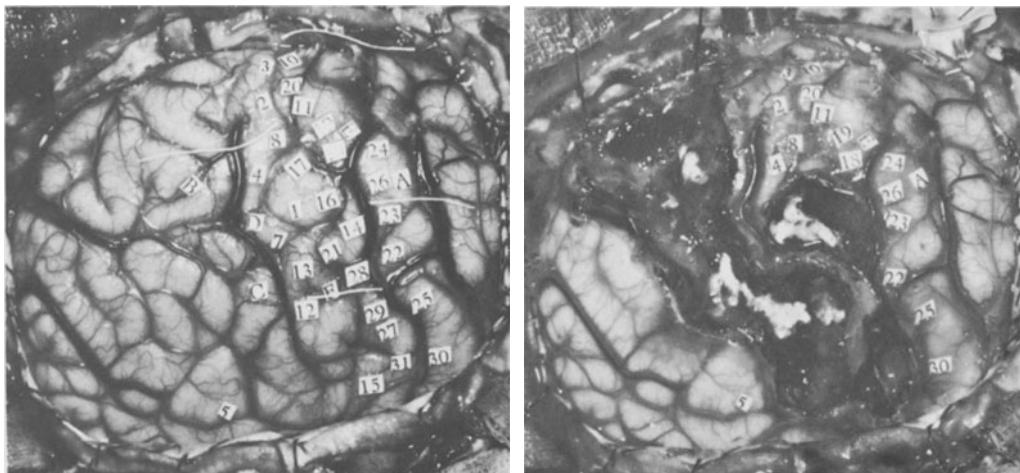


Fig. 8. Pt. J.Du. - Right parietal seizures - bilateral speech representation. 30, 25, 22, 23 precentral gyrus face area responses. 26, 24, 18, 19, 11, 20, 10 precentral gyrus arm area responses. 15, 31, 27, 29 postcentral gyrus face area responses. 28, 21, 13, 14, 16, 1, 17, 4 postcentral gyrus arm area responses. 8, 2 postcentral gyrus trunk area responses. 3 postcentral gyrus leg area response. 5 right, ipsilateral, thumb sensation - second somatosensory area response. 12 left foot sensation - second somatosensory area response

She said the days of the week forward correctly but on trying to say them backward she mixed them up and mispronounced most of them. She was unable to say the months of the year forward and mispronounced the few months she did say. The serial verbal tasks were still more poorly done on the second postoperative day when there was definite weakness of the left arm as well, but she was again able to name all objects shown to her quickly and correctly. The dissociated dysphasic defect continued essentially unchanged for 4 days, then began to lessen progressively. By the 6th day she made only 1 error saying the days of the week backward, and 3 errors saying the months of the year forwards, but was still unable to say them backwards. On the 9th postoperative day she made no errors on saying the days of the week backward or on saying the months of the year forward and was able to say the months of the year backward with only 4 errors. On the 11th day she made no errors on saying the months of the year backward or the alphabet forward, but was completely unable to say the alphabet backward. By the 16th day all gross difficulty with verbal sequences had disappeared but the defect could still be brought out with relatively difficult or unfamiliar tasks. Spelling, which had also been markedly impaired when the sequence defect was prominent, had returned to her preoperative level. Throughout the entire postoperative period naming was normal.

Since the removal of most of the right parieto-temporal speech zone did not result in any interference with speech function at the time of the cortical removal and since the speech difficulty which did develop subsequently was associated with weakness of the left arm and receded with it, it seems highly probable that

this temporary speech disturbance represented the effect of post-operative cerebral edema interfering with the functioning of a frontal opercular speech zone in the right cerebral hemisphere. It seems likely that the other speech functions interfered with by the preoperative left carotid Amytal injection were mediated by the undamaged left parieto-temporal region.

Various right or left sided cortical excisions in these patients with evidence of bilateral speech representation have given support to the carotid Amytal evidence that a division of labor between the two cerebral hemispheres exists in some, but not all, patients with evidence of bilateral speech representation.

Another example is provided by patient S. Sh, a 15 year old left-handed girl who was operated upon for left parietal seizures that had been present since a head injury at 2 1/2 years of age. She had been right-handed up to that time and was acquiring speech at the normal rate. She was tossed into the air in a ship's cabin and struck her head on a light fixture. There was a bleeding laceration of the left parietal region, but no unconsciousness. Early the next day she had a generalized seizure followed by right-sided convulsions which left her hemiplegic and unconscious for two days. Bilateral burr holes showed no abnormal fluid collections. She regained consciousness but remained hemiplegic and speechless for 5 weeks, then improved progressively. Investigation at the MNI 2 years later when she was 4 years of age, and subsequent yearly check-ups because of persistence of occasional attacks, showed only minimal residual evidence of right hemiparesis, a complete right homonymous hemianopsia and speech that was considered normal for her age.

She was finally operated on in 1965 because of increasing severity of her attacks. Carotid Amytal speech tests gave evidence of bilateral speech representation. As in the previous patient, there was dissociation between naming and series repetition, but less marked. Naming was interfered with after both the right and left injections. Series repetition was well done after the left injection, but was badly mixed up after the right.

The entire left cerebral hemisphere behind the level of the postcentral sulcus was removed completely (Fig. 9) except for one small gyrus of the parietal operculum behind the postcentral gyrus which was preserved because of concern it might be serving some speech function, even though stimulation here (point 3) produced only localized after-discharges without interference with speech, as was the case at points 25 and 27 higher up. There was no interference with speech during this removal or during the postoperative period. There was no increase in her minimal slight hemiparesis during the postoperative period either.

The speech difficulty produced by the left carotid Amytal injection, on the side of the operation, must have been due to inactivation of Broca's area, the only remaining speech cortex in this left hemisphere. The speech difficulty produced by the preoperative right carotid injection presumably was due to inactivation of the right parieto-temporal region where the speech functions, which had begun to develop in the ordinary way in the left hemisphere, had developed following the trauma to the left posterior head region at 2 1/2 years of age which had resulted in a complete aphasia that began to regress only after 5 weeks.

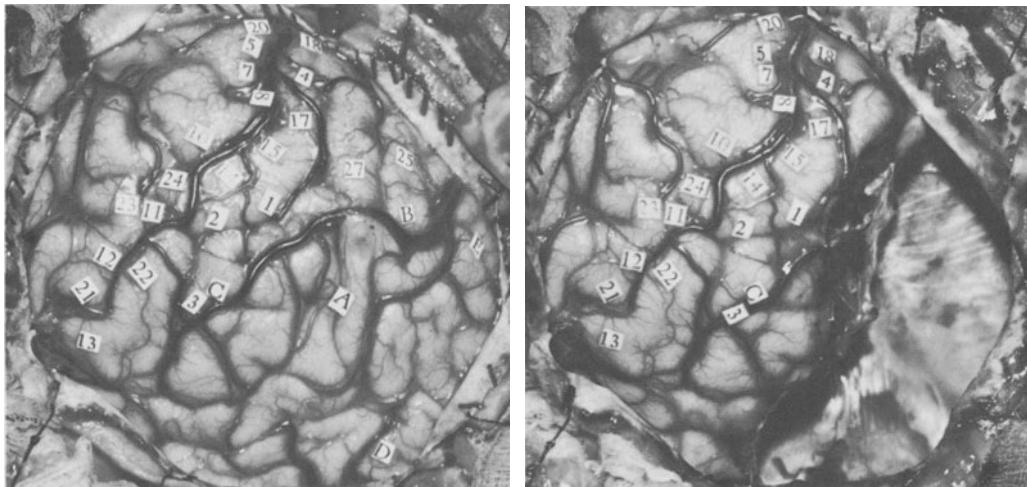


Fig. 9. Pt. S.Sh. - Left parietal seizures - bilateral speech representation. 21, 12, 23, 11, 24, 10, 8, 7, 5, 20 precentral gyrus responses. 13, 22, 2, 1, 14, 15, 17, 4, 18 postcentral gyrus responses. 3, 25, 27 after-discharges

In two-thirds of the 16 patients with bilateral speech representation and evidence of some dissociation between naming and serial repetition tasks, the more marked deficit in the latter followed the right carotid injection and the principal deficit in naming tasks followed the left sided injection. In the remaining one-third, the pattern was reversed.

The findings in these two patients suggest that patients with bilateral speech representation may have the posterior speech area in one cerebral hemisphere and the anterior in the other, in addition to exhibiting a dissociation in naming and series repetition in the speech representations in the two hemispheres.

Our data illustrate the possibility of a qualitative difference in the organization of speech processes in the right and left cerebral hemispheres of some patients with bilateral speech representation. Owing to the fact that all our patients had cerebral seizures, we cannot be sure that such division of labor between the hemispheres is a normal phenomenon in left-handers, but we have hints that this may be so. We have already seen that the incidence of bilateral speech is only slightly higher in the group of left-handers with well documented early lesions of the left hemisphere (Table 2) than in those without evidence of such lesions (Table 1). In addition, 9 of the 15 patients showing a dissociation between errors of naming and errors of serial order (Table 3) belonged to the group without clinical evidence of early left-hemisphere damage (Table 4). It is also noteworthy that this group of 18 left-handers with bilateral speech representation but without early left brain injury included at least 7 patients with familial left-handedness, 3 of whom showed this

Table 4. Quality of dysphasia: Relation of errors of naming (N) to errors of serial order (S) in patients with bilateral speech representation

	No. of cases	N and S associated	N and S dissociated
Bilateral speech cases			
WITH early left brain damage (including 2 right-handers)	17	11	6
WITHOUT early left brain damage	18	9	9

qualitative difference between the effects on speech of left and right carotid Amytal injection, errors of naming being dissociated from errors of serial order.

Summary

These stimulation, ablation, and carotid Amytal test data are crude in relation to the richness, delicacy and precision of human speech, but constitute enormously valuable tools for the neurosurgeon and provide solid and useful guides to help all of us as we grope our way toward better understanding of the way the human brain transmutes commands, ideas, and concepts into speech.

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Discussion

Dr. GLEES: You might have observed in Canada a bilingual patient speaking French and English, where the formation of the second language occurred somewhat later. Did you ever determine whether two different areas for these two languages were coexisting?

Dr. RASMUSSEN: We have had trilingual patients and the speech interference and the dysphasia did not seem to follow any specific pattern. Regardless of the language used, speech was arrested. When the patient was dysphasic, there was no rhyme or reason to which language returns first. Sometimes patients would get one or two words back in each language. Sometimes the first language would come back to a considerable degree before the second language. Sometimes, surprisingly enough, the second language came back first; we have not been able to guess in advance what was going to happen.

Dr. GLEES: Would this be on the side of sensory aphasia too?

Dr. RASMUSSEN: We find it difficult to classify our aphasics in this way because they change from day to day. Our dysphasias may be completely unable to get a word out on the third postoperative day, but on the 8th postoperative day or by the second week their speech is normal. The way in which the speech recovers varies from patient to patient, so that we have rather given up trying to classify them into different categories of dysphasia.

Dr. POECK: When you stimulate at the speech-area you produce, so to speak, negative symptoms. Did you ever observe positive symptoms; for instance, that a patient called a fork a spoon, or was he just unable to call a fork a fork? Did he never produce a semantic paraphasia?

Dr. RASMUSSEN: Yes, I have a couple of examples that I didn't include.

Dr. POECK: A second question: What happens, if you stimulate the corresponding parts of the right side? Do you get interference with speech too?

Dr. RASMUSSEN: Never.

Dr. POECK: Not even with articulation?

Dr. RASMUSSEN: Only if we stimulated the face area of the pre- or postcentral gyrus. There we interfere with speech equally well on the dominant or non-dominant hemispheres, but we never interfere with speech in any way by stimulation in the non-dominant hemisphere of what would be Broca's area in the dominant hemisphere. This is absolutely consistent in many hundred of stimulations, except in the few patients shown by the amyntal speech test to have some bilaterality of speech representation.

Dr. GALBRAITH: In your discussion of speech arrest you mentioned primarily three criteria: one was inability to think of the word, the other was repetition e.g. "that is, that is" and the third was false start in the sentence.

I was struck by the fact that these are precisely the three criteria of GOLDMANN-ELSLER², described in her psycholinguistic research, dealing with non-grammatical pause duration in spontaneous speech. Would you be willing to speculate concerning normal speech?

Dr. RASMUSSEN: It is often been said, that investigating the function of the nervous system by electrical stimulation is somewhat akin to studying the structure of a watch by hitting it with a hammer. So I don't think, that I would have any basis on which to extrapolate the crude effects of our knocking out the function of the speech area with what happens in normal speech. It is, I think, applicable in some sense to disease processes in the speech area, because we are producing a limited lesion by electrical stimulation: limited in extent and in time; I think these stimulation responses have to be looked at as lesions, rather than applying them as indicating this is what happens under normal circumstances.

Dr. GAZZANIGA: What was the dose of amythal used?

² GOLDMAN-ELSLER, F.: Psycholinguistics: experiments in spontaneous speech, pp. 169. London: Academic Press 1968.

Dr. RASMUSSEN: 200 mg. It is important not to go above a 10% solution. In monkeys when we used a 20% solution, in order to reduce the bulk of the injection with the larger doses, we produced microscopic infarction. We never had any histological evidence of a lesion in the monkey study and we never had any complications in what are now over 750 injections in man, as long as we limit ourselves to 10% solutions.

Dr. GAZZANIGA: When you stimulate in a speech arrest zone while the patient is naming objects, do you get an arrest on every naming or in only one-half of the trials?

Dr. RASMUSSEN: That varies on how far we are above threshold, or how quickly we are stimulating. Normally, when stimulating not too often, i.e. once every two minutes, and providing we are at least one or two volts above the threshold, we will produce speech interference with every stimulus. It may be a complete inability to talk with one stimulus or it may produce a jargon or it may produce a misnaming or a perseveration. But I think, this is partly due to the fact that we don't necessarily put the electrode back in exactly the same place or that the resistance of the tissue may change in the area stimulated. In the few fixed electrode studies I have done in Broca's area each stimulus produced arrest of speech.

Dr. CREUTZFELDT: Did you ever try the effect of stimulation, amythal or extirpation on singing?

Dr. RASMUSSEN: No.

Dr. OBRADOR: First question: Where do you put the upper limit of age for the transfer to the other hemisphere in early lesions? Second question: Have you seen any discrepancy between the amytal test and the later removal of speech areas?

Dr. RASMUSSEN: The second is easy to answer: we have never been led astray by the amytal test. The first question is more involved. We have studied five or six patients in whom the following chain of incidences happened: the patient had an injury early in life after developing speech. There was severe speech disturbance afterwards, usually lasting from four to eight weeks. Speech then recovered during the following months. Some years later we had the occasion to do the amytal speech test. Every patient was 5 years older/younger (at the time of injury) in whom there was a transfer of speech function, i.e. who was right-handed and had a lesion of the left cerebral hemisphere with dysphasia afterwards and the amytal test later on showed speech function had returned in the right cerebral hemisphere. When the original brain injury producing the dysphasia occurred after 8 years of age the amytal test has always shown that the speech function is still in the left cerebral hemisphere or, in a few instances, is represented in each cerebral hemisphere.

Excision of Broca's Area without Persistent Aphasia

O. L. Zangwill¹

In 1861, BROCA advanced the view that motor aphasia results from a lesion involving the foot of the third left frontal convolution (ever since known as Broca's area) and viewed by him as the seat of articulate speech. Although the evidence upon which BROCA based his thesis is undeniably suspect, his localization of motor aphasia has stood up pretty well to the test of time and is still widely accepted today.

At the same time, BROCA has not been without his critics. In 1906, MARIE published his celebrated paper bearing the polemical title: *La troisième circonvolution frontale gauche ne joue aucun rôle spécial dans la fonction du langage*. His evidence was based firstly, on the existence of cases of isolated destruction of Broca's area without aphasia and secondly, on the incidence of Broca's aphasia in cases in which absolute integrity of Broca's area had subsequently been demonstrated at necropsy. This evidence was spelled out two years later by MOUTIER (1908), who claimed that out of 108 cases of focal brain lesions with autopsy reported between 1861 and 1906, in only 19 did the facts appear to support BROCA, and in eleven of these the lesion was subcortical. He further referred to 27 cases of destruction of Broca's area without aphasia, in two of which the destruction was bilateral. At the same time, it is only fair to state that DEJERINE (1907) communicated two cases of circumscribed lesion of Broca's area with appreciable aphasia (though in one of these, it is true, there were additional multiple lesions in the right hemisphere).

"Negative" cases, he thought could be explained on the basis of ambidexterity or vicarious function of the area of the right hemisphere homologous to that of BROCA.

In his monumental *Die Lokalisation im Grosshirn* (1914), C. v. MONAKOW concluded that the available facts exclude the theory that lesions strictly confined to Broca's area give rise to complete and chronic aphasia, though he admits that they might produce a temporary aphasia with relatively rapid retrogression. He cited two cases of his own and 16 described by others in which there was initial aphasia but relatively rapid restitution of speech following lesions largely or exclusively confined to Broca's area. In general, MONAKOW had no doubt that the region of the cortex concerned with expressive speech extends appreciably beyond Broca's area to involve a number of related structures, in par-

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ticular, the lentiform nucleus, the insula, and parts of the Rolandic operculum. At the same time, he continued to attach considerable importance to Broca's area, regarding the transitional region between it and the Rolandic operculum (including the deeper subjacent structures) as an "optimal site" for lesions liable to provoke a disorder of speech. He further believed that the incidence of aphasia is more predictable and its remission less rapid in cases of Broca's area lesion than in those with lesions elsewhere in the "motor speech zone".

Since MONAKOW, there have been few systematic reviews of the literature on the localization of motor aphasia but several authors have touched on the issue. METTLER (1949) recalled the work of BURCHHARDT (1891), a pioneer of psychosurgery, who reported two cases of partial or complete excision of Broca's area apparently without aphasia. METTLER himself communicated two cases in which Broca's area ("or at least its major part") had been bilaterally removed "without resulting in the full blown aphasia of verbal, motor or expressive type" which is commonly said to follow its destruction. He also refers to a somewhat similar personal observation by ROBB. JEFFERSON (1949) claimed that his work, as well as that of PENFIELD, had shown that excisions of Broca's area, if care is taken to avoid deep undercuts in the white matter, led at most to nothing more than transient aphasia. PENFIELD himself, in his book written jointly with ROBERTS (1959), refers to one personal case in which removal of Broca's area in a case of tumor (hamartoma) was not followed by persistent aphasia. At the same time, he and his colleagues have never excised Broca's area in cases with a simple atrophic lesion in the treatment of focal epilepsy.

The present writer has recently had an opportunity to study two cases in which Broca's area was either excised or totally undercut at operation and in neither of which was there persistent aphasia. In the first case, the patient, a right-handed man, aged 70, was admitted to hospital on account of personality change, defect of speech and progressive right-sided weakness. Following a gamma scan and left carotid arteriography, surgical exploration was undertaken which disclosed an astrocytoma occupying the whole of the left frontal operculum and extending deeply into the frontal lobe on its inferior surface. The tumor was removed largely in one piece. The surgeon (Mr. J.R.W. GLEAVE) expressed the view that, in this case, there could be no doubt that what is usually defined as Broca's area and all the underlying white matter had been extensively infiltrated with a fairly rapidly growing glioma and that Broca's area had been effectively excised in the course of the operation.

Post-operatively, the patient was mute but speech began to return after 48 hours. Four days post-operatively he was seen by an experienced clinical psychologist (Dr. MOYRA WILLIAMS) who found the patient able to respond to simple commands though his speech consisted largely of stereotyped, automatic utterances with some jargon. Speech improved rapidly over the next week or two, and when first seen by the present writer two weeks after operation, the patient could express himself in a limited way, though with

Table 1. Personal data in two cases with excision or total undercutting of Broca's area

Case	Age	Occupation	Intelligence	Handedness
G.R.	70	Electrical Engineer (retired)	WAIS performance I.Q. 110 Progressive Ma- trices: 50th percentile	Right-handed Both parents and three siblings right-handed
K.W.	37	Refuse Collector	WAIS verbal I.Q. 87 Performance I.Q. 110 Full scale 97	Right-handed Both parents and three siblings right-handed

frequent hesitations and he often left sentences unfinished. On the other hand, jargon had receded almost completely.

Four weeks post-operatively, conversational speech was judged to be almost normal; sentences were well-constructed and the voice well-modulated. There was some difficulty in explaining idioms or proverbs, though some questions were very well answered. For example, when asked to explain the difference between a child and a dwarf, the patient replied: "A child is a normal human being in process of growing up and a dwarf could be a fully matured human being". Specimens of writing and drawing showed nothing abnormal. The patient could name objects and undertake simple calculations. The only deficit that could be reliably ascertained was a certain want of fluency. For example, when the patient was asked to give the names of as many objects falling within a given class as he could think of within one minute, he gave only very few, e.g. the names of nine animals or six flowers. As he himself put it: "I'm just going to think of something and it disappears". Otherwise, speech, writing, and verbal abilities appeared well preserved.

The second patient was a 37-year-old right-handed labourer, who was admitted to hospital on account of increasing severe headache and papilloedema. A left carotid angiogram disclosed a large avascular space occupying lesion in the body of the left frontal lobe. At operation (Mr. J.R.W. GLEAVE), a large cyst subjacent to the middle frontal gyrus was aspirated and a tumor, the main mass of which lay medial to Broca's area, together with the wall of the cyst, was excised. By the end of the procedure, the center of the left frontal lobe, particularly posteriorly, had been removed. Broca's area had been totally undercut though the gyri on the surface remained as a thin covering for the cavity. These gyri seemed totally denuded of commissural or projection fibers.

The patient was mute at first but speech began to return within 24 hours. When first seen by the present writer, two weeks after

operation, the patient named objects correctly and his conversation gave no evidence of dysphasia, though he thought he had had a little difficulty with his speech in the first few days after operation. Explanation of proverbs was somewhat concrete but what he had to say was correctly expressed. He could read and write normally and simple calculations were accurately performed. When asked the difference between a child and a dwarf, the patient replied: "A dwarf is very small and a child is larger. A dwarf is a freak." Fuller psychometric testing revealed a Wechsler Verbal IQ of 87 and a Performance IQ of 110. Some slight difficulty was noticed in defining words and verbal memory tests were performed somewhat indifferently. As in the previous patient, poor performance on verbal fluency tests was very striking.

Table 2. Language status of two patients with excision or total undercutting of Broca's area

Case	Pre-operative	Post-operative		
		Immediate	1 week	4 weeks
G.R.	Gross motor aphasia	Mute at first. Speech began to return af- ter 48 hrs	Expressive speech defect with some paraphasia	Speech al- most normal; some loss on fluency tests
K.W.	No dysphasia or dysarthria recorded	Mute at first. Speech began to return with- in 24 hrs	Mildly dysphasic	Speech nor- mal; some loss on fluency tests

Three months post-operatively, no abnormality could be detected in conversational speech, oral reading or in writing to dictation, and verbal fluency had much improved. The patient's wife had noticed no changes whatsoever in his memory or speech.

The salient features in these two cases are summarised in Tables 1 and 2. The important features to note are: 1. The presence of pre-operative dysphasia in one patient and of post-operative dysphasia in both; 2. The virtually complete recovery of speech in both patients within four weeks; and 3. The lack of any suggestion of left-handedness in either patient or in his family.

In these two cases, it is almost impossible to suppose that the dominant hemisphere for speech was other than the left, as is indeed indicated by the early post-operative dysphasia in both cases and the pre-operative dysphasia in one. Furthermore, the relatively short course of the illness and the rapid restitution of speech in both patients render it highly improbable, to say the least, that the non-dominant hemisphere can have played any significant role in the recovery process. We thus seem obliged to conclude that speech restitution was due to the participation

of those parts of the motor speech system of the left hemisphere which had survived injury.

In a forthcoming study HÉCAEN and CONSOLI (1973) have communicated 12 cases of right-handed patients with acquired lesions of Broca's area. In 5 of these, there was only mild articulatory disorder and/or mild dysprosody, together with a trace of agraphia. In the remaining 7, on the other hand, there was more outspoken language disorder, especially in expressive speech, writing, and calculation, but as a rule also some impairment of comprehension, which might on occasion be persistent. The difference between the two groups, HÉCAEN believes, relates to the depth and extent of lesion as ascertained at operation. In the first, there is reason to believe that the lesion was exclusively cortical; in the second, deeper subjacent structures were involved. He further points out that with deep and extensive Broca area lesions, not only is speech disrupted in its motor aspects but there is a disorganization of all functions of language.

It is perhaps reasonable to conclude that whereas Broca's area undoubtably plays some part in the control of articulate speech - and in denying this MARIE undoubtedly overstated his case - this part seems nothing like as important or as critical as has been traditionally supposed.

A lesion of Broca's area is neither a necessary nor a sufficient condition for the occurrence of aphasia - at all events persistent aphasia - and it seems most improbable that such recovery of speech as occurs in cases such as those described above is due to the vicarious function of the homologous area of the right hemisphere. Although the true role of Broca's area and its subjacent connections remains to be clarified, it may perhaps be said that the awe in which this celebrated part of the brain is traditionally held by neurosurgeons and others is somewhat exaggerated. As JEFFERSON (1949) rightly observed, excision of Broca's area, if care is taken to avoid deep undercuts in the white matter, is unlikely to lead to anything graver than a transient disorder of speech.

I would like to thank J.R.W. GLEAVE, F.R.C.S. for so kindly allowing me to study and communicate the two cases reported here, and Mrs. F.M. HATFIELD for her help in psychological and linguistic assessment. I am also grateful to Professor H. HÉCAEN for permission to cite from his forthcoming paper.

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Discussion

Dr. HÉCAEN: I reviewed my cases of Broca's area lesion and found 19 cases relatively limited to this area. Of these, only two cases had no disturbance in language, but these two cases had congenital lesions. Of the remaining 17 cases, five had very little disturbance of language with only some articulatory or writing disorders. A second group consisted of seven cases with not only articulatory or writing disorder but also very important failures in understanding oral commands or even written commands.

Dr. RASMUSSEN: Was the pre- or postcentral gyrus identified by electrical stimulation in either of these patients? The reason I ask is that slow-growing tumors, like certain astrocytomas, have a great propensity for displacing convolutions and the chain of events in your first patient suggests to me that Broca's area was displaced and interfered with producing dysphasia; then the tumor was removed and the displaced cortex of Broca's area regained its function. Unless the relationship of that part of the cortex to the lower central region was worked out, and unless the surface of the insula was clearly exposed by the removal back to the pre-central gyrus, I think one would have to question whether or not the cortex of Broca's area was actually removed.

Dr. ZANGWILL: I think the answer is in fact no. There has been no routine electrical stimulation. Therefore, one cannot absolutely exclude the possibility which you have suggested.

Neurolinguistic Comments on the Alexias¹

H. Hecaen² and H. Kremin³

The observation that disturbances of spoken speech can be accompanied by disturbances of reading has been known for a long time. It was also recognized very early that reading disturbances could occur independently of expressive aphasic symptoms and even of dysgraphia. CHARCOT has pointed out that as early as 1838 GENDRIN had published findings on patients who were unable to read whatever material was presented to them although they could write (word blindness).

In spite of the earlier descriptions it was as late as 1887 that CHARCOT published the first typical case. DEJERINE had originally been of the opinion that lesions of the angular gyrus lead to global disturbances of written language. In 1892 he published the first anatomical clinical case of pure alexia, i.e. alexia without agraphia except for the inability to copy, and he presented a systematic description of different clinical types of reading disturbances and their anatomical and pathophysiological basis. For DEJERINE pure alexia was a special type of aphasia, while PIERRE MARIE considered pure alexia as a variant of agnosia.

In the following period many papers on reading disturbances were published. In spite of certain theoretical discrepancies there is enough agreement on the anatomico-clinical relations to suggest the following classification of alexias: 1. alexia as a symptom of Wernicke-aphasia (posterior temporal lesion); 2. alexia plus agraphia (lesion of the angular gyrus); 3. pure alexia, for certain authors agnosic alexia (occipital or callosal lesion).

Recently the research in split brain patients (SPERRY, GAZZANIGA) and the anatomical clinical studies by GESCHWIND have again supported WERNICKE'S opinion that pure alexia is a disconnection syndrome due to a callosal lesion.

The impact of linguistics can be recognized in the studies on alexia by MARSHALL and NEWCOMBE (1966, 1971), by WEIGL and BIER-

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WISCH (1970) and by our group (HECAEN, 1967; F. DUBOIS-CHARLIER, 1971).

These studies have supported the classical distinction between verbal and literal alexia. The neurolinguistic analysis, however, leads to the recognition that this distinction reflects structurally different forms of alexia and not only variations of intensity, as suggested by the classical authors. These structurally different types indicate an impairment of the rules of transcoding at different levels, phono-graphematic, morpho-graphematic and syntactic-semantic, the disturbance of which can occur relatively isolated. MARSHALL and NEWCOMBE (1966) have described a case of alexia where the reading errors were clustered as a function of the grammatical category, the semantic paralexias occurring mainly in nouns, and the visual paralexias occurring in adjectives and verbs.

MARSHALL and NEWCOMBE (1971) has described a taxonomic analysis of the reading errors in some patients where the alexic component was predominant in the neuropsychological syndrome. They distinguish three varieties of reading disturbance:

- a) a visual dyslexia, where the paralexic errors consist of confusion of letters or words which are graphematically similar; these errors may also occur predominantly at the end of a word;
- b) a "surface"-dyslexia where the paralexia stem from a partial impairment in the grapheme-phoneme translation and from a disruption in the morphemic structure of the word;
- c) a "deep" dyslexia (syntactic-semantic) where the paralexias are of the semantic type.

WEIGL and BIERWISCH (1970) assume two aspects of the comprehension of written words: the identification of the graphemic structure and the actualization of their meaning, the latter being sometimes impaired in isolation. For the processes underlying comprehension they postulate different steps:

- a) at first there should be the identification of the graphemic pattern "below" the semantic and syntactic level and its storage in short time memory;
- b) the result of this first analysis would be the internal generation of the item to be understood, by means of the information which is stored in the lexicon. The analysis of two cases of alexia led these authors to the consideration that the disturbance derives from a deficit in the subliminal identification of the items where the distinction between lexical and grammatical morphemes is effected; the reading disturbance would be due to a displacement either mainly in the same grammatical class or mainly in a given semantic field. The paralexia would thus be due to an erroneous matching of the result stored after the first analysis and the item generated internally.

H. HECAEN (1967) analyzed his observations of reading disturbance and he confirmed the classical distinction between alexia in WERNICKE'S aphasia, the syndrome of alexia plus agraphia, and

finally pure alexia. Furthermore, the analysis of the observation of pure alexia permitted support of the view that verbal and literal alexia do not reflect different degrees of intensity of the same disturbance and that we are entitled to consider these as two structurally different varieties.

On the basis of this retrospective analysis, F. DUBOIS-CHARLIER (1971) has performed a systematic neurolinguistic analysis of 14 patients where the reading disturbance was a predominant feature of the neuropsychological syndrome. The aetiology of the cortical lesions was variable. The locus of lesion in those cases which were verified surgically was either the temporal, parietal or occipital lobe, with predominance of the parieto-occipital transition. The essential characteristic was that the lesions was located in the posterior part of the left hemisphere in all of the subjects.

The analysis of reading performances revealed three aspects of dyslexia, each of which was represented by a typical case without disturbance of oral language; around these typical cases were grouped some observations which were less clear-cut. The author distinguished:

1. Literal alexia. The common feature is that reading of letters is more impaired than reading of words. The letter read by the patient has no phonemic or graphemic resemblance with the stimulus. When these patients were reading words, they exhibited a strategy of global reading: the patient tended to guess the general meaning of the item. He did not try to read each syllable by itself, consequently there was complete failure in the reading of logatomes and good performance in the reading of mutilated words. In this variety there appeared semantic paralexias and an asymmetric relationship between impaired verbalization and relatively intact comprehension of words and sentences.
2. Verbal alexia. The reading of letters was not very much impaired. The reading of words was achieved by a strategy of analytic deciphering. A characteristic feature was the contrast between this often erroneous spelling and the preservation of reading of isolated letters. The poor performance in the reading of mutilated words and of compound nouns was explained by this strategy of deciphering, where the word is not perceived as a whole but as a group of letters. There was no dissociation between the verbalization and the comprehension of the written material. The failure was very marked in execution of complex written commands and reading a text.
3. Alexia of sentences. The defect is particularly marked in the reading of sentences and texts, the reading of letters and words, in contrast, is very little impaired. As far as sentences are concerned, a certain ability to read is preserved, characterized by paralexias, repetitions, and augmentations. The execution of written commands and the comprehension of texts are very much impaired.

The battery of tests used for these 14 cases with the predominant feature of dyslexia permitted not only the analysis of performance on the different linguistic levels (letter, word, sentence) but it also permitted the definition, for each of the items, of the role of meaning, so that performances where the disturbance was dependent on erroneous denomination (reading) could be differentiated from a disturbance of recognition. The frequency of the words was taken into consideration as well as their length. We have slightly modified this battery for a more specific study of these different factors. These tests were given to 41 right-handed patients with left hemispheric brain lesion. The left-sided hemispheric lesion was the only criterion for selection of cases. Among these 41 patients there were three with pure alexia.

The battery consisted of 30 sub-tests also to be considered as 12 test groups plus three language tests: naming, acoustic comprehension of words, writing on dictation, and copying.

The results of these tests were submitted to a principal component analysis, at first on all 33 tests, and subsequently on the 15 test groups into which they had been formed "*a priori*" (see appendix). The coherence of these regroupings had been established by correlation.

We have tried to regroup the tests by calculating PEARSON'S product moment correlations as an index of their homogeneity (the hierarchical method proceeds by "average linkage").

When we studied the correlations between the results of the patients on these 15 homogeneous test groups we found that the recognition of meaningful words (2) and of sentences (5) and the reading (naming) of meaningful words (9) and of sentences (10) had among themselves a very elevated "r" ($r > 0.9$) while there could be isolated on the one hand the reading of letters (8), of numbers (6), and the recognition of meaningless syllables (3,4) and on the other hand the reading of meaningless syllables (12) and of numbers (7), the disturbances of writing (15), and the recognition of letters (1).

Furthermore we have demonstrated a correlation between reading, recognition of meaningful material, and comprehension of written material (11). Oral comprehension (14) remains an isolated phenomenon.

The analysis of the correlations between the 15 variables of the homogeneous test groups seems to indicate clearly a group of tests which have in common the aspect of meaning (semantic) (test no. 2, 5, 9, 10, 11) representing the score of the reading disturbance following left hemispheric lesions. A further distinction could be made between one the one hand, certain simple operations deprived of semantic content (3, 4, 6, 8) and on the other, a group of more complex operations connecting the reading of numbers and meaningless words with disturbances of writing and the recognition of letters.

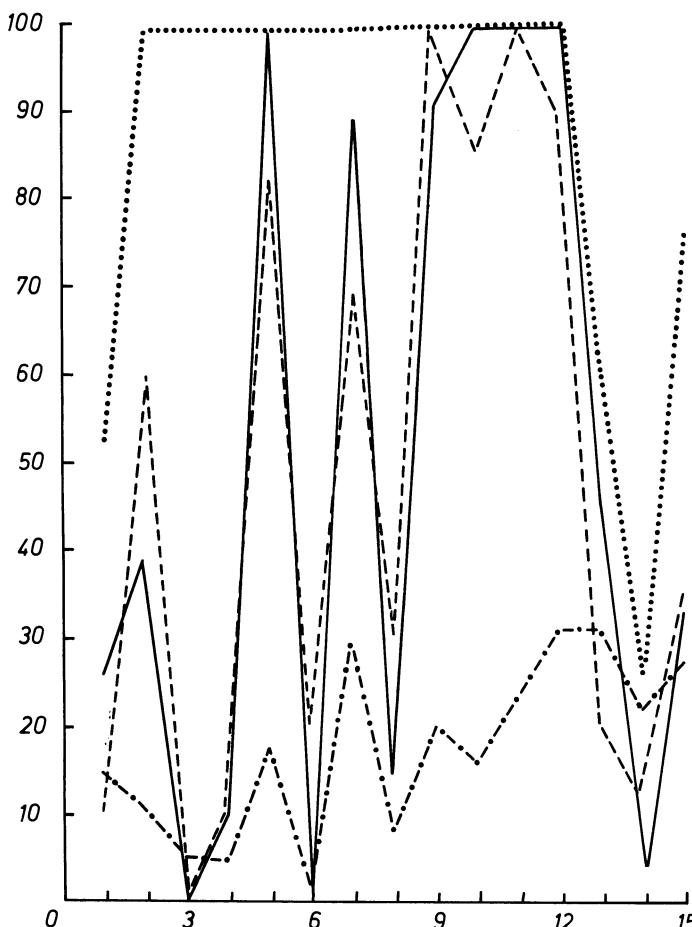


Fig. 1. Profile of performances in the complimentary tests. ----- mean of 38 cases. CLI, - - - SAL, — DEL cases of pure alexia

A second aspect of the analysis aimed at the recognition of certain clusters of patients among the 41 cases. We have found a group of 5 patients very similar to the three cases of pure alexia. These five patients had certain features in common: very severe disturbance of acoustic comprehension of words with preservation of auditory phonemic discrimination, clear deficit of verbal naming, and disturbance of writing; two cases also had disturbance of copying, calculia, and visual field defect. In 3 of these cases there was an impairment in the handling of colors (evocation, pointing, naming). In the 4 verified cases there was a temporal lesion: posterior temporal in 3 cases, and temporo-occipital in one case.

Figure 1 illustrates the mean performances of the 38 cases with left hemispheric lesions and disturbance of oral language and separately shows the profiles of 3 cases of pure alexia. Two of these, SAL. and DEL., appear to be distinguished from the mean profile only by the intensity of the deficit. In case CLI, how-

ever, the recognition of meaningless syllables (3, 4), of meaningful words (2), and of letters (1) is very deficient, as is also the reading of letters (8) and isolated numbers (6), while all the other patients had satisfactory scores in these two tests.

It can also be seen that the intensity of the deficit in the reading of meaningful words (9), nonsense syllables (11), and of sentences (10) as well as the comprehension of written material (11) is such as to warrant the assumption that the differences are qualitative in nature.

This preliminary analysis, which of course calls for further statistical and qualitative evaluation, permits

1. the isolation of cases of pure alexia in a population of patients with reading impairment and disturbances of oral language,
2. the recognition of a certain typology of pure alexias and the recognition of the resemblance to these pure alexias of some cases of alexia (very posterior temporal lesions, including or not including the occipital lobe) which cannot be classified as *pure* alexia because of a concomitant impairment in oral language.

Appendix

The tests applied consisted of the following tasks:

1. Reading of 20 capital letters, presented separately.
2. Recognition of a letter (lower and upper case) in a group of 10 letters (lower case, capitals, bold type, italics).
3. Recognition with the eyes closed of the shape of a letter palpated in the hand.
4. Tactile recognition with the eyes closed of a letter written on the palm of the left hand.
5. Tactile recognition with the eyes closed of a letter written on the palm of the right hand.
6. Recognition of Roman letters in a group of characters foreign to the patient.
7. Recognition, in the middle of a word, of a given letter (transition from upper to lower case, from cursive to printed letters; the letters were chosen for their feature similarity, or for being silent letters or for their position in the word).
8. Distinction between letter and number in a group of letters and numbers.
9. Reading of 50 words chosen according to the following parameters: number of letters (2 to 15), grammatical category, frequency.
10. Reading of 10 nonsense words.
11. Reading of 5 mutilated words.
12. Reading of 6 compound nouns.
13. Reading of 10 words, 8 of which contained a graphic error.
14. Recognition of a given syllable within a word.
15. Reading of digits.
16. Reading of numbers.

17. Recognition, in a list of 5 words (4 Hungarian and 1 French) the French word; vice versa in a list of 5 words (4 French and 1 Hungarian) recognition of the word which was not French.
18. Indicating a picture corresponding to a given word in a multiple choice set of 4 pictures corresponding to semantically and phonemically similar words.
19. Recognition of the outsider in a list of 5 words, 4 of which belonged to the same semantic field.
20. Recognition of a given nonsense word in a list of 5 nonsense words.
21. Grouping of homophonic words among 10 one syllable words presented at random (and eliminating those one syllable words which did not belong to any series).
22. 23. Reading aloud of 10 agrammatical or asemantic sentences, indicating the errors.
24. Execution of simple orders (verb and nominal object phrase).
25. Recognition in a group of 2 sentences of the one describing a picture presented simultaneously.
26. Execution of semi-complex orders.
27. Execution of complex orders.
28. Recognition of the meaning of road signs.
29. Reading a text aloud.
30. Comprehension of a text read by the patient.

The variables of the combined tests are:

1. Recognition of letters.
2. Recognition of meaningful words.
- 3 and 4. Recognition of non-meaningful words.
5. Recognition of sentences.
6. Reading of digits.
7. Reading of numbers.
8. Reading of letters.
9. Reading of meaningful words.
10. Reading of sentences.
11. Comprehension of written material.
12. Reading of non-meaningful words.
13. Naming.
14. Oral comprehension.
15. Writing (on dictation, copying, spelling).

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Discussion

Dr. POECK: You have demonstrated and you have given some references in the literature that show some cases exist which do not fit with the Geschwind hypothesis. But nonetheless there are these cases with the - as we would call it - Déjérine syndrome, i.e. right hemianopia, deficient color naming, and alexia. Here you can demonstrate that the patients have a disconnection syndrome by having them perform cross modal matching within the right hemisphere. If you present a visual stimulus (a letter or an object) only to the right occipital area, the patients can retrieve the model of that letter or object with the left hand without visual control. That is: if you create a cross modal matching situation, you can demonstrate that the elaboration of visual stimuli within the right hemisphere is preserved whereas the transfer to the left hemisphere (required for naming) is lost. Certainly, these patients fit well into Geschwind's hypothesis.

Dr. HECAEN: I agree, but I have said I cannot explain each case by Geschwind's hypothesis.

Traumatic Dyslexia: Localization and Linguistics

F. Newcombe¹ and J. C. Marshall²

The concept of localization of function has undergone several transformations since the last century, when centers for different aspects of language function were confidently described (e.g. LICHTHEIM, 1885; CHARCOT, 1889). The limitations of the "diagram makers" were aptly diagnosed by FREUD (1953) who emphasized the need to study the "functional states of the apparatus of speech". A more flexible approach, explicit in the writings of HUGHLINGS JACKSON (1932), and the work of scientists such as FOERSTER (1936) envisaged different functional levels of organization; and within this framework, localization was related to deficit and implied that "a special area has a definite significance for the appearance of a definite symptom complex" (GOLDSTEIN, 1946).

Rare but well-documented clinical case studies have clearly supported this interpretation of the concept of localization - unequivocally so in the case of dyslexia. DÉJÉRINE'S study (1892) of a patient who had pure word-blindness without agraphia after a cerebrovascular accident remains one of the most elegant demonstrations. The patient initially had a right hemiachromatopsia and then a persistent right homonymous hemianopia. He was unable to read words or musical symbols although spontaneous speech and understanding of spoken speech were intact; he could write to dictation but not read what he had written. His intellectual abilities were otherwise well preserved: he was able to invest money, sing new operatic arias, and orientate himself in unfamiliar surroundings. Some four years later, he had a second stroke which resulted in aphasia, including word-finding difficulties, jargon speech, and dysgraphia. The postmortem, reported by DÉJÉRINE and studied in detail by the neuropathologist, VIALET (1893), showed the first lesion consisting of atrophic yellow plaques in the lingual gyrus, the fusiform gyrus, the cuneus, and the occipital pole as well as in the splenium of the corpus callosum. There was pronounced atrophy of the optic radiations. The recent lesion showed destruction in the area of the inferior parietal lobe and the angular gyrus. The purity of the initial reading defect in this patient and the clear-cut anatomical findings make the case uniquely important. There is little doubt that such pure, modality-specific cases of word-blindness exist; and subsequently both HOLMES (1950) and GESCHWIND (1962) have described patients who could not read visually presented letters or words but were able to decode the same information traced on their hand.

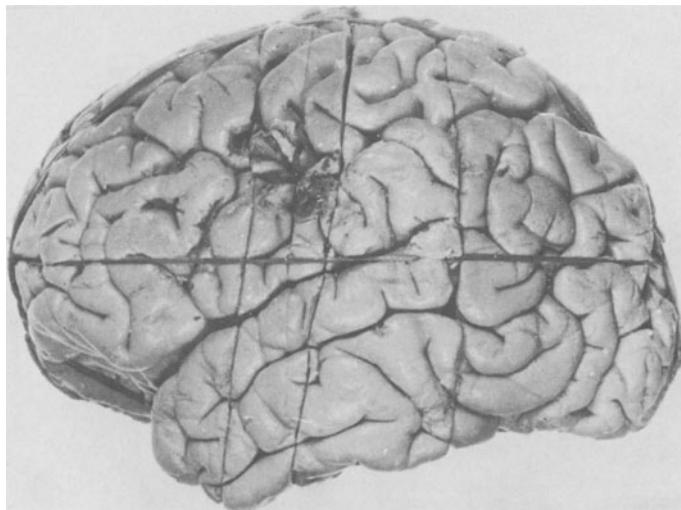
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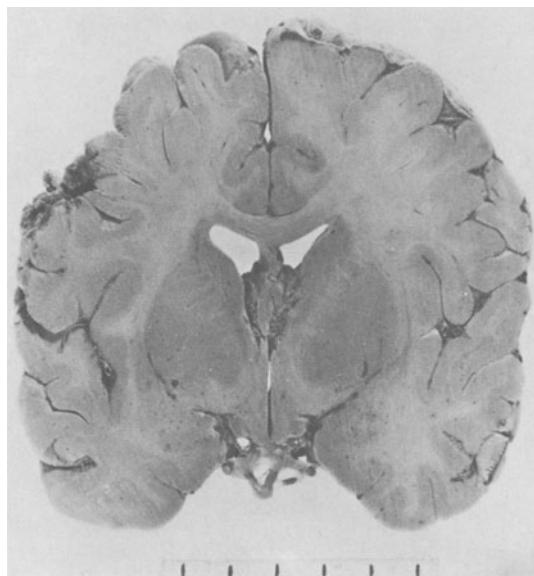
We have seen visual dyslexia in a 58-year-old man, with a butterfly glioblastoma of the corpus callosum and a right hemianopia, who could write and spell orally the words he could not read. But in this case, amnesia and visual impairment were also salient features of the disease. The symptom of alexia without agraphia has been reported by GLONING, GLONING and HOFF (1968) in 27 (3.8%) of their 708 patients with verified lesions of the cerebral hemispheres: and the lesions in the dyslexic group involved the white matter of the fusiform and the lingual gyrus and parts of the splenium of the corpus callosum. Dyslexia, however, is frequently associated with dysgraphia; and both reading and writing may be disproportionately severe in relation to other impairments of language. BROWN and SIMONSON (1957) noted this pattern of disability in thirteen of their hundred dysphasic patients while CASEY and ETTLINGER (1960) cite four such cases (11.4%) among their 35 dysphasic patients drawn from an unselected sample of seven hundred neurological cases.

Dysphasia and dyslexia, attributable to chronic missile injury, are of particular interest in this context since the lesion is usually focal, the pattern of disability is stable, and the age of the subjects and the nature of the lesions are comparable. The value of these cases for the study of cerebral organization has been convincingly demonstrated (POPPELREUTER, 1917; TEUBER et al., 1960); and there has been at least one consistent attempt to link a refined functional analysis of language breakdown to the underlying pathology (LURIA, 1970). Missile injury in the healthy brains of young adults usually causes an extensive fracture of the inner table with clot and bone fragments lying in a cone-shaped track which may reach a depth of a few centimetres, or extend to the ventricle. The injury "resembles closely the effects of experimental excision of an area of cortex and the underlying white matter (RUSSELL, 1947)". Postmortem studies of pensioners who subsequently died from other causes show the focal nature of these lesions. A typical case is illustrated in Fig. 1 which shows a lateral view of the brain at postmortem and the lesion in a coronal section.

Aphasia as an initial symptom has been reported in either one quarter (CONRAD, 1954; WALKER and JABLON, 1961) or one third (LURIA, 1970; RUSSELL and ESPIR, 1961) of large samples of men with missile injury; and the higher incidence in the latter two samples is probably related to the timing and the type of psychological investigation that was carried out. Alexia, as an isolated or predominant symptom is rare: POPPELREUTER (1917) cites eight cases by name and KLEIST (1934) three patients but the latter author mentioned that two of his three cases of visual agnosia were also word-blind. Among the UK series of men who incurred penetrating missile injury to the brain (during World War II) at least half of the men who were dysphasic during the acute, post-traumatic phase also had reading difficulties. RUSSELL and ESPIR (1961 - Chapter XIII) cited eleven men in whom dyslexia was a prominent symptom. The lesions of these men cluster in the region of the angular gyrus (RUSSELL and ESPIR, 1961); and the entry sites, illustrated in Fig. 2, have been geometrical-



a



b

Fig. 1a and b. Missile injury of the brain: appearance of the brain at post-mortem

ly transposed³ from radiographs to a standard representation of the brain (TALAIRACH and SZIKLA, 1967).

³ This technique has been described elsewhere (RUSSELL and ESPIR, 1961; RATCLIFF and NEWCOMBE, 1973).

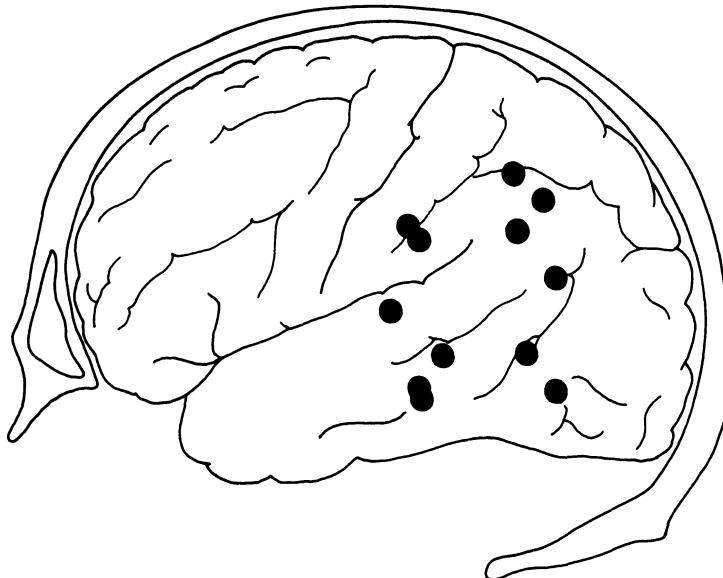


Fig. 2. Left hemisphere missile wounds resulting in dyslexia. (Black circles mark the entry site)

Recovery from dysphasia occurs in about one-third of the missile-injury group within the first year of injury (WALKER and JABLON, 1961; LURIA, 1970); and by eight years more than half of one of the large dysphasic groups had recovered (WALKER and JABLON, *ibid*). The pattern of recovery from dysphasia and dyslexia was not plotted in detail for any of these series but a characteristic report from the men we examined subsequently was of rapid improvement during the first few weeks after injury and then a slower rate of progress for the next year or two. Occasionally - in the case of severe injuries - improvement was said to have taken place for an even longer period. Brief case histories of two of the eleven men with disproportionately severe reading difficulties are presented below.

Case W.G. (no. 630) was wounded on February 12, 1945 at the age of 26, when a bullet penetrated the left temporo-parietal area to lodge in the right parietal lobe. On examination he had a slight nominal dysphasia but could talk and obey commands. A visual field defect was noted but there was no sensory-motor impairment. At operation, 70 hrs after injury, bone fragments and necrotic brain were removed from the track that was followed to a depth of at least six cm and that traversed the left ventricle. A week later, the significant findings on neurological examination were a right hemianopia, left middle ear deafness, dysphasia, and dyslexia. He spoke "rationally but haltingly ... in short phrases", and had nominal difficulties. He clearly identified objects but could not name any digit or any letter of the alphabet although he could match some upper and lower case letters. Three weeks after injury, he could "name objects well and carry out commands" but was still unable to read although he could recognise a few letters. On March 21, it was noted that he could name most of the upper-case letters but made numerous errors when attempting to read words (e.g. SUP → sur; BUNK → bark)

although he could spell fairly well (e.g. newspaper and overhead) and write short sentences (e.g. "the weather is sunny": "there are 42 people in this ward"). By July 4, he was able to read words aloud "accurately but very slowly". Visual acuity was J2 in both eyes. The permanent field defect was described as "an excellent example of segmental defect of the horizontal meridian of the visual field, due to penetration of the intermediate part of the visual radiation by the metallic foreign body."

The pensioner started work as a hatter in October 1945 and in September 1946, he wrote: "I can see quite clearly anything a far distance away, but I am unable to read for more than a few minutes at a time without my eyes watering. It takes me a very long time to read a letter, and especially small print the words seem to run together and more often than not I read the same line twice I can't seem to concentrate on the words". Subsequent reports echoed these difficulties and in 1953, he reported: "I still cannot concentrate enough to read much more than a few lines, which usually amounts to bits in the newspaper". When last seen in 1970, he could read aloud accurately but slowly, and his silent reading rate was about three times slower than that of other pensioners with no dyslexic symptoms. In contrast, scores in tests of vocabulary, verbal fluency, object-naming, and verbal memory were normal. Visual acuity (corrected) was 6/6 for both left and right eye.

Case A.S. (no. 112) was wounded on July 16, 1944 at the age of 26, in the left temporal region. Six hours after wounding, he was "conscious and rational", but had "a marked nominal dysphasia". "Spontaneous speech appears normal and comprehension was but a little impaired." He had "severe dyslexia, with so much distortion of words as to be quite unintelligible ... he tries to read the letters separately and gets that wrong". He had a right homonymous hemianopia to confrontation and a minimal right lower facial weakness. Tone, power, and coordination were normal in the limbs and no sensory loss was detected. At operation, 37 hrs after injury, the bone defect was enlarged to 2 cm in diameter, 20 cc of subdural clot were sucked out of the dural defect, followed by 5 cc of pulped brain. 20 small bone chips were removed but not the metal fragment which, according to X-ray, had been driven in backwards and inwards to a depth of 5 cm. He made an uneventful recovery and his reading improved steadily. He was examined on August 24 and found to have above average scores in tests of vocabulary and block design but the dyslexia was described as "marked". By September 28, he read rapidly from test type but said that his eyes were "easily tired". On perimetric examination, he had a right inferior quadrantic defect which has persisted. There were no other positive neurological signs. He started work as a storekeeper in an engineering firm in December 1944 and in October 1945 reported that he was "rather slow in reading". He had a few fits with unconsciousness of which the last occurred in 1946; but in 1949 he reported: "I have had no fits since I last sent in a report to you but on occasions I have exceptionally strong dizzy turns, and my eyes are more 'blurred' than ever and I find I cannot make head or tail of any reading matter." When he was last seen in 1969, he obtained at least average scores in a wide range of tasks including vocabulary, spelling, fluency, object naming, and verbal learning. He read aloud in a somewhat hesitant fashion, making a few errors (DISTINGUISHABLE → distinguished; PEEPING → popping) and omitting the plural 's', but the difficulty was barely detectable. His letters are unremarkable, but he has to "stop and think about writing". Visual acuity (corrected) was 6/9 for the right eye, and 6/24 for the left eye.

The critical importance of the zone of the angular gyrus and its underlying white matter for reading has been amply demonstrated in clinical literature. MARIE and FOIX (1917), despite MARIE'S reputation as a critic of localization, reported alexia as the salient defect of lesions of the angular gyrus and posterior temporal lobe. He was satisfied that lesions due to missile injury could be more accurately localized than those resulting from cerebrovascular accident or atrophy and admitted that the ensuing damage to zones of functional importance could cause remarkably discrete symptoms of language disturbance: "ces foyers ont à leur tour, par conséquence, des syndromes par déficit souvent remarquablement délimités et fixes ..."

It is clear from the study of the UK series of war pensioners that reading difficulties were related to site and not size of lesion within the left hemisphere. Small but eloquent lesions in the mid temporo-parietal zone occasionally caused a permanent and extensive disruption of language functions including reading (RUSSELL and ESPIR, 1961). In contrast, large anterior, bilateral lesions did not cause dyslexia, even in the acute stage, and even if other aspects of speech or verbal memory were permanently affected. A difference in the anatomical substrate associated with central aphasia as compared with the peripheral dysphasias in which reading is disproportionately affected, has also been noted in other large groups of patients of differing aetiology. A reclassification of BROWN and SIMONSON'S cases, combining groups I and II and then groups III and IV, to give a comparison of the effects of anterior and posterior lesions shows a clear difference ($\chi^2 = 9.17$, $p < 0.01$), with a significantly larger number of cases of severe dyslexia in the posterior group; and these authors comment that reading defects are often associated with small lesions involving the posterior temporo-parietal or anterior occipital region.

The nature of reading impairment will depend to some extent on the structure of the written language as can be seen in the comparison of Chinese idiographic and Japanese phonological script (ASAYAMA, 1914; LYMAN et al., 1938), and in studies of the specific features of the German (WEIGL and BIERWISCH, 1970) and Ndebele languages (TRAILL, 1970). Also, the nature and extent of the reading disability may be influenced by the practice and skill of the reader and the method whereby he was taught to read (BASTIAN, 1898; ELDER, 1900; POPPELREUTER, 1917). It is nevertheless possible to distinguish categories of error, recurring in a wide spectrum of languages; and it is our submission that the structural nature of these errors provides one of the most important constraints on theories of reading impairment, and may contribute to an understanding of the reading process.

Our experiments have been restricted so far to a study of individual word reading; and the long-term aim is to specify in linguistic terms the nature of the impairment, to work towards a taxonomy of errors and thereby a schema of the reading process, and finally to relate these findings to the underlying pathology. Our present schema is exploratory and we anticipate that it will need to be extensively revised before it begins to encompass the subtleties of the problem.

Our recent investigation was mainly confined to those few men who still showed marked dyslexic symptoms, a quarter of a century and more after injury. These cases were drawn from a sample of over three hundred pensioners who have recently been examined in the Department of Neurology at Oxford. The pattern of the investigation has been described elsewhere (NEWCOMBE, 1969) and the reading tests have been designed to examine variables such as letter length, word frequency, and syntax. One such list consists of 60 items: 20 nouns, verbs, and adjectives matched for letter length and word frequency. A second list consists of 40 three-letter words, twenty nouns, and twenty verbs; and additional material has been designed for the study of related words of different parts of speech (e.g. base lexical items and "derived" or "related" words, cf. beg → beggar; high → height). Preliminary accounts of this work (MARSHALL et al., 1970; MARSHALL and NEWCOMBE, 1973) suggested that our dyslexic patients showed different error patterns; and these patterns can also be discerned in patients with acute pathology (abscess, tumor, or closed head injury). The errors in word-reading can be classified as visual (MEDDLE → middle)⁴ as errors in translation from grapheme to phoneme (RID → ride) or as semantic substitutions (CANARY → parrot). More examples of such errors are shown in Table 1. The contrasting patterns of three dyslexic subjects are illustrated schematically in Fig. 3.

Table 1

Visual	Grapheme- Phoneme	Semantic	Neologism	
nap → map	of → off	angel → sacrifice	gin → gin	gin
rid → rig	rob → robe	speak → talk	sound → shound	ſaund
lop → lap	phase → face	berry → grapes	monarch → monarutch	monarʌtʃ
paw → pew	boil → bowl	nephew → cousin	island → izland	izlænd
hit → his	guest → just	cheer → laugh	omit → ommitt	ɔmit

Case AT (no. 464) showed a preponderance of visual errors. Syntax and letter length were not significant variables. He virtually never produced a neologism, or a derivational error.

⁴ The stimulus word in this and succeeding examples is shown in upper-case script, and the response-error in lower-case script, for ease of presentation. In the experiments, however, all stimulus words were shown individually on cards, in lower-case script.

EFFECTS		ERRORS			
frequency	syntax	visual	grapheme-phoneme	semantic	(neologism)
A.T.	X	✓	?	X	X
J.C.	?	?	✓	X	✓
G.R.	✓	✓	?	✓	X

Fig. 3. Patterns of word-reading errors in three dyslexic subjects

Case JC (no. 922) produced a number of neologisms in misinterpreting the sound of the graphemes, often testing out alternative pronunciations of the word (e.g. ROUTE → rote ... rut ... the ... rout). Digraphs were particularly difficult for him. He made fewer errors with nouns than with verbs and adjectives.

Case GR (no. 6) showed an even more striking effect of syntax (see MARSHALL and NEWCOMBE, 1966): many more nouns were read correctly than verbs and adjectives, concrete nouns were easier than abstract nouns and there was a bias to give noun responses when the stimuli were drawn from other parts of speech. The effect of word frequency was marked. There was also a consistent tendency to misread an adjective nominal as its root adjective (e.g. HEIGHT → high) but to read a root verb as its related nominal (e.g. SING → singer). The linguistic interpretation of these errors is being explored (MARSHALL and NEWCOMBE, 1973; WHITAKER, 1972); but we suggest that the errors may result from syntactic bias and inaccurate visual information. No function words or determinants (e.g. "and" "of" "which") were read whereas the other two men had no difficulty in reading them. GR rarely produced neologisms, and could never read a nonsense syllable or neologism.

Brief case histories of these three men⁵ may be of interest in relation to the nature of the injury and the type of reading disability; and schematic representations of their injuries are shown in Fig. 4. These are based on tracings of skull defects, bone fragments, and metal fragments, transposed by the scaling procedure previously mentioned to a standard representation of the brain (TALAIRACH and SZIKLA, 1967).

Case A.T. (no. 464) was wounded on June 30, 1944 at the age of 23. There was a small perforating wound just to the left of the midline in the occipital region a little above the inion. X-ray of the skull showed a bony defect 3 - 4 cm below the lambda measuring 1.5 × 1.2 cm with a compact mass of bone fragments that had been driven in to a depth of 4 - 5 cm. There was no metal foreign body. The wound was debrided within 48 hrs of injury, 3 bone

⁵ All three men were fully right handed and there was no family history of sinistrality.

chips were removed from the superficial 2 cm of brain track and 1 large fragment, about 1.5 cm in diameter, was removed at a depth of about 3 cm. There was no probing for further chips and the wound was drained and the scalp closed in two layers. Examination showed a right hemiplegia, and a visual field defect which could not be tested at that time. The hemiplegia was attributed to a possible intracerebral clot as well as subarachnoid bleeding. For the first fortnight, he spoke little, occasionally answering questions, but did not cooperate in sensory testing; and it was "impossible to say whether or not he could see".⁶ Three weeks after injury he reported a "stutter". By that time, he could see, recognize and name objects and their colors. He could read letters but missed some when spelling long words (e.g. OFFICIAL → offcal). Visual fields, tested to confrontation, showed loss of the lower quadrants including the macula with preservation of the upper quadrants, more to the left than right. There was spasticity of the right limbs and impairment of sensation to light touch and pinprick. Follow-up examination 25 years later showed a spastic hemiparesis, positive finger flexion, and mild sensory impairment to pinprick and light touch. Visual acuity, corrected, was J6 in both eyes; and perimetry showed a complete inferior field defect while the upper quadrants were constricted and incongruous (almost certainly due to his inability to maintain fixation). He still had marked difficulty with reading, writing, and spelling, despite a good vocabulary and fluent though slightly slurred speech. Despite the severe visual field defect his performance in tests of visual recognition (metric and Attneave figures), visual closure (Mooney Faces) and visually guided maze-learning was normal. He worked full-time, from discharge until retirement, including a job as a messenger for a civilian Ministry which he held for over twenty years. He also managed to keep house and look after a wife severely disabled by multiple sclerosis.

Case J.C. (no. 922) was wounded and taken prisoner on February 26, 1945 at the age of 20, when he was found to have a wound 4 cm long and 1 1/2 cm wide behind the left ear. He had a right hemiparesis, more marked in the arm than leg, and dysphasia. At operation two days later, the wound was debrided and the lower parietal and posterior temporal lobes were found to be shattered. Three weeks after injury, he was able to answer questions. He was transferred to the UK in April, 1945 when he was found to have a large herniation in the left parietal region. He was dysphasic, deaf in the left ear and had lost all power in the right arm. He had repeated lumbar punctures to withdraw CSF and the wound was then "excised and slightly undermined". X-ray then showed "extensive bone removal from the left side of the calvarium, mainly left parietal bone but including portions of the left temporal squama and opening into the mastoid cells widely. The defect measured 11 cm × 7 cm. Anteriorly it extended to the coronal suture and its upper margin was 5 cm from the mid-line. Posteriorly, it extended at one point to the left arm of the lambdoid suture. There were no intracranial MFB's or driven bone fragments but two or three small loose bone fragments were seen at the lower margin of the defect where it opened into the mastoid cells. A 5 mm MFB lay in the scalp over the left parietal bone near the vertex. The encephalogram showed dilation of the left ventricle in the region of the atrium and occipital horn. The right ventricle

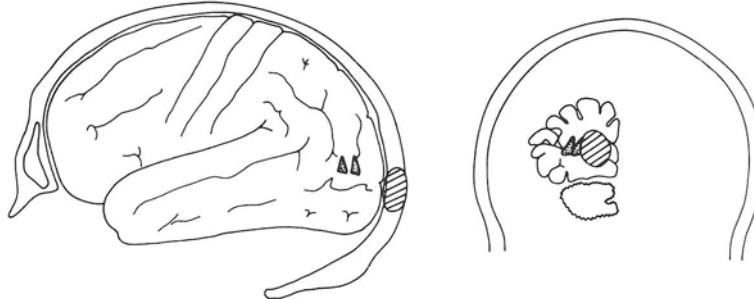
⁶His subjective account was that he was initially "blind", then saw colours, probably red first (cf. POPPELREUTER'S patients) and then shapes. It was easier to identify objects at a distance; and one of his first visual memories was of seeing a mass of green and realizing that it was the grass in the hospital grounds. His vision gradually improved during a period of three to four months, after which no change could be detected.

and the third ventricle were normal. By August 1945 he was said to have recovered from the injury but had a right homonymous hemianopia, spasticity and weakness of the right arm, "a slight speech difficulty", and dyslexia. On examination in 1950, he was found to have a hemianopia, with poor localization in the left visual field, a deaf left ear, very slight weakness of the right upper limb, and impairment of postural sense in this limb without loss of two-point discrimination. Stereognosis was good. His principle disability was dyslexia and dysgraphia with "very little disorder of spoken speech". He had no difficulty in object-naming but had occasional word-finding difficulties, especially when nervous. When examined 24 years after injury, the neurological signs were unchanged. Visual acuity (corrected) was J4 in the right eye, and J6 in the left. Reading, writing, and spelling were severely impaired, digit span was reduced, and he had difficulty in learning paired associate words. In contrast, scores in tests of vocabulary and story recall were within the normal range and his spontaneous speech was remarkably fluent. He was working as a skilled electrician and had in fact been proposed as a Trade Union representative, because of his effective use of language, but could not hold the position because of his inability to read and write.

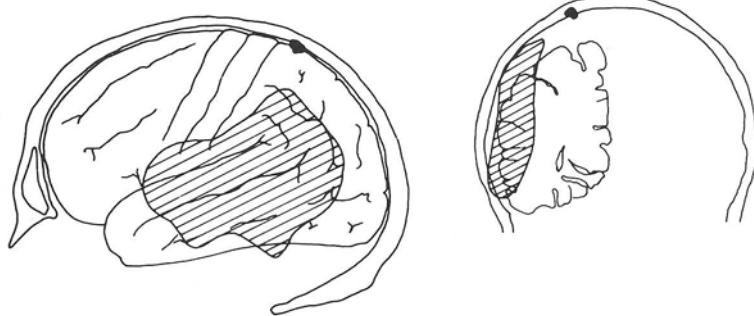
Case G.R. (no. 6) had a severe, accidental injury on June 17, 1944 at the age of 18. A bullet from his own sten-gun entered the brain in the left temporal region, "ploughing up the left temporal and parietal cortex and the vessels of the Sylvian fissure". The patient had a complete right hemiplegia and was in semi-coma. At operation the same day, the ventricle was tapped and the wound excised. "All the scalp tissues were extremely bruised. The bone was shattered in many places; there was a large dural tear about 6 cm in diameter in connection with the exit wound and another tear about 4 cm diameter in connection with the entry wound, and between the two a bridge of intact dura about 3 cm wide". A linear excision was made from the site of the exit wound at the left parietal eminence down to the front of the left auricle. A large fragment of skull was removed, and clot, pulped brain and bone chips were sucked out. There was much bleeding from torn cortical vessels. Ten days later he understood very little of what was said to him and did not speak, but six weeks after injury, he was using two grunts with different inflections to indicate 'yes' and 'no'. He could respond to simple commands and print his name with his left hand. To confrontation he had a right homonymous hemianopia, possibly sparing the macula. There was a severe, flaccid right hemiplegia and complete loss of position sense in the fingers but he could appreciate pinprick and light touch. The neurological findings were to remain substantially the same except that perimetry (November, 1952) subsequently showed a right upper quadrantanopia while in the right lower quadrant only moving objects were detected. Expressive speech improved during the first year to the extent that he could convey the gist of what he wanted to say in telegraphic form and understood most of the questions put to him. Remedial training for reading and writing attempted during the early phase and again in 1952 were not considered successful. He has been examined at yearly intervals during the past decade and no significant changes have been observed in the neurological signs and dysphasic symptoms. He shows a right anosmia, right mild facial weakness of upper motor neurone type, and a profound right spastic hemiplegia with the arm more affected than the leg. Since his injury, he has had infrequent grand mal seizures. Despite the disturbance of expressive speech and the severe dyslexia and dysgraphia, he has obtained average scores in non-verbal standard intelligence tests (Progressive Matrices and WAIS Performance Scale) and high scores in tests of pattern recognition (visual, non-verbal recurring figures, KIMURA, 1963) and visually-guided stylus-maze learning. Visual acuity (uncorrected) is unimpaired. For the first decade after his injury, he occasionally managed

to find casual jobs (e.g. as a nightwatchman) but the combination of disabilities proved too severe and during the last five years he has lived in a Military Home for the Disabled.

A.T.



J.C.



G.R.

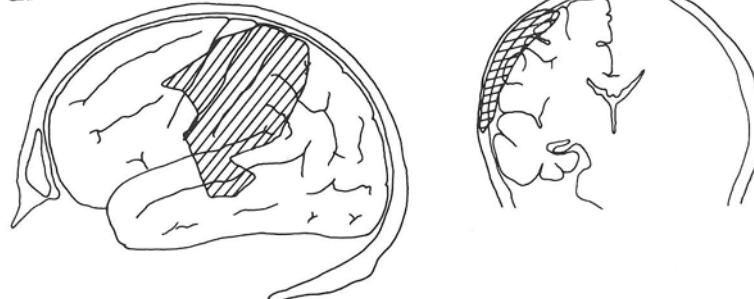


Fig. 4. Schematic representation of missile injury resulting in dyslexia.
Key: Missile fragment ■ Bone fragment □ Skull defect ●

We note that Case AT, who produced mainly visual errors, had a posterior lesion, involving the occipito-parietal region of the brain. In this context, it is of interest that POPPELREUTER (1917), in his authoritative study of war pensioners with oc-

cipital-lobe damage, reported that more visual than phonetic errors were made (cf. MANFRASS who read PAPPE → as 'papier'). At the same time, he clearly demonstrated that these errors did not necessarily stem from visual field defects: other patients with hemianopias and macular defects were able to read. KLEIST (1934) confirmed the latter observation and noted that war injuries were more likely to produce what he called cortical dyslexia. It is clear nevertheless from KLEIST'S summaries that his cases did not show restricted dyslexic difficulties but were impaired in other aspects of language function. The dyslexia, however, was considered to be disproportionately severe; the lesions were on the border of the angular gyrus, and several of the reported errors were undoubtedly visual (e.g. VOR → war; FEIN → sein; HEIM → heil).

Grapheme - phoneme errors, of the type shown by JC, have more recently been investigated from a linguistic standpoint (LURIA, 1970; ALAJOUANINE et al., 1960; DUBOIS-CHARLIER, 1971). Such errors are often associated with ambiguous consonants (e.g. "c" or "g") where pronunciation is dependent on the graphemic context (cf. "gin" and "gun"), silent graphemic consonants (e.g. ride), vowel.digraphs and consonant clusters; and they often occur with stress-shift changes (BEGIN → béggin). Not surprisingly, these partial failures of grapheme-phoneme conversion lead to neologism although these neologisms are "rule-governed", in the sense that they respect the combinatorial possibilities of the English phonological system (HOLMES, 1973). Our case JC who showed a preponderance of such errors had a large lesion in the temporo-parietal region and a second case of the same type reported elsewhere (case ST, MARSHALL and NEWCOMBE, 1973) also had a temporo-parietal injury.

Semantic errors, or the substitution of a word from the same "sphere of meaning" ("Bedeutungssphäre" - BERINGER and STEIN, 1930), are comparatively rare in reading but a familiar phenomenon in spontaneous speech. HUGHINGS JACKSON (1930) suggested that the patient who makes such errors in speech (e.g. COUGH MEDICINE → worm powder) is reverting to an earlier level of organization. Semantic errors in reading have been reported in a small number of cases (LOTMAR, 1933; GOLDSTEIN, 1948; FRANZ, 1930; LHERMITTE et al., 1967; LURIA, 1970; WEIGL and BIERWISCH, 1970; DUBOIS-CHARLIER, 1971; ALAJOUANINE et al., 1960). BERINGER and STEIN'S (1930) detailed analysis of a single case of relatively pure dyslexia is of particular interest in this context. These authors give clear examples of the phenomenon. Their patient read FOX as hare, commenting "when I read it, there first occurred to me 'animal', then it seemed to be 'hare', then 'hens', then hen." However, her reading performance improved "astonishingly" if she was given indications as to the sense of the word. For example, she was puzzled by the word 'sixteen', unable to recognize either the word or the letters, but read it at once when told it was a number; and, when asked to read out names of animals or musical instruments from a mixed list of 15 words, could do so although previously unable to read these words when presented in isolation.

Our patient has produced semantic errors consistently over the past 10 years. He is not necessarily aware of the errors and understands that the task is to read a single word-item not associate to it. This case has already been reported in some detail (MARSHALL and NEWCOMBE, 1966) and the errors are unequivocal (e.g. AFTERNOON → tonight; BELT → strap; FINGER → hand; LITTLE → short; MAD → wild; POOR → cheap; MASTER → pupil; ROB → crooks). This patient differs from our two other cases reported above in that he has a marked, central disturbance of language, with tele-grammatic speech, a moderate nominal defect and difficulty in understanding complex grammatical utterances. Moreover, he has a deep and severe injury incurred at close-range, compared with the majority of pensioners who were injured at long-range. The left occipital lobe, however, was not directly damaged, as far as can be ascertained. It is therefore of interest that visual errors did not predominate and that this pensioner obtained a significantly high score in a pattern recognition task. In many respects, he resembles patients with sensory dysphasia and temporal-lobe damage described by LURIA (1970) who may recognize the meaning of a word (VOLGA → a large body of water ... a river) although not be able to produce it, and who cannot read nonsense words and syllables because "there are no meaningful ideograms to assist" (*ibid.*, p. 352).

We were then led to ask what light these patterns of error shed on the reading process. Our patient who reads CANARY as "parrot" (as KLEIST'S patient, HUFER, made the same error in naming pictures) implies direct access to a semantic library, but difficulty in retrieving the correct address. Our assumption is that the patient who read ISLAND as "izlaend" has processed the stimulus visually, has no direct access to the semantics but searches for the word via its grapheme-phoneme structure; whereas the patient who reads POET as post has used partial or incorrect visual information. Accordingly, we propose a tentative schema (Fig. 5) of the reading process to account for these different types of error. This schema accommodates the possibility of "pure" visual dyslexia without dysphasia, i.e. no difficulty in associating

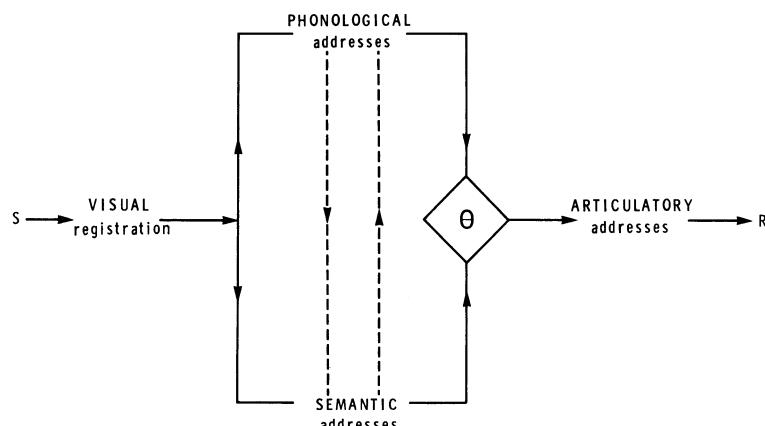


Fig. 5. Schema of the reading process

phonological and/or semantic addresses with letters and words presented in other than the visual modality (e.g. auditorily or tactually), and no other indication of language disturbance. It also provides for the possibility that different stages of the reading process may have been disconnected or partially disrupted. We note the difference between clear-cut disconnection of the type described by DÉJÉRINE (1892), HINSELWOOD (1900), and GE-SCHWIND (1962), a partial disconnection with poor transmission (BERLIN, cited by HINSELWOOD, 1900) and impairment or instability in the various stages (visual, phonological, or semantic) of processing reading material. The critical sites for disconnection syndromes have been reviewed by GREENBLATT (1973) who has recently reported a case of alexia without agraphia and without hemianopia, associated with a left occipital glioblastoma. In this particular case, the left optic radiation and calcarine cortex were intact, connections between the right visual field and the primary visual cortex in the left hemisphere had some connections with the dorsal occipital association areas. GREENBLATT has suggested, therefore, that the critical site of the lesion provoking dyslexia in this particular case was the ventro-medial aspect of the dominant occipital lobe and the splenium of the corpus callosum.

Errors of grapheme-phoneme translation, and semantic errors have in our experience been associated with more severe and permanent dysphasic symptoms; and we note the association with temporo-parietal lesions. But postmortem data are lacking.

Our taxonomy has been concerned with errors in word-reading. A corollary approach is to examine the difference between the reading of letters, words, and sentences. This approach, pioneered by HINSELWOOD (1900) and POPPELREUTER (1917), has been subjected to detailed experimental investigation by HÉCAEN and his colleagues (see HÉCAEN, 1967). In our experience of chronic missile-injury cases, however, it is extremely rare to discover "letter-without word-blindness" and, in fact, GR is the only case showing a trend in that direction: he can name only 10 - 12 letters of the alphabet, but reads many words of which he cannot name the letters individually. HINSELWOOD considered that such patients had learned to read words idiosyncratically; and it may be that they can subsequently use such imagery despite letter-blindness (RICHARDSON, in preparation).

A study of individual word-reading is necessarily circumscribed, although this very fact allows for considerable experimental control over the linguistic variables. It does not, however, take into account differences between the reading of single words and the reading of narrative; and it does not consider the further problem of deciphering handwriting. Impairment of the latter skill may be the final residual symptom of dyslexic difficulties; and we have noted it in an intelligent 22-year-old man some three months after surgical excision of small ruptured angioma which had filled from the left posterior cerebral artery and drained into the left transverse sinus.

Our attempts to establish a taxonomy are based on the notion that different types of error not only elucidate the reading process

but have implications for rehabilitation and retraining. We suggest, however, that these analyses of error must be related to an understanding of the processes of remission and spontaneous recovery. With these considerations in mind, we have studied, over a period of two years, the partial recovery of reading in a patient whose dyslexia was one of the main sequelae of a large abscess in the left cerebral hemisphere (cf. a preliminary account in NEWCOMBE and MARSHALL, 1973). The changing error pattern over time and indeed the continued improvement over time suggest not only a physiological recovery from the secondary consequences of the lesion but relearning. The decrease in errors in reading our 60 word (N.V.Adj.) list, over a period of 127 weeks, is shown in Fig. 6. There is clearly no evidence to suggest whether this

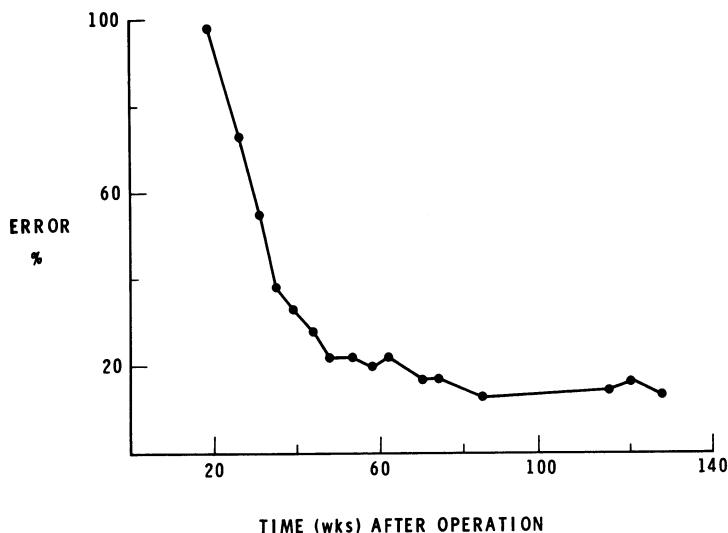


Fig. 6. Spontaneous improvement in word-reading after surgical treatment of a left posterior cerebral abscess

relearning has involved "new" areas of brain. But repeated exposure to words, including a percentage which can be correctly read, may facilitate the process of generalization of grapheme-phoneme rules and other regularities of the lexicon. Longitudinal studies of the error pattern may assist rational programmes for remedial training.

Finally, our concept of localization assumed specialization of function within the left hemisphere for the various functional systems involved in language. Their interdependence is unquestioned; and while "pure" cases of dyslexia or other selective disturbances of language function undoubtedly exist, they are rare because the lesions provoking dysphasia are often extensive. We recall KINNIER WILSON'S (1926) approach to the problem in a neglected but illuminating monograph on aphasia. He spoke of a

physiological "centre", which "indicates the focus of activity of the particular system concerned, and does not of necessity correspond exactly with its anatomical correlate: a 'process' is not localisable in the same sense as a morphological unit". LICHTHEIM (1885) also was well aware of "the restricted foundations on which we may safely build, and what a space theoretical reasoning has still to occupy in the discussion"; and he justified the proper use of diagrams: "we must not recoil from the consequences deducible from our hypothesis. In proportion as we draw these conclusions, we shall obtain the necessary data whereby to correct, or if need be to abandon them." Within such a flexible conceptual framework, it should be possible to elaborate and test schemata of the reading process, which will accommodate those "pure" and critical cases that undoubtedly exist, be firmly linked to physiological findings, and also carry significant implications for the remedial prognosis.

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Discussion

Dr. HÉCAEN: Did you find a patient with semantic aphasia, but with recognition of letters?

Dr. NEWCOMBE: Yes, but he had very poor letter recognition; he could name about half of the letters of the alphabet.

Dr. HÉCAEN: Have you studied writing performances?

Dr. NEWCOMBE: With this man? Yes, but not in such detail. It was very similar but his writing was much worse than his reading. He made semantic confusions when asked to write individual words to dictation. (e.g. COUSIN → nephil (i.e. "nephew"); DANGER → warnet (i.e. "warning"); STAR → moon; CAKE → bun).

Dr. RASMUSSEN: Do you have any comments on the rate of recovery in these various types of dyslexia? Are there some types that tend to recover more quickly and more easily or are they heterogeneous?

Dr. NEWCOMBE: Our impression is that the semantic aphasics have a rather poor prognosis, perhaps because they tend to have severe, deep lesions in the temporo-parietal region; and they have visual and phonological problems in reading as well. Our few cases of semantic dyslexia also have a moderately severe dysphasia, more

than twenty years after injury; and recovery of language functions has been limited. In contrast, our first case - the man with the occipito-parietal injury - was virtually blind in the first weeks after injury, but was reading as well as he does now, some eighteen months after injury.

VI. General Discussion

Localization of Normal Function

Moderator: T. Rasmussen

Dr. RASMUSSEN: Let me say immediately that this discussion raises a number of semantic problems, which are difficult to solve; however, stating the problems will clarify the air. The first problem is to define the borders of this discussion; the term "cerebral" may mean different things to different people; moreover, we have not talked in our papers about the localization of functions of the cerebellum and the brainstem and, finally, it may be said that it is illusory to discuss localization of function without considering the "final common pathway". What is localization, its nature, and extent? What are its implications? What is its role in the various levels of the CNS and the final common pathway?

We shall probably not be considering other localized control of functions, for instance, that of the pituitary hormones or the localization of consciousness, but rather concentrating on the motor system.

Dr. ZÜLCH: There was perhaps some misunderstanding by the formulation of the title of this symposium. Actually we did not want to restrict our discussion only to "cerebral" localization. However, this term seemed the best and shortest translation of the German "Lokalisationslehre", which has no restrictive meaning.

Dr. MEYERS: Perhaps we should start out by considering the localization of function within the corpus callosum and anterior commissure and by relating these facts to the known connections of these tracts. Studies of localization of function within the forebrain commissures are particularly instructive inasmuch as specific portions or even the entirety of these tracks may be destroyed in animals without interfering with the sensory processing or the mnemonic functions of either the one or the other of the two hemispheres.

Our own studies using cats, monkeys, and chimpanzees, have provided straightforward and unequivocal answers to these questions of localization of function. First, a strict localization of function does exist. For example, the splenium and the anterior commissure, either acting together or separately, can mediate the transfer of visual pattern discrimination learning between the eyes in chiasma-sectioned monkeys or chimpanzees (1). At the same time, other regions including the genu, the rostrum, or the entire body region of the corpus callosum even when taken together are incapable of mediating any degree of training transfer. That the splenium is involved in transmitting visual information is easy to understand inasmuch as this bundle of fibers

interconnects those specific regions of the occipital lobes of the two hemispheres which receive commissural fibers, i.e. the various portions of area 18 (7). In addition, it should not come as a surprise that the anterior commissure can also transmit visual information since this fiber bundle interconnects areas 20 and 21 of the temporal lobes. These same areas of cortex (areas 20 and 21) also receive heavy projections from areas 18 and 19 of the ipsilateral occipital lobe and represent cortical regions which themselves have been shown, through lesion work, to be involved in visual learning and memory.

Studies with the intermanual transfer of tactful discrimination learning have shown that tactful information is transmitted through the posterior body region of the corpus callosum in the rhesus monkey (3, 5) again, other commissural regions including the splenium, the anterior commissure, and extensive portions of the anterior corpus callosum are unable to sustain any transfer of tactful learning and, thus, do not support tactful information transmissions. Studies have also been carried out with chimpanzees on the transfer of learned motor skills between the hands, i.e. in latch-box solving can the chimpanzee perform with one hand what he has learned with the other? These studies have indicated that either or both the anterior and the posterior portions of the body region of the corpus callosum can mediate the transfer of such motor skills (2, 6, 8). These results differ from those which were obtained in working with the purely sensory, tactful discrimination tasks where no component of acquired motor skill can be identified. The purely tactful sensory discriminations cannot be transferred by the anterior body region and depend entirely on the posterior body. These results suggest that the learning involved in acquiring motor skills include one component from the somatic sensory system (which accounts for the transfer of the learned motor skills when only the posterior body region of the corpus callosum remains) and a second component from the precentral motor cortex and presumably "motor" in type (which accounts for the intermanual transfer of motor skill learning when only the anterior body region is preserved). Stated in another way, the transfer of learned motor skills can occur through more widespread areas of the commissure than can that of pure tactful roughness discrimination learning.

Thus, we have presented evidence for a strict localization of function within the forebrain commissures. However, strong evidence also exists for an equipotentiality of an equivalence of function of different fiber strands within the various distinct portions of the commissure in the handling of specific sensory information. For example, studies with cats have shown that the posterior two thirds of the corpus callosum is that part which is concerned with visual information transmission in this species (4). Yet, any bundle of fibers located anywhere within this portion of the commissure provided it exceeds a certain critical size is capable of transferring visual pattern discrimination tasks between the eyes in chiasma-sectioned animals. Accordingly, these studies, taken together, place us in the peculiar position of, on the one hand, insisting upon a specific and closely identifiable localization of various sensory functions within various

portions of the commissure, but at the same time, they force us to the conclusion that, within those specific morphologic sectors, a nearly complete equipotentiality of the various component bundles is obtained with respect to the transfer of specific discrimination tasks.

A similar interpretation is apparent with respect to functional localization within the various regions of the cortex of the two hemispheres. Studies carried out with rhesus monkeys have shown that extensive lesions outside the parietal lobe, which may affect any or even the entirety of the other cerebral lobes, fail to disturb contralateral hand performance on previously learned tactual discrimination tasks (9). At the same time, lesions located anywhere within the parietal lobe, when of sufficient size, may disturb the performance on tactual tasks. However, re-learning of these tasks will proceed in all instances except in those cases where the entire parietal lobe has been removed. Closely similar findings are also obtained with respect to vision and the effects of lesions of the occipital and posterior temporal lobes. Thus, we are forced again to the conclusion that a strict localization of function exists with respect to specific regions of the cortex. That is, learning and memory functions which relate to the several sense modalities are carried out in different zones of the cortical surface. However, within these specific identifiable functional sectors of cortex, further lesion work has demonstrated a considerable equipotentiality of function.

The connectionism of the corpus callosum supports the above interpretations. That is, the different zones of the corpus callosum serve to interconnect the different specific zones of the cortical surface and these connections are always strongly homologic in their distribution (9). For example, the splenium of the corpus callosum interconnects only the occipital regions; the posterior body region of the corpus callosum contains all those fibers which pass between the parietal lobes; the anterior body region interconnects the posterior frontal regions; and, finally, the genu and rostrum interconnect the prefrontal and the orbito-frontal regions of the cortex. At the same time, the anterior commissure interconnects areas 20 and 21 of the temporal lobes leaving the zones of cortex of the anterior temporal zones almost entirely devoid of commissural connections. However, the homology of the interconnectionism of the corpus callosum extends far beyond the gross pattern which has just been described. That is, specific zones of the cortical surface which project fibers across the midline to the cortex of the opposite hemisphere, send fibers to the same loci contralaterally as they do ipsilaterally. For example, if a specific region of the *juxtaparietal area 18* sends fibers to its homologic locus contralaterally and also to a specific area of the contralateral *area 18 proper*, it also will send fibers to that selfsame *area 18 proper* zone ipsilaterally. Thus, we have seen that, just as a remarkable homology of interconnectionism exists between the various zones of the cortical surfaces in the two hemispheres morphologically, so a remarkable reduplication of the activity of the cortex exists with respect to the functional characteristics of these zones.

Dr. RASMUSSEN: We have obtained very similar information in humans on a lower functional level; for instance, with regard to motor and sensory functions after the restricted removal of the pre- or postcentral gyrus.

Dr. BACH-Y-RITA: When we study anatomical lesions the effect is strongest on the projection fibers and here it is certainly hardest to repair the functional reorganization. Certainly, FOERSTER and LURIA were of this opinion. Lesions without strict projection characteristics may be easier to reorganize, and these areas may have many different sorts of input. However, in our studies the visual cortex seemed to have only one sensory input in the strictest way; although we have noted other forms of input of unknown significance; they had longer latencies and were therefore not direct projections, coming from the auditory and skin systems.

Dr. KUYPERS: Our earlier findings (10a) indicate that the distribution of the cortical fibers in the spinal cord of the newborn rhesus monkey is different from that in the adult, and that immediately after birth cortical fibers do not yet establish direct connections to motoneurons. In three-day-old rhesus monkeys many cortical fibers can be detected in the funiculi with the Nauta technique but only a limited number of fibers enters the gray matter as yet and hardly any are distributed to motoneurons. In the next six months the number of cortical fibers encountered in the motoneuronal cell groups progressively increases and reaches an adult density at approximately the age of eight months. This is in keeping with the electrophysiological findings (10b). In keeping with these anatomical findings, a newborn rhesus monkey does not show any relatively independent finger movements in picking up food morsels from a well and in this respect behaves therefore in very much the same way as a pyramidotomized adult monkey (10c and d). LAWRENCE and HOPKINS (10e) showed further that when a baby monkey is pyramidotomized at the age of one or two weeks the animal at the age of two years still does not show any relatively independent finger movements in retrieving small food morsels from a well, despite the fact that the animal otherwise does not show a defect in walking, climbing, and reaching. The cortico-spinal and probably in particular the direct cortico-motoneuronal connections therefore seem to be critically involved in providing the capacity to execute relatively independent hand and finger movements. Obviously these findings argue for a rather rigid localization of function (10a - e).

Dr. RASMUSSEN: There is a parallel observation in man, where a lesion of the pyramidal pathway at birth is rarely detectable by the physician in the first 3 to 5 months of life.

Dr. ZÜLCH: May I remind you here of the timetable of "maturation" of the movements of a baby in the first year, which is probably in correlation with the myelination of the pyramidal pathway (11a - c).

Dr. CREUTZFELDT: One question I would like to ask Drs. KUYPERS and BACH-Y-RITA: Can one find a deficit of synapses in these cases?

Dr. KUYPERS: These motoneurons carry many terminals from local interneurons. A few missing terminals will therefore be difficult to detect.

Dr. CREUTZFELDT: So it seems, that neurons, especially dendrites, don't like to be without synapses.

To come back to the question of multiple sensory input, I think that much of the "poly-sensory" input to specific cortices acts on a general arousal level, but is in no way specific. It may change the receptivity of such an area - for its specific input as, for instance, sleep does. There are, on the other hand, true multisensory areas in the cortex, but their somato-topic organisation is not quite clear. In the midbrain (superior colliculi), "environmental space" appears to be mapped: in the deeper layers of the colliculi neurons are found which respond to different sense modalities as long as the stimulus comes from the same direction in space. In the cortex, only some observations of this kind have been mentioned (12, 13).

Dr. DENNY-BROWN: I would like to discuss the definition of "function". Anatomists like to use this term, whereas the physiologist very carefully tries not to use it. The anatomist, for example, would define a discrete finger movement as a function and would correlate this directly with activity in the cortex of the opposite hemisphere. There are several objections to this. If you see an animal grooming the skin with the limb opposite hemispherectomy you will realise that the pyramidal tract is not essential for discrete finger movement. The significance of the cortical contribution is, I think, particularly well exemplified by the result of high dorsal column section of the kind GILMAN (14) and I have reported. These monkeys had good placing reactions in the lower limbs, but in the upper limbs they completely failed. They right themselves without using the upper limbs at all and do not reach for objects with them. And yet from time to time they will use them very discretely and delicately for grooming. This type of movement must be reflex; yet it can be directed by vision by extrapyramidal pathways. Dorsal column section clearly eliminates a very important source of input for the exteroceptive aspects of the cortical part of "function". Moreover, it also abolishes a very important source of the perceptual process. For instance, after high cervical dorsal column hemisection there is a visual inattention on the same side in the first week. The perceptual process of the corresponding hemisphere has been unbalanced by loss of one large input. The phenomenon is concerned with that perceptual entity which is poorly defined as "attention" and which is not localized in any one area of the cerebral cortex. The disorder relates to the process of extinction, i.e. the vulnerability of perceptual function on one side resulting from a cerebral lesion. It is not important where the lesion is, except in relation to size. A relatively small parietal lobe lesion, particularly in the interparietal fissure, will result in a very considerable degree of extinction in relation to all sensory input from the corresponding side of the body. A frontal lesion has to be larger for a corresponding degree of extinction than a parietal or temporal lobe lesion. Physiologically the extinction

and inattention resulting from dorsal column, parietal, or area 8 lesion points to a defect in the same unitary function.

Dr. RASMUSSEN: It's interesting that this is not seen in man in large cortical excisions unless you go deep into the white matter. We have removed the whole parietal lobe behind the postcentral gyrus in a number of patients, and SUZANNE CORKIN (15) wrote a thesis on the inability to demonstrate any real disturbance in the standard cortical sensory modalities.

Dr. DENNY-BROWN: The paper of HECAEN and PENFIELD (16) was very interesting in that respect. The trouble there is that the depths of the intraparietal sulci tend to escape the neurosurgical lesion.

Dr. RASMUSSEN: In the cortical excisions we have performed, we went right down to the corpus callosum and the cortex of each convolution in the excised area was completely removed by subpial suction. These patients were well studied both pre- and postoperatively and there were many opportunities to investigate them in detail one or more years later. Another interesting thing is the fact that a small lesion in the postcentral gyrus produces a sensory defect in two-point localization, graphesthesia, stereognosis, joint-sense etc. in all patients. The second interesting point for localization: if a lesion in the postcentral gyrus is within the arm area (as defined by threshold electrostimulation) the defect of the cortical sensory modality is always in the hand, not in the face nor in the foot. If the excision is made in the face area of the postcentral gyrus, there is a decrease in two-point discrimination in the face and this is the only impairment one finds with no deficit in the cortical sensory modalities in the arm or leg. So there is, as Dr. MYERS said, a rather discrete localization of the 3 primary divisions of the postcentral gyrus and also for the precentral gyrus, as far as motor function is concerned. But within each of these divisions there is not the same degree of localization. If you have a small excision with a diameter of 3 mm in the thumb area of the postcentral gyrus, you will get a mild defect of all of these sensory modalities in the whole hand.

Dr. OBRADOR: There are many approaches to these problems of localization.

I can't forget OTFRID FOERSTER who as a clinical neurologist clearly demonstrated many fundamental facts of the localization of function in the central and peripheral nervous systems. Yet, we have to face a fact which is well known by clinical neurologists and neurosurgeons i.e. how tremendous big lesions can be and yet have no clinical signs. This is particularly well shown in slow growing tumors.

Dr. RASMUSSEN: Or, we may have patients with a subdural hematoma without any signs. In severing some tracts of the spinal cord we produce immediate effects. But these immediate effects will lessen to a considerable extent after a few weeks. FOERSTER wrote about this subject very extensively. We must never forget the

great amount of reorganization of function that may occur in the nervous system.

Dr. ZÜLCH: I hope that by the end of this symposium we will have more detailed information about the organization, function, and the topography of the nervous system. This may promote new experimental work and stimulate new clinical observations. Moreover, we may learn what kind and amount of reorganization takes place in the first years after pre-, peri- and postnatal lesions, in contrast to the clinical pictures of reorganization later in life after cerebral trauma or infarct. Perhaps then we will be able to give a better definition of terms like "plasticity" (BETHE), "diaschisis" (v. MONAKOW), "Katastrophenreaktion" (GOLDSTEIN) or "Zusammenbruch der Arbeitsgemeinschaft" (OTFRID FOERSTER).

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Cerebral Dominance

Moderator: H. Hecaen

Dr. HECAEN: It seems useful to ask if the specialization of each hemisphere is for all the tissue of that hemisphere or only for certain areas according to some particular modalities. Furthermore, one may ask if this specialization occurs in the surface areas of the hemisphere or also in parts of the subcortical formations, as some experiments with stereotaxic operation seem to show. You can ask also whether this functional specialization corresponds to some differences in the topography of the representation and is more focused on the left side for both parts of the body, or is it in the right more diffusely organized and mainly for the contralateral part of the body. Another problem seems to me to be the "innate" or "acquired" character of hemispheric specialization. There is some evidence against the innate character in examples of acquired dysphasia; on the contrary, patients with neonatal or perinatal cerebral lesions have a similar defect as adults. Another question to which, however, a partial answer has already been given, is the relationship between hemispheric cerebral specialization and handedness. Finally, it seems very important to know whether hemispheric specialization is specific to human beings or whether you can find some precursor of this in animals. Some people speak about dominance of the left part of the brain for vocalization in birds. Recently BUTLER and FRANCIS (1) found that in baboons there was some preference for rotation for the right or the left hemisphere. In a paper by HAMILTON (*Neuropsychologia*, 1974) it was shown that there is preference for the left hemisphere for discrimination of patients with a multiple orientation, but both hemispheres were equal for discrimination of faces, mirror images, and the asymmetric models. It seems to me that these are questions and problems which can elicit a discussion.

Dr. POECK: You ask whether the hemispheric specialization is valid for all parts of a given hemisphere; I shall go even as far as to ask, is there any specificity of the left frontal lobe apart from Broca's area at all, i.e. is there a consistent non-verbal deficit that is observed in patients with left frontal lesions which is not observed in patients with right frontal lesions?

Dr. ZANGWILL: Let's say that there is a consistent minimum verbal deficit with left frontal lesions well anterior to Broca's area. And such a patient does not present dysphasia in a clinical sense, i.e. a limitation of speech, or limitation of vocabulary or a simplification, which can be brought out very easily by psychometric tests as Dr. BRENDA MILNER now has shown.

Dr. POECK: That's what I mean.

Dr. HECAEN: BRENDA MILNER (2) finds greater deficits in performances on the maze test, more frequently with right frontal lesions than with left frontal lesions.

Dr. RASMUSSEN: Certainly with the Wisconsin card sorting test, which I find difficult to understand, the psychologist can pick out patients who have, for instance, epileptic damage in the convexity of the dominant frontal lobe. The same defect is not produced by lesions, damage, or excisions of the orbital or the medial surface of the frontal lobe or in the frontal lobe periphery.

Dr. POECK: The card sorting test has something to do with concept formation and the patient has to find out the concept behind this task, which the examiner did not tell him before.

Dr. GAZZANIGA: Certainly, the right frontal lesion will produce that deficit too, though not as severely as the left.

Dr. RASMUSSEN: There is also quite a difference with the maze test. It's just the reverse.

Dr. POECK: Is this a quantitative or a qualitative difference?

Dr. RASMUSSEN: Qualitative.

Dr. GAZZANIGA: A lesion in either frontal lobe will produce a deficit versus the normal range.

Dr. RASMUSSEN: BRENDA MILNER is astonishingly accurate in identifying whether an epileptogenic lesion is lateralized to the dominant or non-dominant frontal lobe. If there is a discrepancy between her findings and the EEG; then we immediately review all aspects of the patient's seizure problem and laboratory findings since the case is clearly a complicated one, and it often turns out to be a multifocal problem.

Dr. JUNG: I should like to demonstrate some examples of cerebral compensations at a higher level of artistic creation. Four painters with vascular lesions of the right hemisphere, who are described in another paper (4) had a visual neglect of the left side of differing degrees and duration. Two of these, CORINTH and RÄDERSCHEIDT, showed a very severe left-sided neglect during the first year after the stroke and compensated it by assiduous exercise in drawing and painting.

The complete series of paintings and sketches by RÄDERSCHEIDT, who lived here in Cologne, during his compensation efforts which he continued until his death 2 1/2 years later, has been preserved by his widow. I am very grateful to Mme. GISELE RÄDERSCHEIDT for allowing me to study this material showing the gradual compensation. Pertinent pictures are published in color in Fig. 9 of the paper mentioned previously (4) and some other examples had been reproduced in a popular article (5). These should be described

first before I show CORINTH'S unilateral neglect which is less well documented during the period of compensation.

RÄDERSCHEIDT'S self-portraits, compared to portraits before the stroke, clearly demonstrate the time course of artistic compensation of his right hemispheric lesion within one year. RÄDERSCHEIDT had a hemianopsia to the left, a severe left-sided visual neglect, a prosopagnosia, and slight left hemiparesis. Two and 5 months after his stroke he deleted the left side of his face in self-portraits (Fig. 8b and c in (4)) and then gradually in a further series of paintings he succeeded in drawing the left side. Nine months after the stroke he painted rather symmetrical self-portraits such as Fig. 9c in (4).

However, the compensation is incomplete as shown by closer inspection. The paintings 3 to 9 months after the lesion also show severe defects of color distribution in the left field. The color is well composed only on the right side, on the left it is coarse and inappropriately placed with large brush strokes. Thus the defect and its compensation concerns both form and color disorganization of the left side. When I discussed this with Dr. TREVARTHEN from Edinburgh he called attention to several other differences which come out with his "chimera" technique of half faces adding two lefts and two rights together. When each the left and right sides are added to this mirror image in a "chimera" (Fig. 10, in (4)) The differences are shown more clearly. Also the emotional expression is quite different; for the right side of the face there is sharp observation whereas the left side has a depressive expression.

CORINTH'S left-sided neglect is known only from few drawings, reproduced in his autobiography (3) and by SINGER (2). Fig. 1 shows these drawings. LOVIS CORINTH suffered from a right-sided cerebral lesion due to a stroke at the age of 53, in December 1911, with a lasting left-sided hemiparesis.

CORINTH continued to be a creative painter and draughtsman for 14 years. During the first year after the lesion he produced the study sheet of head drawings shown in Fig. 1a. In the incomplete face of the middle part, (below left of the portrait of his wife) he drew some sort of a defect (scotoma?) on the face. Art historians who published CORINTH'S drawings didn't recognize the defect and H.W. SINGER even filed this drawing in his book (6) under the wrong sequence of drawings of the year "1904". But CORINTH himself, in his autobiography (3) dated the reproduction of the right part "1912", i.e. during the first year after his brain lesion in December 1911. Therefore it may be justified to reproduce the drawing with the corrected date and to add another drawing made 9 years later (Fig. 1b) which shows a re-appearance of the left-sided neglect in 1921 after it had been compensated in all his drawings from 1912 to 1920 and also from 1922 - 1925. Thus one may explain the disturbance by fatigue (4).

The drawings may now be reproduced 50 years after CORINTH'S death as documents of his untiring productivity as a draughtsman in



Fig. 1a and b. Unilateral neglect of the left side in two pencil drawings of the painter CORINTH, 1 and 9 years after his right hemispheric lesion. a) Study sheet of head drawings made in 1912 (about 10 months after his stroke which occurred in December 1911). The facial drawings neglect the contours and forms of the left side beyond the mid-line structure. The left eye is either lacking or displaced or unclear. Left contours are only completed in the horse profile. From SINGER (4). b) Reappearance of left-sided neglect in a self portrait dated 25th January 1921, nine years after the stroke. Only the contours of the right side are well drawn, the left structures appear deformed and the shoulder is deleted. Although shadows of the left face mask some defects of drawing, the contrast to the sharply delineated right side is apparent. From CORINTH (1)

spite of his handicap due to the left-sided paresis. The examples demonstrate that even severe defects of nonverbal functions of the right hemisphere in painting and drawing can be compensated in the course of time, although not completely.

Two other painters, O. DIX and J. THIEL, compensated the drawing disturbance after a similar right parietal stroke within several days and weeks.

These examples should demonstrate how compensation and reorganization of functions is effective at a higher level of art performance.

Dr. HECAEN: I have seen this in another famous painter, but he could not compensate because he died fifteen days afterwards.

Dr. NEWCOMBE: Do you have any idea which group of patients neglects persistently and which group does not show neglect.

Dr. JUNG: No, except that the lesion might be larger in those with delayed compensation; but we have no postmortem findings in these painters.

Dr. NEWCOMBE: I was not referring specifically to painters, but to neurological patients in general. We find that gunshot wound patients with hemianopia fall into two groups: the majority who recover from unilateral neglect spontaneously and a very small group who have the defect for years afterwards. We have a few patients who - 30 years after missile injury - are still bumping into people on the hemianopic side; and we wonder why this small group has failed to compensate.

Dr. JUNG: Recovery from neglect may be an unstable compensation in others. The instability of compensation of unilateral neglect may be illustrated by the selfportrait of CORINTH (Fig. 1b). In this drawing his left-sided performance again decompensated 8 years after the unilateral neglect had disappeared. Meanwhile, CORINTH had made very good pictures without left neglect but in 1921 he produced this portrait, which shows drawing defects in the left face and shoulder. We first suspected that this might have been due to a second stroke. His son THOMAS CORINTH, however, told me that the painter had had no other cerebrovascular accident in 1921 and until his death in 1925. All later portraits are without neglect. Therefore, this transient left neglect may have been a short-lasting decompensation due to fatigue.

Dr. GLEES: Please describe once more the lesion.

Dr. JUNG: Both CORINTH and RÄDERSCHEIDT probably had a right parieto-occipital hemispheric lesion, the motor symptoms being more pronounced for CORINTH, the visual for RÄDERSCHEIDT. CORINTH certainly had a severe, lasting left hemiparesis and probably a left homonymous hemianopia, but precise neurological findings and autopsy verifications are lacking. CORINTH'S left hand could only be used to hold a copper plate, pressing it with his left hand against the body whilst he etched with the right.

Dr. POECK: Let me take up another problem: is there any evidence to support the old Jacksonian idea that, in contrast to propositional speech, emotional speech has something to do with the right hemisphere? I have personally never seen anything to support that.

Dr. PREILOWSKI: I think there is some evidence from hemispherectomy cases, where the left hemisphere has been taken out and some emotional speech has remained.

Dr. ZANGWILL: I saw one of these patients with Dr. SMITH some years ago. There is no question that his automatic speech was swearing, exactly like severe motor aphasics. So there seemed to be no doubt in this particular case from which side the improper language was coming from. And by implication one would imagine that in most ordinary aphasics with large anterior left hemispheric lesions they swear with the right hemisphere.

Dr. DENNY-BROWN: With regard to compensation I would like to say that the patient reported by MEYER, HORENSTEIN and me (7) 16 years ago still has the same extinction, and I have seen a lady of 68 who had an infantile parietal lobe lesion, who still had very remarkable degree of extinction. When the lesion involves the interparietal sulcus, extinction is a very resistent disorder. Though the patient may compensate in general behavior, testing will show the same defect as before.

Dr. ZÜLCH: May I remark here that none of our patient with right- or left-sided hemispherectomies showed extinction (8).

Dr. DENNY-BROWN: There is something I would like to comment on in relation to Dr. ZANGWILL'S paper. This relates to Broca's lesions. At first I should say that I don't know whether I am alone or not with my very strong opinion that vision in most people is very important in speech, as is most obvious in patients with echolalic aphasia remaining after a severe but not necessarily very extensive lesion in the region of the angular gyrus. These patients repeat everything that you say to them (in the manner of echolalia). The most remarkable thing about this performance is that if you stand behind them, they don't repeat the words. So this is a visually determined speech performance that is completely reflex. If you exclude vision by blinding the patient, the result is just like covering a parrot, there is no speech; no matter how loud you shout at them, there will be no response. Such speech would be what I have called a "visuo-social phenomenon". Also, if you watch a young child learning to speak, he watches his mother's lips carefully when trying to speak his first word. However, this obviously is not the only way speech can be learned, for it can be slowly acquired after congenital blindness. This brings me to the question of Broca's area. I have reported (9a/b) an interesting patient with a very well localized, quite small vascular lesion from an embolism, which damaged only the cortex of Broca's convolution, and did not undercut Broca's area. The lesion extended slightly above Broca's area into the lower frontal gyrus, but did not affect any of the remainder of the cortex. That man survived about 6 - 8 weeks and then died of a cardiac episode. His speech disorder was what ALAJOUANINE has very well described as "phonetic disintegration". It is a perseveration of the first syllable. In the beginning the patient had quite severe lingual and labial apraxia as well, but this cleared up in the first week; however, he was left with this very peculiar difficulty in beginning words, e.g. the labial "p", in "Please, where is the telephone". He would say: P-P-P- and then this P-sound would contaminate every subsequent word for a time and then you get a few more words out until he came to another labial "telephone" and he had the same difficulty starting that word. Certain words involving labial syllables were incomprehensible as a result. In this particular patient there was no difficulty in comprehension, though we were aware that the French writers in particular always described a difficulty in comprehension with Broca's disturbance of speech. But I found that Broca didn't describe any disturbance of comprehension; these patients have a disturbance of comprehension only when the lesions are a little more extensive in the Island of Reil. The importance of this in the present context is that this

patient watched you very carefully as he spoke. Now this is really just the opposite of the patient with semantic aphasia, who has great difficulty in speaking if he sees a person who he is trying to speak too, but has very much less difficulty speaking on a telephone ("visual avoiding"). I want to ask Dr. HECAEN whether he differentiated in his statistics the patient with very complete auditory memory or auditory speech memory from those with typical visual speech memory?

Dr. HECAEN: I am afraid I cannot answer this question. I did not look at this aspect. But do your patients have some difficulty in writing?

Dr. DENNY-BROWN: Yes. The disorder in writing also consisted in the perseveration of the labial syllables. Conversely, following subcortical lesion, every word is slurred, dystonic, or spastic. This did not appear with a pure cortical lesion. In phonetic disintegration it appears the patient has difficulty in attaining a posture of his lips and mouth for enunciation of a particular syllable, and then has difficulty changing that particular posture for the next few syllables. It is a type of apraxia.

Dr. HECAEN: That's a question of semantics, I think.

Dr. RASMUSSEN: I just wanted so say that I like your term "hemispheric specialization" rather than "cerebral dominance" because it gives the right hemisphere more of its true place in the hierarchy of function. In this general consideration of cerebral dominance one interesting aspect is the fact that in a certain number of people who have early damage of the left hemisphere, speech was transferred to the right hemisphere; however, the right handedness remained. They still preferred it as the dominant hand. When dealing with a right-handed patient who has had a history of an early injury it is possible that speech may have been transferred and developed in the right hemisphere even though he is still right handed.

Dr. WOOLSEY: I was wondering whether there are any known examples of individuals who had lesions such as you were speaking of, i.e. who had one language at the time of the lesion and who undertook to learn a new language afterwards. Was there any evident better performance in the new language with certain defects in the original language at the same time. In other words, was the new language learned by the second hemisphere?

Dr. HECAEN: I don't know of any case of that sort.

Dr. PREILOWSKI: I just wanted to make a short comment on lateralization of functions in subhuman primates. I think it was Dr. JUNG (10) who once summarized a conference and concluded about non-human primates that since they did not have any speech obviously there could be no lateralization or specialization in these animals. I personally think that there is more to lateralization than speech. Investigators so far have mainly tested for hand preference in monkeys and apes. This is not sufficient. In most cases tests were used in which motor control could have been ex-

ercised through the ipsilateral as well as the contralateral hemisphere. I think the question of cerebral dominance in non-human species is open until more specifically lateralized behavior requiring cortical control have been investigated and until functions relevant to a species have been checked, such as for example communication through facial expressions and auditory signals.

Dr. HECAEN: Do you know of any documents on this subject in apes?

Dr. PREILOWSKI: Yes, there were a few studies (11). But again, only hand preference was investigated and not lateralized performance.

Dr. HECAEN: I do not mean manual preference but hemispheric specialization.

Dr. PREILOWSKI: No, there are none to my knowledge. Although investigators have used hand preference as a test of specialization; but I don't think that this is justified.

Dr. NEWCOMBE: Returning briefly to humans and to your opening remarks about hemispheric asymmetry considered in terms of the distinction between verbal and nonverbal functions and the simultaneous versus the successive approach, I think there are data which do not fit very plausibly into this neat dichotomy: for example - data on visual recognition and spatial orientation. It is unlikely that these non-verbal activities can be referred exclusively to the right hemisphere: there are patients with left posterior lesions who are impaired in visual recognition (12), and orientation (13) tasks; and both hemispheres may be responsible for some aspects of spatial orientation (14). I think we might have to revise our concepts regarding the nature of hemispheric asymmetry and hemispheric interaction, with more emphasis on the *strategies* used by subjects to solve problems.

Dr. HECAEN: I agree.

Dr. YAKOVLEV: I would like to refer to the extensive and detailed architectonic and comparative metric studies of the cortical fields of the left and the right hemispheres made in the thirties and forties at the state Institute of Brain Research in Moscow by a team of several investigators under inspiring leadership of OSCAR VOGT'S pupils in Soviet Union. Seven human cerebra were exhaustively studied. It is of some interest in the context of the present discussion that fields 45 and 47 of the inferior frontal gyrus showed a greater surface area and higher structural differentiation in the left hemispheres of 5 right-handed individuals and in the right hemisphere of one left-handed and (curiously!) of one individual whose autopsy revealed a "status inversus viscerum" (15). Otherwise no statistically significant differences were noted in the surface areas and structural differentiation of the cortical fields of the two frontal lobes in terms of prevalence of one hemisphere over the other - both hemispheres exhibited a great individual variability. The author of these interesting studies of the frontal lobes (16) concluded that the

differences found in the fields 45 and 47 correlate with the special role of these fields in the function of human speech.

Dr. PLOOG: Was this extensively published?

Dr. YAKOVLEV: Yes, this long series of studies has been published in Russia, some of them with the authors' summaries in French or in German, in "The Contributions of the Moscow Brain Institute" six volumes with atlases, Gosisdat 1935 - 48, Moscow-Leningrad.

Dr. ZANGWILL: I would just like to return very briefly to a semantic problem which you have raised and which Dr. DENNY-BROWN commented appropriately on. I think that Dr. ZÜLCH reminded us yesterday of Hughling Jackson's dictum to localize a deficit like aphasia and to localize a function like language are two quite different things. These days very few people believe that. It was supposed that a deficit gave one a clue as to the locus of a normal function. This led of course to the concept of a "center" and this has an interesting history. The idea of a "center" began from the reflex model and came to denote the focus of a reflex system as, e.g. a respiratory center. However, as the idea was carried further, i.e. higher to the cerebral cortex, the idea of centers started to get mixed up with psychology; or perhaps contaminated by psychology would be a better way of putting it. And there we had the idea of a brain center, as something in part physiological and in part psychological, the psychological side being envisaged in earlier days in terms first of a store-house for imagery which was supposed to be destroyed by a lesion, or in some cases as a generative center, which produced a particular activity by its own endogenous action. So aphasia became to be regarded as either the destruction of centers or destruction of connections between centers. This idea has been amazingly persistent though people don't actually use the term today. However, a lot of the thinking in 19th century "Lokalisationslehre" in terms of centers is still, I think, with us. Now, obviously there have been reactions against this from COGHILL HERRICK (17), GOLDSTEIN (18) and others. The idea of the centers were dropped and a kind of rather vague "wholism" replaced it, but I think we are now seeing that wholism has been just as inadequate as the "center theory" in explaining functions. We are now looking for some other way of regarding the problem which involves, on the one hand, clinical and experimental evidence of localized deficits; and on the other hand, a controlled study of behavior. I think this is what I tried to say this morning when I was slightly critical of Dr. HASSSLER. I think we now really have to look at behavior as that attitude which is produced by the nervous system or to look at the nervous system as the instrument of behavior. We have to sort out the forms and varieties of behavior in so far as they relate to the activities of specific neurological systems as defined by anatomical, neurophysiological, pharmacological, and other techniques. As I see it, we are now moving toward a new area in localization theory in which we are trying to get at the analysis of functions, to define functions in terms of the breakdown of patterns as disclosed by clinical pathology and experiments like SPERRY'S split-brain work. The latter seems to me to give us enormous encouragement in trying

to understand how functions are built up by hemispheric cooperation, and competition, in the normal subject.

Dr. BACH-Y-RITA: I want just briefly to focus the discussion on the specific functions. I think we might be in danger of overlooking the specific importance of the less specific ones. I think this is degrading the potential importance of facilitation as one of the less specific activities. They are equally important in normal function, but we don't notice these until they are extensively destroyed. I think LASHLEY (19) pointed out very well the example of the stroke patient who is paralyzed in a particular accident and left in an emotional state which requires immediate responses. Then he can perform actions under an emotional stress that are undoubtedly to be considered by the so-called facilitation as well as the more nebulous and difficult ones to identify.

Dr. GLEES: Some of us have to go back to teach students, and I am personally very confused now about these speech areas. We have taught the existence of the Broca and Wernicke center, but apparently in the meantime these have become invalid. But I would like to be informed what to teach.

Dr. RASMUSSEN: I would not say that the concept of a Broca- and Wernicke center is invalid. I would say that the concept of an anterior speech zone in the frontal region and the parieto-temporal speech zone posteriorly is a certainty. I think the concept or the information that we have accumulated from so many sources about these speech areas are really refinements of the original and basic concepts; we are only trying to get a better idea of how they are interrelated and how they are integrated. I think the richer the speech the greater the part of the brain that is involved, I think this is one of the problems with the localization area. If you exempt the production of pituitary hormones by the supraoptic nuclei, there is almost no function we can speak of which you cannot narrow down into a very limited rigorous basic minimum or expand it into a something which is obviously going to require the whole brain and this is, I think, our big problem. Each of us has our own idea of where we are going to draw the line in our concept of localization of functions.

Dr. ZÜLCH: We have even grater difficulties with the localization of movement, which seems so simple. I just took out my old Hughlings JACKSON (20) book in order to try to find out what he said about the "level concept". I was stimulated to this by Dr. HASSLER'S concept of the three levels. JACKSON said that strictly before Ferrier's motor zone is the highest level and without this highest level there is no motor performance. Well, in the meantime we know from prefrontal leucotomy, and from all sorts of standard leucotomy, that this is not true. This is a very interesting clinical and neurosurgical contribution to the problem of where the area, the system, and the region is localized which creates a pattern of movement, and which triggers it to realization.

Dr. YAKOVLEV: I remember an episode from my student days. There was an old professor of international reputation. He gave a lecture on the paramidal tract to a class of students and I was one of

them. He described the Betz cells, their fibres, the decussation, and how they get to the anterior horn neurons and to the muscles, and how "voluntary" movements are performed. It was a very elaborate and instructive lecture. After the lecture a student went to the professor and enquired: "Herr Professor, when I move my finger is it my Betz cells that move it?" The professor, somewhat perplexed for an instant, nodded affirmatively murmuring: "ja, ja." "My God!" exclaimed the student, "and I always thought it was I who moved it!" (Laughter). The epistemological conundrum of the student follows brain research like a shadow.

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Plasticity of the Nervous System¹

Moderator: P. Bach-y-Rita

Introduction

Central nervous system (CNS) plasticity is the major factor in functional recovery following brain lesions in man. The concept of plasticity is broad; further, it is difficult to identify the structures and mechanisms underlying the plasticity. However, that plasticity is present is apparent from the clinical evidence of functional reorganization following some CNS lesions.

The question of CNS plasticity is intimately linked with concepts of cerebral localization, the neural substrate of the various functions of the CNS. Some functions are more localized than others. For example, LURIA (16) considers that the localization of such processes as visual and auditory perception in circumscribed sensory areas is less likely than the localization of the respiratory or patellar reflex. However, he notes that in the cortical representation of the special senses such as vision and audition, the cortical projections are only a small part of the functional system of that part of the brain. The high specificity of the neuronal structures which project a particular receptor system to the cortex underlies the fact that lesions in these areas often lead to irrevocable defects, and compensation is possible only within very narrow limits.

Plasticity has been defined in many ways. In its broadest terms it includes the capacity for any adaptational changes, including learning. BETHE (5) considers plasticity to be a general principle of living organisms. It is the ability to adapt to changes and to meet the dangers of life. In particular, it is the capacity of the CNS to reorganize following insult, and to restore adequate function. In a more narrow sense, I have defined sensory plasticity as, "The ability of one sensory system (receptors, afferent pathways and CNS representation) to assume the functions of another system" (3), with the qualification (4) that the functions of specialized receptors, such as retinal rods and cones, cannot be performed by other natural receptors, but must be supplied by artificial receptors (e.g. a TV camera).

This discussion on plasticity will be concerned principally with the restoration of function following a CNS lesion. In this re-

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gard. LURIA (16) described the restoration of functions as "... a radical reorganization of the destroyed activity in which after brain injury the deranged function is restored by means of entirely different neuronal structures unaffected by the trauma". This statement can serve as the basis of the following questions: What is the extent of functional reorganization following structural changes? What are the mechanisms underlying this functional reorganization? How might these be related to the plastic CNS mechanisms which underlie sensory substitution? Further, the factors necessary for clinical functional reorganization will be considered. Some aspects of these (e.g. experimental lesions, sensory augmentation studies, and plasticity at the level of single CNS neurons) have been discussed elsewhere (4) and in this volume (see p. 205ff., 313ff.).

Factors Essential for Functional Recovery

In a group of patients with comparable CNS lesions, recovery will vary greatly. Factors that produce the functional reorganization in those with partial or total recovery include: 1. CNS plasticity, 2. training, 3. motivation, 4. the possible avoidance of spasticity by prompt and extensive physiotherapy, and possibly by the development of centrifugal inhibitory mechanisms. These inhibitory mechanisms are comparable to those involved in many aspects of learning and may, in addition to the avoidance of spasticity, underlie much of the functional recovery.

FOERSTER (cited in 23) was a pioneer in revealing the crucial role of training. Many others have confirmed this. Motivation is of equal importance. CHOW and STEWART (7) were able to obtain both behavioral and neural recovery following visual deprivation in cats, whereas previous workers obtained little if any recovery. A major difference was that CHOW and STEWART (7) used forced training methods as well as encouraging performance by gentle treatment and food reward. In the case of recovery following a stroke described by AGUILAR (1), the extremely high motivation, the reinforcement of the performance efforts by the patient's family, and the long and arduous physical therapy were undoubtedly all contributing factors to the recovery.

In unpublished studies, RASMUSSEN (personal communication) noted that recovery of good function following facial-hypoglossal nerve anastomosis occurred only after several years of arduous training. In order to develop selective control of the facial musculature, RASMUSSEN directed his patients to push their tongues against a specific tooth as they attempted to accomplish a specific movement, and to practice this action daily in front of a mirror. Those who continued to do so were able to recover selective control which was never possible during the first two years without the conscious pushing of the tongue against the tooth. However, during the third year of practice the patients obtained selective voluntary control without tongue movements.

Functional reorganization is often a process that proceeds for many years. HARLOW (12) found evidence for recovery even in the last (sixth) year of his study of monkeys with brain lesions.

Long-term recovery can be seen in man as well: in the facial-hypoglossal anastomosis cases studied by RASMUSSEN (personal communication) recovery often continued for four to six years.

Neural Substrates

GERARD (11) considers that the entire course of biological evolution has had as its main theme the development of organisms which are more easily modified by the environment. GALAMBOS (10) considers that genetic factors provide a substrate for plasticity (adaptive modification) and also restrict its extent and character.

Central nervous system plasticity may be more dependent upon reorganization of function than on restoration or transfer to another specific CNS locus. It is probable that some pre-lesion link between the neural control mechanisms and the remaining neurons and fibers is necessary for the functional reorganization. Such pre-lesion connections may have been buried in the "subliminal fringe," and thus not previously evident. It has not been demonstrated that completely new supraspinal control of motor functions can be established post-injury. However, RAISMAN (17) has shown that when one afferent input to the septum of a rat is sectioned, another afferent source occupies the vacated synaptic sites, and several studies (reviewed in 4) have demonstrated competitive synaptic organization in the visual system. It is generally noted in textbooks that brain cells do not regenerate after lesion, but what is generally *not* noted is that nerve cell bodies are a small part of the mass of the brain. Most of it is composed of dendrites, axons and glia. Even when measurements are confined to the neurons, SHOLL (19) has shown that the surface of the perikaryon only accounts for about 10% of the neuron surface. The studies cited here certainly demonstrate the capability of axons and dendrites to grow, and for synapses to be established, in response to functional needs. These capacities form the plastic neural substrates that allow functional reorganization following CNS lesions.

How is the reorganization accomplished? New synapses are established (e.g. 17), and existing synapses "facilitated," with potential connections being transformed into actual connections (e.g. 13) while other synapses are inhibited (6). The "subliminal fringe," evidenced by such phenomena as the temporary disappearance of paralysis during an emotional disturbance (14) or, on a cellular level, the involvement of additional neurons in the motor cortex to a particular stimulus as the stimulus becomes part of a conditioned response (22), is undoubtedly utilized in functional reorganization following CNS lesions. The "subliminal fringe" may also be revealed by drugs: for example, chloralose increases the amplitude of evoked responses in zones of convergence (2), and ROBERTSON (18) noted that thiopental reversibly increases the receptive fields of cat visual cortex cells as well as the types of stimulus to which the cells respond. Although these drugs may act primarily by blocking inhibition, they nevertheless uncover synapses and pathways that already exist, but are not utilized under normal circumstances.

Inhibition may play an important role in the functional disability produced by brain injuries. Spasticity may in part be caused by the absence of selective inhibition, while paresis may result from excessive inhibition. RATNER and PERELMAN (cited by 16) have described the effect of Prostigmine in cases of brain injury accompanied by paresis of the limbs. The Russian authors consider that Prostigmine (which suppresses cholinesterase activity and thus potentiates the action of acetylcholine) selected the group of movements that were merely inhibited from the general paresis. Further, PERELMAN (cited by 16) has presented evidence that the de-inhibition of function was not limited to the motor system, but could also restore sensation.

Cortical areas are not exclusively concerned with a single unique function; each area is involved in multiple functions. This multiplicity of functions offers a substrate for functional reorganization. Further, LURIA (16) points out that functional reorganization can occur by the transfer of the impaired process to a higher level of organization. He notes that this usually can only be achieved by long and special training. LURIA (16) discusses the theory of the various structural levels of nervous processes in relation to the restoration of damaged functions and notes, "The fact that each action has both main and 'background' levels, able to replace each other in various ways, and Man's ability not only to reorganize his actions within each level but also to shift these actions from one level to another, produce forms of 'plasticity' which do not exist in the animal world".

Equipotentiality (15) and specificity are not entirely mutually exclusive concepts, and both are likely to be involved in functional reorganization following CNS injury. WEISS (21) noted, "The specific diversity of chemical constitution - the principle of 'specificity' ... would continue to operate in the developed nervous system as an instrument of maintaining functional order, as well as of restoring order after structural or functional disturbances."

LASHLEY (15) considered that the performance of any function is dependent on two variables in nervous activity: (a) the reaction mechanisms which, whether of instinctive or of learned activity, are related to a definite pattern of integrated neurons whose threshold of excitability is variable, and (b) the availability of such a neuronal pattern, and the ease with which it can be activated, which depends on less specific facilitatory effects. The general level of facilitation, which may also include "subliminal" inputs from many CNS structures to many other structures, may, therefore, play an important role in CNS activity.

Although the total amount of cortical tissue remaining may play an important role in the restoration of certain functions, it is equally important to note, as WEISS (21) did, that "... nothing could be more misleading than the impression that embryonic neurogenesis merely fabricates blank sheets on which experiential input from the outer world is then to inscribe operative patterns".

Thus, the principle factors underlying functional reorganization after a lesion include: 1. the CNS neural substrates of the plas-

ticity (the effectiveness of these substrates is evidently inversely related to the age of the patient), 2. motivation, and 3. training. The reorganization may be partial, allowing for adequate but not highly efficient function to occur. Further, functional reorganization may be a continuous process with gradual improvement of function over the course of many years. Therefore, a fourth factor is: sufficient time for the functional reorganization to occur. All four of these factors (and possibly others as yet unidentified) are apparently necessary for the functional reorganization to occur. In connection with motivation, an essential condition of the functional reorganization is that the particular activity is *needed* by the patient. The greater the need, the more likely it is to take place (16).

The process of functional reorganization following CNS lesions may be loosely compared to learning a new language. The CNS substrate exists in most humans, but is not called upon unless a need occurs. Motivation and training are necessary: Children learn more quickly and are more able to completely acquire the accent, grammar, and subtleties of a language. The absence of learning is *not* *prima facie* evidence of the absence of the capacity to learn the language: either adequate training or motivation may have been absent, or training may have continued for an insufficient time. Great experience with language training has led to the development of methods that produce highly efficient results. The amount of training required is usually related to age. In fact, young children require no further training than exposure to the language. However, with increasing age, exposure alone is insufficient: Numerous examples exist of immigrants to the USA who even after 50 years of residence are unable to speak English.

Although the CNS lesion may not be incompatible with life, the quality of life is certainly reduced unless a considerable amount of functional recovery occurs. Thus, a stroke patient may live at a reduced level for many years with hemiplegia and aphasia. (Comparably, the long-term resident of the USA who has not learned English can exist within his cultural sub-group without being able to participate in many of the activities that surround him.) Each small increment of functional reorganization will improve the quality of his life.

Future work on CNS plasticity should include an exploration into the neural substrates, by specific laboratory and clinical studies and by the exhaustive studies of "natural" experiments, specifically of those unusual patients who recover from CNS lesions that are usually more severely debilitating, (e.g. the cases of AGUILAR and of RASMUSSEN, described above), especially when histopathological reports are available for correlation.

Training methods initiated in the last century and continued by many workers such as FOERSTER (8, 9), BETHE (5), and LURIA (16), should continue to improve. Motivation of the patient may often reflect the attitudes of the physician, the therapist, and the family. When little recovery is expected by those who surround him, it is indeed an unusual patient who can continue to be motivated. He *must* be highly motivated in order to continue the

enormously difficult, tedious exercises that may have to be performed every day for years, as the cases of RASMUSSEN and of AGUILAR (described above) have shown. Finally, time for recovery must be provided. In a practical sense, this may be the most difficult factor. Therapy is expensive and long-term therapy is often limited by economic factors.

Summary

Central nervous system plasticity has been defined; these comments have been largely limited to plasticity related to functional reorganization following CNS lesions. The history has been briefly reviewed and recent experimental and clinical evidence has been examined. The principal factors in functional reorganization have been identified as, 1. the existence of CNS substrates, 2. motivation, 3. training, and 4. sufficient time for recovery. Suggestions for future research have been made, and some factors related to improved clinical approaches to CNS lesions have been mentioned.

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Discussion

Dr. ZÜLCH: For the discussion of plasticity I can here point to the restoration of the synergies which I have described in detail in my paper. There I emphasized the fact that the synergies are better developed and less strictly linked in their segments, the earlier the damage to the pyramidal system occurs, i.e. the earlier they are "called into action". Whether this means at this particular time, when the myelination is not yet complete, that other morphological connections are linked in a system which Sir HENRY HEAD called "overwired" or whether the better motor performance is based on more active "functional" connections has to remain open today. In patients in the "stroke age" flexor/extensor

synergies of the leg return, but there is usually only a very poor restoration of flexor synergy of the arm. This is in complete contrast to what I described in children. However, a patient aged 35 who had been hemiplegic for one year because of a benign tumor and had also developed synergies, could already produce the synergic movements in the first few days after hemispherectomy. Usually after vascular or traumatic lesions of the pyramidal pathway the development takes 3 - 5 weeks for the leg and 4 - 10 weeks for the arm. We may then ascribe this phenomenon of the different quality of the synergies to "plasticity".

Another even more interesting example for "plasticity" may be the result of various transplantations of nerves and muscles. Here I have tried to functionally split off the mass-movement of the three branches of the facial nerve by intensive training in front of the mirror, however, without any effect. My working hypothesis was that in the re-innervation of the several facial nerve there was an overshoot of the sprouting fibers, up to 20 - 100 times the original according to DOGLIOTTI (1). But the regrowth into the distal part was undirected and, according to the misregeneration theory of LIPSCHITZ (2), all three divisions of the nerve receive fibers from all parts of the proximal segment, i.e. a complete intermingling takes place. This is considered the cause for the subsequent mass movements. It could be possible now, I guessed, by training and coordinated galvanic stimulations to reinforce the fibers of one branch, which are part of the correct (old) connections and to suppress and to bring to atrophy the "wrong fibers" in the reinnervated branch which are not functionally reinforced during the training. Yet, I did not find any change in such patients as compared with the ordinary clinical course leading eventually to the global (mass-) movements after facial nerve palsy.

FOERSTER'S observations about the retraining of movements after grafts of the spinal accessory or hypoglossal nerve onto the facial nerve are of particular interest here. I have theoretically discussed whether it would not be possible by modern micro-surgery to split for instance the various components of the spinal accessory nerve up in the main root and to sew the parts up separately to the three different divisions of the facial nerve. Perhaps it would be easier to "connect" a cortically planned movement like turning the neck by the sternocleidomastoid muscle after transplantation with a new desired movement, i.e. contracting the zygomatic and similar muscles and then showing the teeth. OTFRID FOERSTER himself described his experience (3) with the repair of the severed facial nerve by the (total) spinal-accessory, that in the first phase movements of the face were only possible by a willed movement (elevation) of the shoulder. In time - FOERSTER observed - the patient learned to separate these and to move his face without an "associated" movement of his shoulder. FOERSTER ascribes this to a functional reorganization of the cortical area for shoulder and the corresponding facial movements.

Dr. RASMUSSEN: I was very interested to hear you talk about facial palsy because over the past 15 years I have had some experience

in patients with facial-hypoglossal anastomosis. A number of years ago I began to ask these patients to perform exercises when the tone was restored in the face and some sort of movement began to return. Then I would instruct them everytime they went into the bathroom to push the tongue against the tooth, which they found by experiment would produce the most symmetrical retraction of the lips. And we told them to do the exercise only when they were in the bathroom looking at the mirror. It is very interesting that these patients came back after one year and had a mass reflex facial movement. When I asked them to retract the lips, they were able to retract the lips quite well. When I asked a patient how he did it, the answer was: "I push my tongue against this certain tooth". When he returned a year later there was even better movement of the lips and he was again asked how he did it. He gave the same reply, "I pushed my tongue against this tooth". When asked 3 or 4 years later how he retracted his lips, he replied "I just pull the lips back!" When I reminded him "but the last time you were here and did that, you said that you pushed your tongue against a tooth, he answered "I don't do that anymore, I just think about it."

Dr. ZÜLCH: Does this contradict me?

Dr. RASMUSSEN: No, what I am saying is that it is possible for the brain to make new connections, because initially in order to do this his brain sent the message out to the tongue, but after this had been practiced for a while, his brain does this by short-circuiting the tongue. The interesting thing is that patients who do not do the exercise never get that transfer.

Dr. ZÜLCH: But this is exactly what FOERSTER (1934) described in his special work on the repair of the VIIth nerve by anastomosis to the XIth and XIIth nerve. The point is not whether one learns to move one side of the face first by intending to move the tongue in a particular way, which later is not necessary. This learning process is exactly the same as with the repair of extensors in the arm by flexors. The point is: can you split up the global movement of all three branches of the facial nerve, once a global reinnervation has taken place, either by regeneration of the severed nerve or by anastomosis? And therefore I ask a crucial question: Did he grimace when using his tongue in swallowing?

Dr. RASMUSSEN: No, he did not, he moved only the tongue.

Dr. BACH-Y-RITA: We should analyze the factors leading to recovery in those unusual cases that reveal an extraordinary recovery. This should lead us to determine how that particular person accomplished recovery. The most important element of learning to me is the development of inhibitory control. What you have here is a big mass of input and there is no way the brain can learn which of the central nervous system connections should be connected, and how to block out all the others. And these are things we really have to learn. I think if we are going to find the system, we must take advantage of whatever possibilities exist.

remote as they may be. If one works 8 months to train a subject who has had a cortical lesion to move his finger, and he does not get results, I don't think the conclusion is at all justified "it is impossible". I think the other conclusion that I would draw is at least equally justified, i.e. that we haven't found yet a specific training mechanism to do this. For instance in our studies with vision substitution we have greatly refined our training approaches. We can do now in an hour what used to take a week, because we found specific activities that encouraged the development of perceptual mechanisms and there has to be some sort of interneuronal substrate.

Dr. ZÜLCH: I claim to be one of the first since the last war to have introduced rehabilitation, any sort of exercise, and physical training into clinical neurology. Maybe the difference is that I still believe in pathways and I am a "localizer" in the sense of HUGHLINGS JACKSON, although HENRY HEAD has already reminded us that the brain is "overwired".

May I come back to Dr. RASMUSSEN'S observation, because this is an excellent example. Again I ask: the crucial point is was he able to inhibit innervation of the facial nerve entirely when he used his tongue? Because use of the tongue does not give very many possibilities of isolated movements - you can move it up, down, left, and right and you may learn to inhibit movement; but when, for instance, he was talking or swallowing, didn't any muscles of his face make an associated movement?

Dr. RASMUSSEN: I would not say never. When he was asked to put his tongue out right and left, there would be never more than the slightest flickering movement; however, this was quite different from the situation when he was examined after one year. There was never any movement when he swallowed.

The interesting thing to me was that in every patient who really worked at it, by the fourth, fifth, sixth, or seventh year, it had entirely disappeared. And the other thing is that in these patients who did the practicing, their facial movements were better in the sixth year than it was in the fourth year. There was continuous improvement. But the patient who said: "I really didn't do the exercises!" never developed this ability to move the facial muscle without voluntarily moving their tongue.

Dr. ZÜLCH: What did the eye do? Have these muscles been examined by electromyography?

Dr. RASMUSSEN: That varied. Sometimes there is always a little closure of the eye. The most spectacular example was a woman who worked very hard and she had practically no movement of the eye about nine times out of ten. One time out of ten there was a flick of the eye, but this lessened progressively through the years in a very interesting fashion.

Dr. ZÜLCH: Theoretically, the best way would be to split up the hypoglossal nerve into the bundles which serve different muscles and movements, and then suture those to the various branches of

the facial nerve using the microtechnique. Then one could have an almost ideal reinnervation.

Dr. RASMUSSEN: With the microscope that may be possible.

Dr. CREUTZFELDT: Such functional restorations are indeed amazing. But there are many examples of this kind. One can, for example, train oneself to innervate individual muscle fibers if one gets the right feedback, e.g. through an oscilloscope connected to the EMG. In the cases mentioned, the patients had to look into the mirror and could thus control their facial movements from another cortical area than they were used to before. In the same way, they can train their right hand to guide their left hand, if it is paralysed, or to use a computerized prothesis. But is this really plasticity in the sense we are talking about?

Dr. PREILOWSKI: I would like to add something to the question of whether we are really talking about plasticity which is also related to the difference between emotional and voluntary movements. Is it not true that when muscles are transposed and people acquire excellent control in new directions, that under stress they fall back into their old patterns?

Dr. BACH-Y-RITA: When they revert under extreme fatigue or emotional stress, this just indicates that the "initial" organization has not been changed; you have only superimposed something on top of it. You said you were not sure that this would be accepted as plasticity; you reorganize the sense of superimposing control in another level. In other words, you have been able to change the hierarchy of the innervation.

Dr. ZÜLCH: I just have a small point to make about the examination of patients with disorders of movement. I feel a little uneasy about many statements we make on the motility of patients. I shall try to make my point just on one observation. We have patients after vascular accidents who have, for instance, a proximal paresis of arm and leg with a better preservation of finger and toe movement; in contrast to the Wernicke-Mann type which has a distal pattern of paresis. Now, one could be inclined to assume patterns of defects of the precentral gyrus where such combinations could be "represented". However, in detailed clinical observations we have found that this is the case in pontine infarcts, i.e. in vertebrobasilar insufficiency. I have been searching the literature for a description of the situation of the various bundles of the pyramidal pathway in the pons, in parallel for instance with the spinal segment where the most medial groups of the anterior horn cells supply the proximal limb muscles and where the most external ones supply the distal muscle groups. I have not found any details about the pons apart from some hints of Dr. KUYPERS. But this example shows how inadequate and false our conclusions about localization and plasticity may be if we do not know such simple facts as the site of the various bundles of the pyramidal pathway in the pons.

I have seen one patient who was tetraparalytic after he had a basilar thrombosis. The only movements he could do during six

years of observation were isolated movements of the three fingers. Now we are trying to solve the question of localization in the monkey, but have not yet come to a conclusion.

Dr. KUYPERS: What you have just described fits very well with my own findings in the cat, and those of Dr. LAWRENCE and myself (4a/b) in the rhesus monkey (5). Moreover, these functional findings are in keeping with various anatomical findings concerning the terminal distribution of the descending pathways, which presumably are responsible for the control of movements. On an anatomical basis, three groups of descending pathways can be distinguished: two of these originate in the brain stem and the third one originates in the pericentral cortex. The largest descending brain stem system originates in the reticular formation, the vestibular nuclei, the interstitial nucleus of Cajal, etc., and functionally subserves primarily the steering of the body and integrated limb-body movements as well as synergistic movements of the limbs. When the animal has only this system available, he can right himself and pick up food morsels by means of a synergistic arm-hand movement. The other brain stem system presumably comes mainly from the red nucleus and provides the additional capacity for independent movements of the limbs, particularly their distal parts. When this system is also available to the animal he can now pick up food by reaching out and opening and closing the hand on a stable arm. The cortico-spinal system was found to amplify these brain stem controls but in addition, probably on the basis of its many direct connections to motoneurons to distal extremity muscles, also provides the capacity to execute relatively independent finger movements. On the basis of your findings I would suggest therefore that in the case of your patient the lesion involved the brain stem pathways but spared at least some of the cortico-spinal connections, which therefore leaves the patient with some capacity to execute relatively independent finger movements.

Dr. ZÜLCH: I think, at least in man, that ipsilateral movements are not possible at will. However, one can, as I have reported earlier, show that there are "identical" "mirror"-movements as associated phenomena, which probably "travel" along the ipsilateral share of the pyramidal pathway.

Dr. MYERS: We have spent some time today on the plasticity of the nervous system - first, with respect to peripheral nerves and then to the spinal cords. I would like now to discuss the remarkable plasticity of the cortex. We shall use the parietal lobe as our example. We have taught corpus-callosum-sectioned monkeys difficult roughness discrimination tasks using one hand. After overtraining through this hand, some part of the opposite parietal lobe was surgically removed. If the *hand* components of areas 3, 1, and 2 were removed, the animal was unable thereafter to perform the discriminations properly but he could relearn it with this hand with retraining (6, 7). When the *face* or *leg* components of areas 3, 1, and 2 were removed, no such deficit appeared. When areas 3, 1, and 2 were removed in their entirety (including the *hand*, the *face*, and the *leg* components), though discrimination performance was lost, relearning again proceeded well. Similarly,

areas 5 and 7 were removed in other animals and whether it was the one or the other or both of these two areas which were removed, a loss in performance was again evident but relearning was again possible. Thus, those difficult tactual discrimination tasks could be relearned either when those areas of cortex which are classically considered as being the receptive areas (areas 3, 1, and 2) were totally removed, or, when, instead, the posterior, so-called associative areas of the parietal lobe (areas 5 and 7) were removed. Indeed, only when the entire parietal lobe was removed did the ability to relearn the tactual discrimination tasks entirely disappear. So the parietal cortex shows a considerable plasticity in its functional capabilities and even a plasticity which doesn't seem to recognize the distinction between the receptive or the associative zones of cortex. In other words, the plasticity of the parietal lobes is such that almost any part of the parietal lobe can carry out its function and a total removal of the lobe, i.e. a loss of the entire functional sector is required for a total loss of discrimination function.

Dr. WOOLSEY: It seems to me that the question here is whether this is plasticity or not, or whether it is a temporary dysfunction following surgery with subsequent recovery due to the components which are already present in this cortex. The cortical areas with their connections to the motor system are certainly going to have their overall function interferred with by any surgery we impose. But after the immediate effects of surgery are over, these areas will begin to function again making what contribution they can. As HUGHLINGS JACKSON said long ago, as cited by O. FOERSTER (8), compensation by an area can only be realized to the extent that it made or was capable of making a contribution before.

Dr. MYERS: You are suggesting that the need for relearning is due to the surgery itself?

Dr. WOOLSEY: I would suggest that, following a partial lesion of the parietal lobe, temporary defects develop from which the animal subsequently recovers through training or in a matter of time. For example, there was a very striking contrast between experiments on behavior done by JACOBSEN, with so-called premotor cortex lesions, and those of T. PINTO-HAMUY. JACOBSON (9) trained his animals to perform latchbox tasks and then operated on them. They lost their ability but then he retrained them and the ability returned. T. PINTO-HAMUY (10) worked on animals in our laboratory. The animals were trained and surgery was performed. Four to six months passed without the animal being subjected to retraining. The animals were then presented with the boxes and they did just as well, in fact even better, than before operation.

Dr. PREILOWSKI: I don't know if I understood you correctly, but could these results not also be explained by equipotentiality of several areas?

Dr. WOOLSEY: I thought that the animals recovered their ability to do the special test simply because they were given a long enough period in which to recover their general motor abilities

and they were then able to carry out tasks, which they couldn't carry out immediately after operation.

Dr. GALBRAITH: Just one comment about a striking example of functional reorganization in man. That is the situation of congenital agenesis of the corpus callosum as compared with the split-brain. I have had experience with only one such agenesis patient; when he was given split-brain tests, there was a remarkable ability to make correct judgements.

Dr. RASMUSSEN: We have tested several such patients and have obtained the same results. I think this has been verified in other institutions as well.

Dr. PREILOWSKI: I would like to make one more comment. I have always been doubtful when there was talk of restitution of motor functions because evaluations were hardly ever made of the exact extent to which the functions returned and of the quality of pre- and posttraumatic performance. Do we really know whether a patient uses all of the available nervous mechanisms, or is he perhaps using only a small portion of the fibers of a functional circuit? Perhaps we saw only the performance of one half of his capacity for a specific task before the lesion. After the insult he uses his remaining capacity and we describe his performance as unchanged?

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The Concept of Diaschisis

Moderator: M. S. Gazzaniga

Dr. GAZZANIGA: This last session is devoted to the discussion of diaschisis. I thought I would begin with the clinical story. This has been very extensively discussed by LURIA (1), who claims that after stroke there is a disinhibition of the diseased area that can be enhanced for instance by drugs. The actual drug therapy is not in use anywhere, as far as I know, outside Russia. In general I think, the experience of most neurologists is that there is very little improvement in stroke patients as a result of physical therapy. STERN (2) and others have worked on basic sensory motor functions and higher cortical functions. STERN took two control groups and sent them through an extensive physical therapy program. He took another control group and did nothing with them. At the end he assessed their recovery and it was exactly the same. Similar observations were made on recovery from stroke using classical means of speech rehabilitation, and no matter what was done, there were no improvements other than what time alone could do.

This leads me to think there really is little improvement at this point on VON MONAKOW'S concept of "diaschisis." There is an initial dysfunction resulting from an actual brain lesion. This dysfunction can be widespread in the brain, but finally and gradually through normal repair processes the brain returns to whatever level it will naturally attain. There is some data to support this idea, as for example the work of KEMPINSKI (3), where he showed that following unilateral cortical ablation there is depressed electrical activity on homotopic points of the opposite hemisphere. The problem with this work is that the time course is so widely different from what is usually described in the clinic. The phenomenon he reports are all over in one hour, while in the clinic, of course, this lasts from six weeks up to six months. Furthermore, there is the metabolic work of HOEDT-RASMUSSEN (4), which shows that the cerebral blood flow is changed bilaterally after a stroke. These changes correlate well with the clinical course of diaschistic processes.

What I would like to consider is the behavioral recovery of function. When this is found I think it usually can be explained in terms of preexisting behavioural processes being reordered by the patient or animal to recover from the detrimental effect of a particular brain lesion.

Here I would like to mention two experiments. First in rats, in which bilateral lateral hypothalamic lesions had been made to produce a state of adipsia, we tried to see whether we could get an adipsic rat to drink. Classically, they are reported not to

voluntarily drink for weeks and they have to be fed with wet mash. Our rats also refused to drink, showed all the classic adipsic signs and the probability they would drink in half an hour's time turned out to be zero. During this phase of acute adipsia, however, they would, in half an hour, run and exercise within an activity wheel for about 150 seconds. Then we placed a proviso. If they wanted to run, they had to drink first; so by licking a few times on a drinkometer, the wheel was freed and they could run. What happened? The adipsic rat instantly started to drink water. In other words, these adipsic rats, because of the altered environment, wanted to run but in order to do so they had to drink.

After this experiment we thought we would see whether an animal with an infratemporal lesion would discriminate an order to run. This proved unsuccessful because as we found out, a monkey who was given the opportunity to run will do anything not to run. When given the opportunity to run, they stood in the box and kept the wheel motionless; so we changed the proviso on them. Initial training involved food reward, but following learning the proviso was changed to running. When the stimulus comes on, the wheel starts to run and if they hit the button it stops. These monkeys literally lived by the response panels because they just did not want to run at all. Then when a lesion is made which should produce a learning deficit in being able to perform a pattern discrimination, we found that in post-operative testing that they instantly performed correctly. The point here is that we have a situation where pre-operative training on two different behavioral contingencies seem to insulate the brain from the detrimental effect of this lesion. In other words, the animal experiencing this discrimination training had the opportunity to solve the problem in a number of ways, which means that there are a number of different brain mechanisms involved in that process. Thus it would seem highly unlikely that one lesion will eliminate all of one behavior. What I am trying to say is that it is sometimes depressing to brain researchers to find how many ways the brain can solve a problem.

In the clinic, by using a special language system we can see what would be called classically recovery of function in global aphasia. Here, we took Dr. PREMACK'S chimpanzee language system (9), where he lists various examples of a natural language and on a series of 12 patients with severe global aphasia, we were able to teach them the language.

Dr. PLOOG: Were the patients just confronted with the symbols and no instructions?

Dr. GAZZANIGA: Yes, without instructions. It is a point worth noting, that just as the adipsic rat will drink in order to run, an aphasic patient will learn a system if you picked a proviso that he wants. He also must want the reward that the experimenter offers, which we forget all too often. In neuropsychology, we often administer beautifully standardized tests, while the patient is looking out of the window, so to speak. When there is a zero response the neuropsychologist reports a deficit. I have

now to remember that I am the moderator, perhaps I should ask now what do you know about diaschisis? The literature seems to leave the question open as to understanding this phenomenon in solid physiological terms.

Dr. OBRADOR: There is one point I want to raise for discussion: we know the "diaschisis" in the old Monakow sense - when you cut some important efferent nerve pathways, like the pyramid, this results in a depression in the form of a spinal shock. I wonder how far such a "diaschisis" spreads through the central nervous system, for instance, whether it needs some preferential pathways? That is to say, is there initially any area within the central nervous system where "diaschisis" arises that is not correlated with specific anatomical connections?

Dr. ZÜLCH: I have some observations which may be relevant to this problem of diaschisis. If you make a hemispherectomy because of a tumor and the patient has not yet had a hemiplegia with a subsequent restitution in synergies, directly after hemispherectomy he will show a completely flaccid paralysis without any possibility of movements in the form of synergies. These patients recover only after months. But if you perform a hemispherectomy on a child with a birth lesion, who has developed the usual synergies, it can use its synergies immediately after the hemispherectomy as well as before the operation.

Now this is the general rule. But we had one case which was different from this pattern. This was a man who had a slow-growing glial tumor, which was thought to be inoperable by some neurosurgeons and was therefore radiated. As a consequence he had probably delayed radiation necrosis and subsequently he had a complete flaccid hemiplegia from which he recovered with synergies and spasticity. One year later a hemispherectomy was performed because we were concerned about the growing tumor. However, the hemisphere showed only radiation necrosis and no tumor tissue was found. The important observation was that after two days the synergies of this patient were like the old pattern although he had had his pyramidal lesion and hemispherectomy as an adult. I think that the anatomical substratum for these synergies, which is well below the cerebrum and somewhere in the brain stem, had already been "called into action" long before the operation and therefore was not "hit" and thrown out of action by the operation, as in a patient who is hemispherectomised for a tumor. Here in this last case "diaschisis" (or whatever that may be in neurophysiological terms) did not sever the mechanism of a "lower level", to use the terminology of HUGHLINGS JACKSON. Here were three different examples of the reaction of the motor system to hemispherectomy, which may pertain to the problem of "diaschisis".

Dr. CREUTZFELDT: I would like to give an example from neurophysiology about diaschisis. As you know, there is a connection between the visual cortex and the superior colliculi, i.e. between the retino-geniculate-striate and the so-called second visual system. The question is whether the collicular units are functionally dependent on the visual cortex. Collicular units of cats are specifically sensitive to stimuli moving out of the

foveal region. After acute decortication, STRASCHILL and HOFFMANN (6) found that these properties of the collicular units remain the same. However, WICKELGREN (7) and others did chronic experiments and reported that 1 to 2 weeks after the cortical ablation the units had lost their characteristic direction sensitivity. In fact, recent experiments of STRASCHILL and HOFFMANN have shown that the direction sensitivity may not be completely abolished even after chronic cortical ablation, but the units are less responsive and more easily disturbed by anesthesia. This indicates that the lower system develops different functional properties once the cortical afferents have degenerated.

Dr. ZÜLCH: I am afraid that we have to close now for time reasons. Diaschisis seems to be an interesting problem as shown by the few examples we have heard and which we should all think over again and perhaps discuss again at a later meeting.

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