FUNCTIONAL EXPLORATION OF THE BRAIN

FUNCTIONAL EXPLORATION OF THE BRAIN WITH STEREOTAXIC TECHNIQUES*

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AFTER the pioneer work of Horsley and Clarke in animals and Spiegel et al. in humans, several other stereotaxic instruments and technical improvements were described in the literature. All these methods had a common aim—to locate specific cerebral structures through small burr holes, using bone or intracerebral landmarks as reference points. Interaural line, inferior orbit, habenula, pineal body, ventricles and other structures have been used as references. The main problem has been to find appropriate anatomical correlations. Some technical difficulties concerning distortion of brain preparations have been described but the greatest handicap has been anatomical variations. Radiological studies of the skull of each patient before the operation may help; however, neurosurgeons are generally aware that anatomical variations limit the accuracy of stereotaxic methods and considerable work has been done to learn the margin of possible error, which may be several millimeters. A second limitation often overlooked is the existence of physiological variations. Even with ideal anatomical conditions, if we were able to hit systematically a cerebral target—a point of the pallidum for example—the effects of electrical stimulation probably would vary in different patients. The purpose of this paper is to comment on this functional variability and to discuss different types of exploration which may improve the accuracy of stereotaxic techniques. Our experience is based on stereotaxic exploration of the brain in a large number of monkeys and, in collaboration with Dr. Hannibal Hamlin, on manual placement of intracerebral electrodes in a group of 30 patients.

Electrical Stimulation. A well known fact emphasized a long time ago by Sherrington and confirmed often in the operating room is the unpredictability of stimulations of the motor cortex. It is true that there is a somatic distribution, with leg represented in the upper part and face in the lower part of the precentral gyrus, but it would be risky to predict the result of the stimulation of a concrete point in area 4 because the shape of sulci and gyri do not correspond exactly to motor representation. When a surgeon tries to remove the motor area of the hand, for example, anatomical landmarks are used for general orientation but it is the functional exploration that is decisive to delimit the excision. In deep structures the problem is

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similar. Electrical stimulation of the posteroverentral nucleus of the thalamus in the unanesthetized monkey produces offensive-defensive reaction but again it would be difficult to predict the results of stimulation of a specific point in this structure. However, from the motor cortex we can expect motor activity and from the posteroverentral thalamus emotional responses. Analysis of somatic, autonomic and psychic effects evoked by electrical stimulation may help to identify anatomical structures and to pinpoint functional localization in each case. This is well known in surgical therapy of pain in which electrical exploration is usually performed before the permanent interruption of pathways. Something similar might be done in stereotaxic techniques, especially when electrodes are left in the brain for several days. Multiplicity of leads allowing the exploration of many points is particularly useful. One problem, however, must be mentioned. Several authors, from Sherrington to Penfield and Jasper, have mentioned a "cortical instability"; stimulation of the same points at different times gave different results. If this is true, interpretation of functional exploration would be most difficult. However, we must consider that during surgical operations experimental conditions are not constant. Level of anesthesia may change and even with local anesthetic many factors are difficult to control, such as physical and mental stress of the patient, position and pressure of the electrodes, moisture on the cortex, local circulation and temperature of the brain, impedance of the contacts, etc. Variation of these factors could be responsible for the cortical instability. In our studies with intracerebral implanted electrodes in both animals and humans these factors, on the contrary, were constant, and stimulation of the same points gave similar results throughout the observation period. In one monkey, for example, electrical stimulation of one point in the motor cortex evoked extension of the contralateral arm with similar motor characteristics for 6 months of observation and many other animals have confirmed reliability of results. In humans with implanted electrodes reliability of motor effects evoked by electrical stimulation of area 4 has also been repeatedly demonstrated and other effects such as déjà vu or increase in friendly verbalization were evoked by electrical stimulation of the frontotemporal region with the results being specific and repeatable, with a significance demonstrated by statistical analysis. It should be emphasized that effects of electrical stimulation of the brain could be predicted after functional exploration, but prediction would be difficult and often wrong when based only on anatomical data.

Spontaneous Electrical Activity. The claim of Kornmüller concerning a correlation between electrical activity and cerebral cytoarchitectonics unfortunately has not been confirmed. It is true that, as described by Penfield and Jasper and others, the occipital, parietal and temporal cortex have a regular rhythm of about 10 cycles per second while the sensory and motor cortex exhibit a faster frequency and different pattern, but these correlations are too gross for the purpose. Within the brain, also, it is easy to differentiate the rather flat activity of the septal areas from the spiky pattern of the
Fig. 1. Local after-discharge evoked by electrical stimulation of three pairs of adjacent contacts (1–2, 3–4, 5–6) of the right needle (RT.ND.). Observe that in each case the evoked after-discharge was different. The pattern of each was reliable and its study could be used for functional identification of cerebral structures. RT.ND. = depth electrodes in the temporal lobe. RT.FP. = subdural cortical electrodes on frontal lobe. Contact #1 at the tip, contact #7 at the top of each array of electrodes. Dot on diagrams = top of depth electrode shaft. (Epileptic patient)
hippocampus but up to now fine differences in electrical pattern within discrete anatomical structures have not been demonstrated and therefore study of spontaneous electrical activity does not add accuracy to the stereotaxic technique. Knowledge of spontaneous electrical pattern could, however, be useful to detect gross errors in the location of contacts. Also a mechanical shifting in the position of implanted leads could be identified by analysis of spontaneous activity because local electrical patterns are in general very reliable.

*Evoked Electrical Activity.* Local after-discharges evoked in the temporal lobe of a patient by bipolar electrical stimulation of three pairs of adjacent contacts of one array of electrodes are shown in Fig. 1 (square unidirectional pulses 100 c./sec., 0.5 msec. of pulse duration, 8 V.). In each case stimulation of contacts spaced 8 mm. apart evoked different patterns of after-discharge. The shaping up of the activity probably depended upon local functional factors and also upon neuronal connections which may be considered a part of the functional characteristics of the area. The interesting fact is that different areas exhibited different types of evoked after-discharges and this may be important in the identification of cerebral structures. In addition, the problem is closely connected with basic problems of epilepsy and deserves further investigation. Existence of different seizure patterns in areas with anatomical proximity and reliability of each pattern through periods of months have been repeatedly demonstrated in monkey experimentation.

*Action of Drugs.* In previous studies in unanesthetized monkeys with intracerebral electrodes we developed a battery of tests to analyze the possible site of action of drugs that affect the central nervous system. Local electrical activity, thresholds for minimal motor responses, thresholds for local convulsive effects, recovery time of convulsive capacity and thresholds for after-discharges could be modified specifically in different cerebral structures by several drugs; 14 per cent CO₂, for example, had a minor action on the precentral gyrus while it increased 640 per cent the threshold for electrical after-discharge in the amygdaloid nucleus. Trimethadione did not affect the thresholds in the amygdala but increased them considerably in the thalamus and precentral gyrus.

The same cerebral area might respond specifically to different tests. For example, in one point of area 4 parenteral administration of diphenylhydantoin did not modify the threshold for minimal motor activity but increased the threshold for motor convulsive activity.

The use of implanted electrodes thus permits the study of site of action of drugs and also of the problem in reverse, which is the identification of cerebral areas by their functional characteristics. Stereotaxic techniques are still in the process of being developed and more knowledge of the physiology of the brain is needed, but we may expect in the future that the combination of the different types of exploration described in this paper might lead to functional identification of many cerebral areas.
FUNCTIONAL EXPLORATION OF THE BRAIN

SUMMARY

Stereotaxic exploration of the brain has two main handicaps: the anatomical variation and the less well known functional variation. Somatic, autonomic and psychic effects evoked by electrical stimulation of the brain are reliable and specific. They may be used for functional identification of cerebral structures. Recording of spontaneous electrical activity of the brain characterizes large areas but has a limited use for discrete localization. In some areas evoked local electrical after-discharges have typical patterns which may be useful for identification. Several tests are mentioned which are specifically modified by drug administration; by these means site of drug action may be studied and cerebral structures may be functionally identified.

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274 SYMPOSIUM ON STEREOTACTIC SURGERY


DISCUSSION

DR. BAILEY: Now, symposia have the advantage of giving the audience a general oversight of the extent of the problem and also of some of the possibilities for solutions up to date. Such a symposium is also very frustrating for the participants because no one of them, except by the indulgence of the Chairman, has time to develop his subject as he wishes. Since symposia are organized after this fashion and the Chairman has to exercise more or less arbitrary control over them, we have been able, however, to preserve enough time, since I understand that this symposium is supposed to run until twelve o'clock, for a bit of discussion which will be begun by Dr. David Cleveland of Milwaukee.

DR. DAVID CLEVELAND: After listening to the presentations this morning, I have enough questions to carry us on until three o'clock, I am sure. However, I shall avoid that and limit my remarks to a relatively few.

First, however, we should give credit to Drs. S. W. Ransom and Loyal Davis for reviving the Horsley-Clarke apparatus in the early thirties. It was with them that I did my first work in stereotactic surgery, making lesions in the paraventricular nuclei and in the hypothalamus. Dr. Ingraham and Dr. Magoun pioneered in a physiologic experimental manner with the Horsley-Clarke stereotactic apparatus, and we have all benefited by their experiences.

Dr. Bailey has described—and rightly so—the need for functional and physiologic testing with the stereotactic apparatus in humans, as well as in animals.

I might say that from 1936 until 1943, I carried out a series of experiments in the basal ganglion, using the Horsley-Clarke apparatus in monkeys and in cats. After many, many experiments over these years, I obtained information which I felt was relatively valueless. I had nothing new to offer, nothing to publish. Since we have been doing work on Parkinson’s disease, as many of us have been forced to some extent, we have operated on 36 patients and the majority of these patients have had physiologic testing by stimulation before injection. Our results so far have been on the negative side. We have not been able to tell by stimulation tests when our needles or cannulas are in the area of the basal ganglion, or the globus pallidus in particular. We are warned, however, when the needle or cannula is in the internal capsule.

Dr. Wycis’ talk on the use of the stereotactic apparatus in the convulsive disorders is indeed interesting. I have one question. Has he ever seen convulsive disorders in Parkinson patients or in epileptics who had Parkinson’s disease and, if so, what has been his experience with doing a chemopallidectomy in such a case?

We owe a great deal of credit to Dr. Cooper for stimulating interest in this disease. Much has been done before him, of course. Dr. Meyers is one of the pioneers whose work stimulated interest in this field. But Cooper certainly has brought it into the public eye and created a need, or at least a demand for this type of work. I think his studies have been excellent.

In our laboratory we have tried to demonstrate the anatomical landmarks of the globus pallidus. Our findings agree with Dr. Cooper’s quite closely. We have found that the medial globus pallidus is about 1.2 cm. wide and 1.4 cm. long in its greatest dimensions. I have noted in the various films and slides shown today that there seems to be quite a variation between the location of the needles in the globus pallidus. Some are ahead of the sela and some behind the sella, some are above and some below.

In our anatomic studies, we have found that the medial portion of the globus pallidus lies approximately 15 to 17 mm. from the midline. With the needle at 10 mm. we have always
reached the internal capsule. The anterior third of the globus pallidus lies at the posterior portion of the sella. The posterior portion of the globus pallidus lies approximately 9 mm. behind the dorsum of the sella.

With those findings in mind, we have tried to define our landmarks accordingly. Dr. Cooper has mentioned and shown that a line passing from just 1 cm. ahead of the external acoustic meatus at the zygoma, through the upper tip of the third ventricle to a point \( \frac{8}{3} \) to 9 cm. lateral to the midline and \( \frac{2}{3} \) cm. behind the foramen of Monro will pass through the globus pallidus. This has been our experience also.

Dr. Bertrand’s apparatus is indeed unique, and I am sure has a great deal of localizing value. I wonder about the use of the core-removing snare. I worry about the ultimate danger of producing hemorrhage. He says he turns it part way, and then releases the snare before turning it again.

The only experience I have had was with a snare leucotome. As I released the snare, I caught a vessel in the loop and pulled it out with the leucotome. Years ago I attempted to do a prefrontal lobotomy by that method and I have never used it since. I wonder if Dr. Bertrand has had any similar experience with it. I feel it carried potential danger.

I also understand that he stays 15 mm. from the midline, passing his instrument straight down to the globus pallidus. I am sure that in doing this, i.e. staying that close to the midline, the cannula will pass through the lateral ventricle and increase the operative danger. Certainly, a chemical pallidectomy should not be done in this way. I consider that Dr. Cooper’s \( \frac{5}{3} \) cm. lateral approach point is an excellent landmark to use.

Regarding stereotaxic surgery, I have had no experience with the convulsive disorders, or other disorders mentioned, including intractable pain. Stereotaxic surgery, except for gross structures, should be limited to the university hospital or the hospital where meticulous control and technique can be developed. It should not be used where it cannot be controlled scientifically. For the average individual, stereotaxic surgery should be used toward the destruction of gross structures rather than the making of accurate small localized lesions.

We have devised a simple instrument for making lesions in the globus pallidus which is based on the same principle as most of the others, including Dr. Cooper’s. It enables the making of a gross lesion in the globus pallidus by a simple means.

[Slide] This is the instrument which after a 30 to 40 cc. pneumoencephalogram has been performed, either by the cisternal or lumbar route, and the anterior horns, foramen of Monro and third ventricle have been visualized radiologically, is attached to the skull at points A and B and fixed at C. Point A, in the skull, should lie 1 cm. in front of the acoustic meatus at the level of the zygoma. Point B should lie 8 to 9 cm. lateral to the midline, so that in the anteroposterior view of the skull, a line passing from Point A to Point B would pass through the upper tip of the third ventricle. Point B should be placed in a plane 14 to 16 cm. posterior to the nasion, depending upon the size of the skull. A wire passing across the scalp, from A to B, should lie or be visualized in a direct lateral roentgenogram, \( \frac{3}{4} \) cm. behind or posterior to the foramen of Monro. Point B should be moved anteriorly or posteriorly to the point where the plane AB will lie \( \frac{1}{2} \) cm. behind the foramen of Monro.

These landmarks have been carefully defined by Cooper and verified by others. The axis extending from A to B in the above plane will invariably pass through the center of the medial globus pallidus. Following the determination of plane AB, a burr hole is placed in this plane \( \frac{5}{3} \) to 6 cm. lateral to the midline on the point A side. The dura mater is opened sufficiently to allow the insertion of a suitable cannula or coagulation needle. The instrument is then fixed at points A, B and C, as illustrated. [Slide] The transverse wire D is attached to the instrument at A and B, so that it represents axis AB projected out of the skull. The cannula guide E, with its pointing wire F, is then attached to the guide with the external wire pointing toward the inner canthus of the eye. The cannula will always go in the same direction as the pointer in the exact plane of axis AB. When F is pointed from the dural opening to the internal canthus of the eye, the cannula will pass directly through the dural opening to axis AB to a point \( \frac{2}{3} \) cm. lateral to the midline or in the center of the medial globus pallidus. The distance that the cannula should be inserted to reach axis AB can be determined by measuring the dis-
tance from the upright wire on F to the transverse wire D. In this way, the entire measurements can be made accurately, external to the skull, without guesswork or trial. The position and localization of the cannula are verified by roentgen ray and then the cannula is fixed to the paracranial tissue by chronic 000 sutures, and to the skin by silk or cotton sutures. The cannula guide is then moved from the cannula by elevating the holding plate H and sliding the guide away from the cannula. The guide, itself, is then moved from the skull. When the guide is fixed at A and B, axis AB remains constant regardless of the rotation of the guide on AB. Any point on axis AB can thus be reached in the same manner as a spoke of a wheel always reaching the hub.

A large number of our patients with Parkinson's disease are complete charity patients, and because the Cooper balloon cannula, which is superior to others, is expensive, we have used a simple polythene tube over a stylette in the same manner as the Cooper cannula.

The technique of injection has been adequately described, but in brief it is that of injection of 2/10 cc. of novocain, to determine the physiologic effects following the slow injection of a small amount of alcohol and Hypaque, 1/10 cc. in 5 min.; 4/10 cc. being the most injected at one sitting.

The guide can be used in a similar manner for either electric coagulation or coring, if preferred to alcohol injection.

In summary, I believe that we have a good method. Stereotaxic surgery has a definite place in our neurosurgical armamentarium, but the more complicated type of stereotaxic surgery, requiring more complicated instruments, will for some time have to be limited to centers where they can be handled and evaluated properly. We should all be cautious in doing this work and not do it blindly without experience or study.

Dr. RUSSELL MEYERS: Taken in the aggregate, the papers we have been privileged to hear at this symposium provide a cogent summary of observations and inferences relative to stereotaxy as currently applied to problems in human neurology. The authors have dealt ably with matters of basic as well as clinical scientific interest and have succeeded in bringing us up to date in respect of a technical agent that has been usefully employed by neuroanatomists and physiologists for over a quarter of a century and which, it seems safe to say, is destined to become within the foreseeable future an integral agent of neurosurgery. If any doubts as to the potential uses of stereotaxy in human problems have existed up to now, this morning's symposium must surely have dispelled them. A start—a commendable start—has been made; it now remains for us to exploit this agency to the fullest possible advantage of our patients.

I. At this point we might pause to consider some of the more extended meanings and implications of the papers just offered. In this connection, I venture to delineate certain IDEALS that might advantageously be adopted in respect of stereotactic procedures at large, regardless of whether employed principally for basic research in neuroanatomy, physiology and pathology or for the amelioration of human suffering. Ideally, then, the use of stereotaxy should entail:

1. **No mortality.** This item requires little elaboration except to say that an obvious exception prevails where stereotaxy is used in animal experiments expressly concerned with inquiry into the mechanisms of death itself.

2. **No morbidity.** The stereotactic agent should produce no neural behavioral deficit, overt or covert, beyond that deliberately planned by the operator. In particular, as used in clinical neurological problems, patients should not be expected to exchange one neurological deficit for another, even when the stereotactically induced deficit (e.g., a spastic hemiparesis) is manifestly preferable to the pre-existing deficit (e.g., a severe hemitremor).

3. **No inadvertent damage to tissues** disposed along the path of the physical agent; or neighboring upon or lying remotely away from the structure and/or the projections that engage chief attention. It is especially desirable that the stereotactic agent should spare all blood vessels that happen to traverse the path followed by the penetrating instrument and
those that course through the site of intended lesion, destined to irrigate structures lying at some distance beyond the lesion. It should be remarked that in the recent history of neuroanatomy and physiology, the unwitting production of damage of this sort has often equivocated the interpretation of "function" and gravely compromised therapeutic results.

4. Precise placement. The stereotactic technic employed should enable the operator to bring the effective tip of the pick-up or coagulating electrode (or hollow needle or catheter) directly into the intended neural structure on the first pass, one hundred per cent of the time.

5. Controlled extension of lesion. Once the tip of the physical agent has been brought to rest at the intended site, the stereotactic device should permit the operator expeditiously to produce a lesion of any predetermined polyhedral figure having any prescribed axial orientation.

6. Selective discrimination among structures. The measures employed up to now for producing stereotactic lesions have, for the most part, entailed relatively crude agents which can best be characterized as non-discriminating. Thus, mechanical leucotomies and rotating snares, aspirators, electrocautery and chemical solvents commonly injure all tissues—neurocytes, myelinated and unmyelinated nerve fibers, glia, neurophil, ground substance and blood vessels. It would obviously be advantageous to possess a stereotactic agent capable of selective discrimination, not only among macroscopic and microscopic but also among microscopic structures (e.g., cortex as contrasted with subjacent "U" fibers; neural and glial tissues, with blood vessels; neurocytes, with nerve pathways; myelin, with axis cylinders; enzymes, with carbohydrate molecules; keratin molecules, with phospholipids, etc.). That the pursuit of this ideal is no science-fiction dream will be brought out in our later discussion of ultrasonic stereotaxy.

7. Unfailing achievement of the envisioned pathophysiologic or clinical therapeutic result.

II. Admittedly, the seven ideals delineated above are high and, in the present circumstances, quite beyond our ability to realize. Yet, if we are to improve our efforts continually, they appear to be no less than what we should be prepared to adopt. If we are dissatisfied with the present circumstances of our knowledge and therapeutic effectiveness in the neurological realm (as I take generally to be the case), then improvement, if it is to be economically accomplished, entails the taking of certain deliberate steps. The first of these consists in specifying the desirable state of affairs. Here is where preset IDEALS prove most serviceable. The next step is to assay dispassionately the present state of affairs, identifying as completely as we can those respects in which we fall short of the envisioned aims. This then leads to a consideration of the likely reasons for our shortcomings. Next, we must cast about, in and beyond our repertoires, for possible solutions, adopt the most promising of them, even if tentatively, and contrive to implement them. Finally, we must develop a yardstick with which we can reliably measure whether we have moved from the present to the desirable state of affairs; and if so, by what route(s) and how far. Needless to say, our yardstick must be employed as free as possible from bias.

III. It lies beyond the scope of this discussion to deal intensively with all the matters alluded to above. We should, however, take advantage of the moment to consider the limitations that conspicuously compromise our present efforts.

It is clear in the first place that there are at least two necessary conditions of effective action. These consist in the possession of (a) a dependable stereotactic instrument and (b) reliable "maps" or coordinates of the brain. We may pass lightly over the former as being a virtual fait accompli. It amounts, at least in principle, to a problem in three-dimensional space analysis, the solution of which lies easily within the capacities of geometers, trigonometers, engineering physicists and precision toolmakers. We do not lack for stereotactic instruments capable of meeting our severest demands for accuracy.

It is the second of the mentioned necessary conditions—that of acquiring reliable brain coordinates—that poses a knotty problem. In general, our basic difficulty stems from the existence within any species of individual variations—a circumstance that has vexed neuroanatomists and physiologists as it now troubles the neurosurgeon.
Several coordinate systems have been drawn up for cats and for monkeys since the first such tridimensional maps were introduced by Horsley, Clarke and Henderson.* These differ among themselves in many particulars, so much, in some respects, as to be irreconcilable if not frankly contradictory. It is apparent, of course, that their differences are dependent upon differences in the authors’ own abstractions, i.e., their ideas of the “common denominators” shared among the particular brains of the cats and monkeys they have studied as related to those of cats and monkeys in general. This makes it understandable why, when an experimenter adopts a particular coordinate brain map for his purposes, he so often finds himself afar from the mark.

The method employed in the experimental laboratory to compensate for such disparities between “map” and “territory” as actually explored is to sacrifice the animal and implement a histological check-up. Animals exhibiting “proper hits” are retained and failures are rejected or reserved as “controls.”

Unfortunately, this method of sacrificing the subject and subjecting the brain to intensive histological check-up is not accessible to the clinician and is unlikely so to be until and unless our ethics undergo a radical change. In the instance of the human, then, our only recourse

must be to the realm of therapeutic effect, i.e., to the observable degree of success and failure as related to some manifest neurologic disorder. Thus, in the case of hyperkinesia, the degree of success of the stereotactic procedure must be evaluated in terms of the degree of abolition of the abnormal movements.

We must now inquire as to why the difficulties subtended by individual differences have been so persistent. The answer appears to reside in the fact that the brain coordinates introduced by Horsley and Clarke and followed in almost all experimental work since 1930 have been based upon reference points of the skull. The underlying principle has involved three spatial planes, mutually intersecting at right angles. One corresponds to Reid’s line, from the inferior orbital margin to the middle of the external meatus or some line parallel to this; a second to a line erected perpendicular to the first and passing through the middle of the external meatus (the internarial line); and a third corresponding to the midsagittal line.

In 1948, Dr. Robert Hayne and If exhibited a series of three separate coordinate systems for the human brain based upon our studies of 26 cadavers. One set of coordinates seemed applicable to dolichocephalic, one to mesocephalic and one to brachycephalic shapes of head. We were at that time impressed with the unreliability of any one abstract formulation for the human and expressed the opinion that coordinates would eventually have to be prepared not only for each of the three principal anthropologic types of head, but for variations in size within these types. We suggested that these might be feasibly arrived at by developing mathematical factors for correction and actually used these factors on matrices to overcome the effects of fixation and shrinkage.

Our early misgivings concerning the reliability of brain coordinates based upon skull landmarks was shared by other workers, including Drs. Spiegel and Wycis,‡ whose 1952 atlas made use of the pineal shadow as the prime point of intersection of the three “zero” planes. More recently, the unpublished studies of Drs. Bailey, Amador and Blundell in Chicago have convincingly demonstrated the low degree of reliability that obtains when bony landmarks are employed and the uncertainty that attaches even to the use of arbitrarily selected points in the human brain itself as “zero” landmarks.

These are formidable matters. The question now arises, is it in any way possible to get around such difficulties? One suggestion I should like to offer is that we agree henceforth to


abandon further attempts to use skull landmarks as the bases of human brain coordinates. The non-correspondence of skull and brain appears by now to have been so convincingly established as virtually to doom further efforts along these lines. The alternative is to make conveniently demonstrable brain structures the points of reference from which coordinates in the three spatial dimensions can be erected. But even this is not enough. We shall probably find it inadvisable to employ any one set of zero planes based upon a single cerebral structure, such as the pineal shadow. It would seem to me more feasible to construct separate coordinate systems, depicting the cerebral structures clustering around certain arbitrarily adopted landmarks of the brain. Thus, we might make a series of maps of the minor variations of structures neighboring upon the posterior margin of the mid-portion of the anterior commissure, such as has been utilized by Drs. Sweet and Kjellberg. It should be possible by similar procedures to set up fairly reliable coordinates of the structures clustering about the fornix bordering upon the foramen of Monro; the posterior or habenular commissures; a tangent cutting across the anterior margin of the pons and intersecting some other structure conveniently demonstrable by pneumoencephalography; and so on.

With a general "target" furnished in this manner we should then need some device by means of which the bull's eye within the more general target could be "hit." Such would involve a certain amount of trial and error, as explicated in the procedure described this morning by Dr. George Austin. Unfortunately, with the ordinary devices now at our command, such trial and error would entail a good deal of local tissue damage. What we need, obviously, is some means of making a relatively harmless, reversible lesion. The use of procaine hydrochloride, as introduced by Narabayashi and Okuma,\(^*\) was a move in this direction. Unfortunately, one cannot be sure of the limits that might be respected by injected aegnecies; nor could one be sure that a more enduring lesion, produced by a chemical solvent injected later, would necessarily follow the same pathways of diffusion as the procaine.

IV. This brings us to a consideration of the use of ultrasonic beams in stereotactic work. I wish that my collaborator, Professor William Fry, physicist at the University of Illinois, were here to explicate the matters which he has been so instrumental in developing. In brief, however, an instrument capable of precise stereotactic control has been fashioned and employed on well over 300 experimental animals, depending for the production of cerebral lesions upon the "phased" intersecting of four ultrasonic beams having a frequency of 980,000 c./sec. delivered by two pairs of piezo-crystal transducers arranged at polar opposites. The brain appears not to be damaged along the lines of convergence or divergence of these beams. The tissues at the point of intersection are bombarded at an acoustic particle acceleration of 400 cm./sec. and the exposure period can be varied from one to several seconds. Any predetermined position, size and geometric form of lesion can be produced by such a device. The lesions are clear-cut and are attended by negligible damage to bordering tissues. By a proper arrangement of parameters it has been recently proved possible to produce a transient, reversible effect, for example, by "buzzing" the lateral geniculate body, to temporarily abolish "photic driving" of the occipital pneumoencephalographic recordings. The transient effect having in this way established the correctness (or incorrectness) of the target "hit," it can be followed by ultrasonic parameters such as to produce an enduring effect.

The chief limitation of this modality inheres in our knowledge of the physiology of the structures selected for "buzzing." For example, we have a useful yardstick for the geniculate bodies, motor nuclei, etc., but lack such for the other structures, such as the mammillothalamic tract, which have been precisely interrupted by ultrasound in the experimental animal.

Ultrasonic beams exhibit the desirable property of selective discrimination. Curiously enough, the most susceptible intracerebral structures appear to be the myelin sheaths, after which, in order of susceptibility, come the axis cylinders, neurocytes and, lastly, blood vessels.


Whether further critical discriminations can be produced by ultrasonic beams remains for us to explore.

During the past two and one-half years Professor Fry and his staff at the University of Illinois and the Neurosurgical Division at the University of Iowa have collaborated in building an ultrasonic apparatus adaptable to human use. This is now in the final stages of assembly. Our immediate intentions are to deal with two major areas of clinical interest: the hyperkinetic-dystonic disorders and the problems of intractable pain posed by postherpetic neuritis, phantom-limb pain, Déjerine's thalamic syndrome and causalgia.

We have recently designed an ultrasonic scanning device by which it is hoped we may be able to search safely within a general target, say, the paleostriatum, to find the bull's eye, say, the ansa lenticularis. The possibility, already realized in animals, of making reversible lesions, the effects of which will pass off in 5 to 10 minutes while the patient is being observed, will, it is hoped, enhance our efforts. Once the critical site has been identified in this way, it will be a relatively simple matter to change the parameters and buzz the site for the production of an enduring lesion. It should be possible for us to report on the first human cases at the next meeting of this society.

**Dr. J. Lawrence Pool:** Because of the importance and comparative novelty of pallidal surgery, we should like to contribute our modest experiences and then ask a question.

We too have been using the leucotome method although we do the entire procedure, including air studies, at one stage under local anesthesia, and use Polaroid film to speed radiological localization. Like Dr. Bertrand, we have also found that a 2 to 3 mm. advance of the instrument may sometimes be necessary to achieve any relief of tremor or rigidity.

Of 28 operations on 19 patients, 10 were leucotome procedures, 9 ligations of the anterior choroidal artery, 6 electrocoagulations (including 2 by the Guiot approach), and 3 chemopallidectomies. There were 14 cases of Parkinson's disease.

Marked relief of tremor and/or rigidity followed 13 operations in 10 patients and some improvement in 4. Thus the rating of operative improvement was 61 per cent and of case improvement, 74 per cent. Only 1 of 4 reoperations on the same side led to improvement. Marked bilateral relief of tremor and/or rigidity, however, occurred in 3 of the 4 patients who had a two-stage bilateral procedure. The fourth patient died. Two postoperative deaths have led to an operative mortality of 7 per cent and a case mortality of 10 per cent. Both were poor-risk patients; only 1 followed use of the leucotome.

Approximately 50 per cent of those patients who were improved as to tremor and rigidity, however, showed little or no postoperative gain in general ability because of continued poverty of volitional activity. Some of these were patients who were hypokinetic or retarded in the initiation of thought, speech and action prior to pallidal surgery; others suffered from a rapidly progressive disease process. We feel that such patients are victims of widespread cerebral pathology, as indicated by clinical and psychometric studies, pneumoencephalography, and the gross pathological appearance of the brain at operation.

However, in 2 other such patients having no significant relief of tremor or rigidity, pallidal surgery led to distinct lasting psychological improvement.

May we ask Dr. Bertrand and other speakers if they have noted a similar dissociation of postoperative effects suggesting that dyskinesia, hypo- or bradykinesia, and psychological state may be separate components of the advanced Parkinsonian syndrome, each subserved perhaps by a different pattern of pathological and physiological disturbance? These are obviously important considerations both as to research and the selection of patients.

**Dr. Bailey:** It may be that some of the patients are unable to pay $20 for a catheter, but everybody knows that any neurosurgeon can easily buy a $55,000 instrument. Still, even the neurosurgeon, I think, wouldn't object to having the price of these instruments brought down somewhat.

There is nothing I like so much as a good free-for-all and I wish it were possible to continue this discussion. Unfortunately (and I did not make the arrangements), luncheon will be served in this room and it is necessary that we evacuate it immediately.