JOSÉ M. R. DELGADO*
HANNIBAL HAMLIN†
YALE DAVID KOSKOFF‡

Departments of Physiology and Psychiatry, Yale University; the State Hospital for Mental Diseases, Howard, Rhode Island; and Montefiore Hospital, Pittsburgh, Pennsylvania

ELECTRICAL ACTIVITY AFTER STIMULATION AND ELECTROCOAGULATION OF THE HUMAN FRONTAL LOBE§

In his Salmon Lectures in 1950, Fulton[10] suggested that radical lobotomy should be abandoned in favor of more restricted lesions in the medioventral quadrant of the frontal lobe. Delgado and Rosvold[9] and Rosvold and Delgado[16] have shown that frontal lobe syndrome in the monkey may be produced by electrical stimulation or electrocoagulation of small areas in the head of the caudate nucleus, a structure which is within the limits of the medioventral quadrant of the frontal lobes.

As a form of therapy for human patients we have performed electrocoagulation of certain points in the frontal lobes which were selected after functional exploration by means of electrodes implanted within the brain for a period of several days. A discussion of the preceding work in animals[4, 5] and of the technique[6] has been published elsewhere. Implanted electrode techniques in human patients have also been used by Brazier, *et al.*,[1] Heath,[14] and Sem-Jacobsen, *et al.*[17]

In this paper we submit information concerning electrical activity observed in the frontal lobes of nine patients after electrical stimulation and electrolytic destruction of selected points in these lobes.

MATERIAL AND METHODS

Five cases of schizophrenia, three of intractable pain, and one of anxiety neurosis were studied. Lobotomy had been recommended for these patients, and electrodes were implanted as a preliminary procedure in all of them and as alternative treatment in seven. The electrodes remained in the brain for the minimum time necessary for functional exploration and electrocoagulation. The average time was two and a half

* Associate Professor of Physiology and Psychiatry, Yale University School of Medicine.
† Consultant in Neurosurgery, State Hospital for Mental Diseases, Howard, Rhode Island.
‡ Senior Neurosurgeon; Director of Research and Medical and Surgical Services, Montefiore Hospital, Pittsburgh.
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days; one case required four days; in another patient, operated upon under local anesthesia, 24 hours proved sufficient. In five patients, two multilead needle electrodes were placed in each side of the frontal lobes in the coronal-sphenoidal plane, 2 cm. anterior to the coronal suture. In the other four, one needle electrode was similarly placed in each frontal lobe, and one plate electrode was slipped below the dura over each side of premotor and motor cortex, providing a total of 24 leads. Additional data concerning this group of patients and information on spontaneous electrical activity will be published elsewhere.[7]

The needle electrodes were made of seven silver wires of graduated length, 0.1 mm. in diameter, insulated with Teflon. Four mm. of insulation were scraped from the tip of each of the seven wires; these contacts were spaced 8 mm. apart. The leads were cemented together with plexiglas and soldered to a subminiature seven-pin socket to form an electrode about 0.5 mm. in diameter. The plate electrodes were of similar delicate construction, the contacts being tiny balls on the ends of the silver wires which were encased in 1 mill gauge polyethylene sheet. Additional technical details may be found in a previous publication.[6] Needle and plate electrodes were placed in the brain through 2 cm. burr holes, with the patient under Pentothal-nitrous oxide general anesthesia. In one case a local anesthesia was used. Recording equipment included a Grass 8-channel electroencephalograph, a Grass stimulator type S-44, a DuMont dual beam oscilloscope type 321, tape recorder, and still and motion picture cameras.*

Electrical recordings and electrical stimulations were bipolar. Monopolar coagulations were performed through the same needle electrodes by applying 6 mA D.C. for about two minutes, using a constant current device designed by Mauro and Delgado.

RESULTS

Potentials evoked by single shock stimulation. A. Ipsilateral transmission. In patients having four needle electrodes it was possible to stimulate through the leads of one needle and to record from the leads of the other in each frontal lobe. In this way potentials evoked in the same side of the stimulated area were studied. A representative example is given in Figure 1. Recordings of electrical activity were taken from linkages 1-2, 3-4, and 5-6 of the right external electrode (RT EXT). Point 1 was always the deepest lead and point 7 the most superficial. Single, unidirectional square waves of 4 V. and 1 msec. pulse duration were applied every three seconds for about 30 seconds through different depths of the right medial electrode. The leads of both needle electrodes were at approximately comparable depths, the right external slightly deeper than the right medial.

Single shocks, delivered between leads RT MD 1-2 (the deepest), evoked a spike followed about 50 msec. later by a sharp wave in leads RT EXT 1-2. The stimulus artefact was visible in the other two channels, but the evoked response was small in linkages RT EXT 3-4 and was absent in

* The motion picture was presented at the Fifth International Congress of Neurology, Lisbon, 1953.[18]

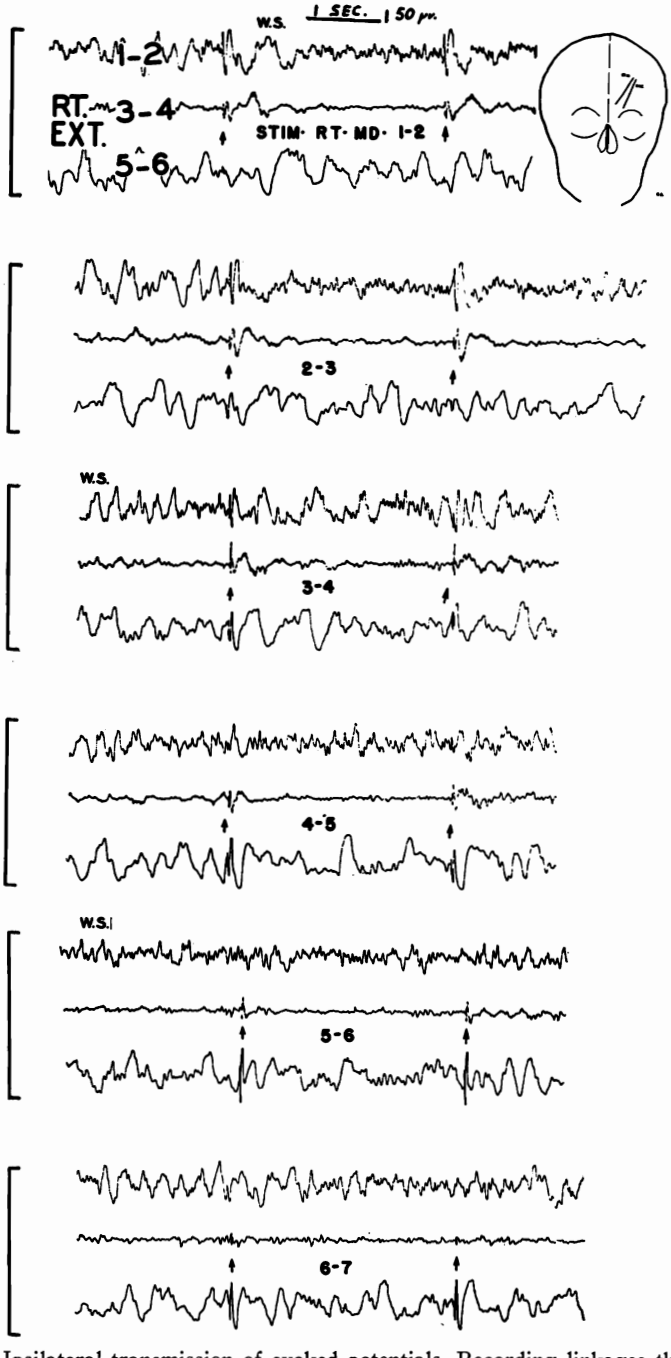

FIG. 1. Ipsilateral transmission of evoked potentials. Recording linkages through the right external needle electrode (RT EXT) were kept constant. At the arrows single shock stimulation was applied through different leads of the right medial electrode (RT MD) as indicated in the recordings. In all figures lead 1 was deepest, lead 7 most superficial.

RT EXT 5-6. Electrical stimulation through intermediary points evoked responses which were more noticeable from the recording leads located approximately at the level of the stimulating leads. When stimulation was applied through the most superficial points, RT MD 6-7, the evoked response was apparent in the most superficial leads and absent in the deepest points of the right external electrode.

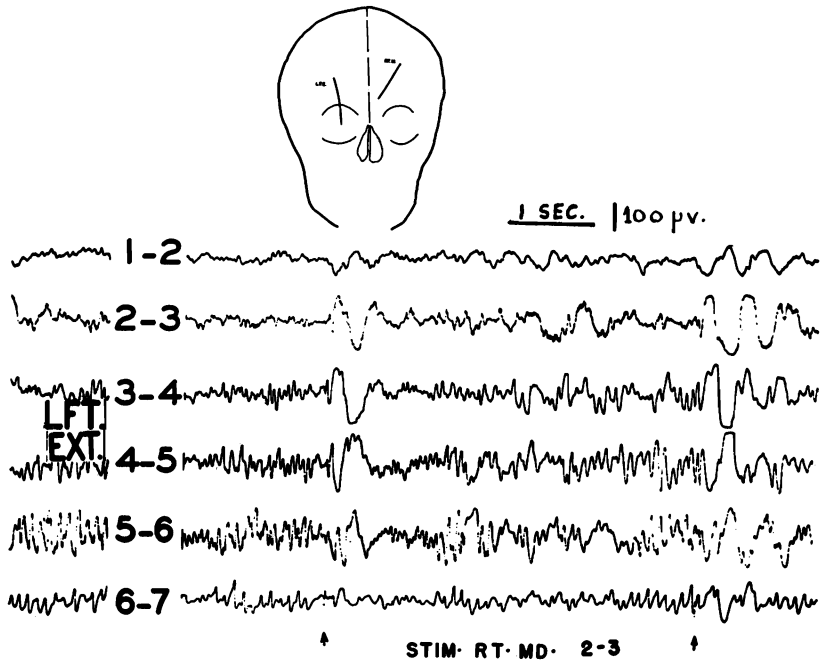

FIG. 2. Contralateral transmission of evoked potentials. Recording through the left external electrode (LFT EXT). At the arrows single shock stimulation through leads 2-3 of the right medial electrode (RT MD). Observe reversals between leads LFT EXT 3-4 and 4-5.

B. Contralateral transmission. When single shocks were delivered to one side of the frontal lobes and recordings were taken from the other side, responses consisted in general of a small sharp wave followed by one or more slow waves of decreasing amplitude. The evoked potentials mainly affected areas deeper or more superficial, according to the relative position of the stimulating points. An example is given in Figure 2 in which recordings were taken from the left external electrode (LFT EXT) and single unidirectional square waves of 4 V. and 1 msec. pulse duration were applied at the arrows, leads RT MD 2-3. Highest amplitude of response and

reversals were found in linkages 3-4 and 4-5, which were at a depth comparable to the stimulating leads. The evoked response was minimal at the deepest (LFT EXT 1-2) and at the most superficial (LFT EXT 6-7) linkages.

The amplitude of the evoked potentials was related to the voltage of stimulation without affecting the delay of the response in general. An example is shown in Figure 3. Electrical stimulation was applied in the depth of the right frontal lobe and oscilloscopic recordings were taken from the left side. Leads of the upper channel were at about the same depth as the stimulating points. Leads of the lower channel were about 16 mm. higher. Stimulation was increased two volts at a time from 2 to 8 V. The delay of the slow wave response in the first channel was about the same at all voltages tested (a little over 200 msec.). Amplitude of evoked responses increased when the stimulating voltage was augmented. At 8 V. the first slow wave was followed by another one of less amplitude and similar duration.

Effects of repetitive stimulation on electrical activity. Frequency of pulses 60-100 c/sec., pulse duration 0.1-1 msec., and voltages up to 30 for 5-10 seconds were tested in all the patients at different depths of the frontal lobes. Electrical stimulation within the frontal lobes using 100 c/sec., 1 msec. pulse duration and 10 V. for 5-10 seconds often evoked afterdischarges in both sides of the frontal lobes (Fig. 4) which lasted for 5-60 seconds and were followed by slow waves for a period of a few minutes in the stimulated side. A quick return to the pre-stimulation pattern was usual in the nonstimulated side. The pattern of afterdischarge generally showed high voltage, irregular activity of 1 to 8 c/sec. and occasionally high voltage rapid spikes. Patterns different in frequency and amplitude occurred at different depths. Wave and spike activity was less often observed. Afterdischarges were evoked with lower thresholds in the superficial than in the deep points of the frontal lobes. At threshold levels of stimulation the afterdischarge might be limited to the stimulated side only, and on a few occasions to only the stimulated point. The afterdischarges more often spread to superficial than to deep areas. In some cases it was possible to see all points of the stimulated side and the two or three most superficial of the other side involved in an afterdischarge, while the electrical activity around the deepest points of the nonstimulated side remained undisturbed. Often, when several afterdischarges had been evoked, it was possible to trigger the corresponding side by electrical stimulation of some previously unresponsive areas. For example, in one patient stimulation of RT NDL 1-2 with 60 c/sec., 1 msec. pulse duration, and 5 V. for 10 seconds produced no effect.

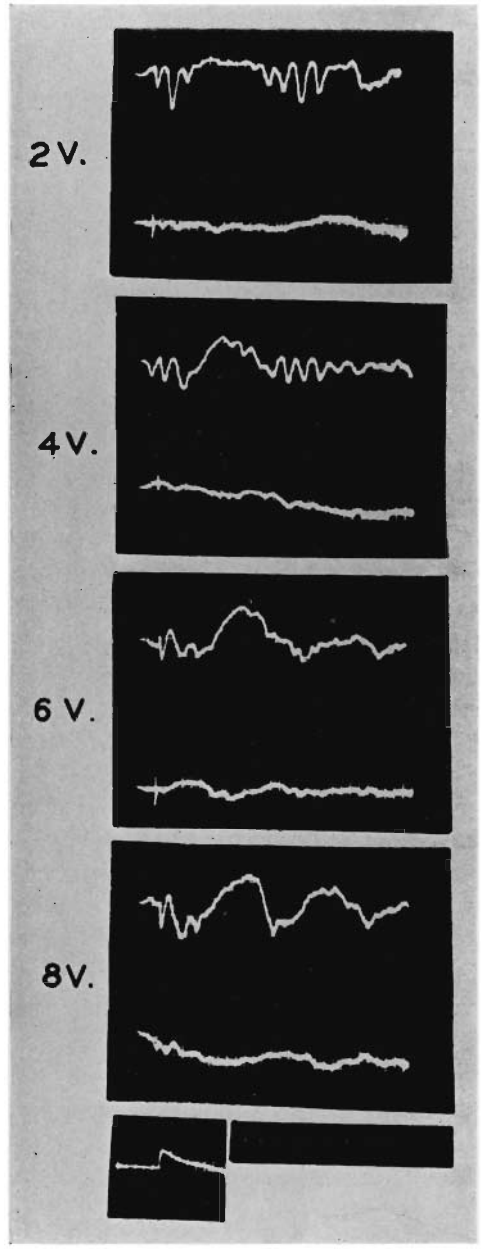

FIG. 3. Single shock stimulation with increasing voltages was applied in the depth of the right frontal lobe. Leads connected to the upper channel were in the left frontal lobe at about the same depth as the stimulating points. Leads connected with the lower channel were in the left frontal lobe 16 mm. higher. Observe in the upper channel the increase in amplitude of response without modification of delay. In the lower channel there was no response. Calibration: 50 μV., 0.1 sec.

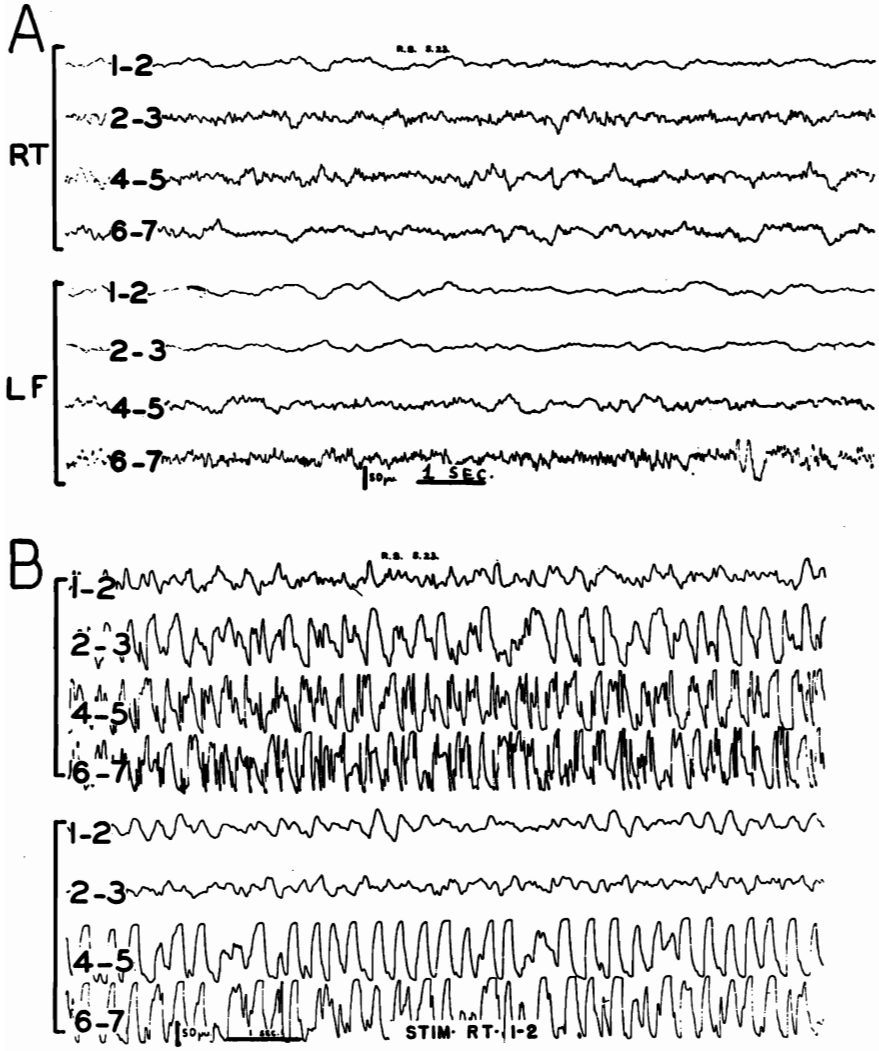

FIG. 4. *A*. Spontaneous electrical activity of the frontal lobes before stimulation. *B*. Electrical stimulation through leads 1-2 of the right external electrode evoked an afterdischarge which in this case affected both sides of the frontal lobes. Behavior, conversation, and motor activity of the patient were not modified during the afterdischarge.

Then points LFT NDL 5-6 and 6-7 were stimulated with the same parameters and several afterdischarges were evoked. A few minutes later stimulation of RT NDL 1-2 was repeated with the same parameters and one afterdischarge of about 20 seconds' duration was evoked in all linkages of the *left* frontal lobe, without modification of the electrical activity of the right

side. Afterdischarges evoked by electrical stimulation of the frontal lobes were in general restricted to this area of the brain, as evidenced by plate recordings from other areas. However, in some instances, especially when high voltages were used and the most superficial points stimulated, the evoked activity spread to the premotor and motor areas and was recorded directly from these regions through the plate electrodes. The spread of seizure activity from the frontal lobes to the motor area was a slow process, requiring several seconds to reach the ipsilateral motor area and longer to affect the contralateral motor area. The development of a seizure pattern in these regions was also slow and often took 20 or more seconds to show well-organized waves and spikes. The end of the seizure activity was independent in both areas. In general it ended first in the frontal lobes and was succeeded by slow waves, while the motor area was still producing waves and spikes at full strength.

Effect of evoked afterdischarges on the patients. General behavior, motor activity, and conversation were not apparently modified by afterdischarges localized to the frontal lobes. One patient, for example, was looking at a magazine and making pertinent comments to the interviewer. Electrical stimulation of point RT MD 1-2 (100 c/sec., 1 msec. pluse duration, 25 V. for 5 secs.) evoked one afterdischarge of 15 seconds' duration affecting both frontal lobes, and was followed by slow waves which lasted about five minutes in the right frontal lobe. During all this time the patient continued looking at the magazine, turning pages and talking with the interviewer, who did not observe any change. The normality of the behavior of the patient was in marked contrast to the gross abnormalities in the electrical activity of his frontal lobes. On the contrary, in a few cases in which the afterdischarges spread from the frontal lobes to the motor cortex, a motor seizure with loss of consciousness followed. The patients were out of contact for one or two minutes and then seemed to recover completely while the electrical activity of the frontal lobes still showed slow swings away from the pre-seizure pattern. One patient was stimulated (RT EXT 1-2; 100 c/sec., 1 msec., 10 V. for 5 secs.) while he was reciting poetry. He suddenly stopped; when stimulation was discontinued, he commented that he had felt a funny sensation in the head and was unable to think of the words of the verse. "My mind was blank," he said, "as if I had drunk a lot of beer." This effect was repeated several times and tape recorded. Fake stimulations and stimulations of other points failed to produce the described sensation. In other patients stimulation of different points evoked motor, sensory, and autonomic effects, which will be described in another publication.

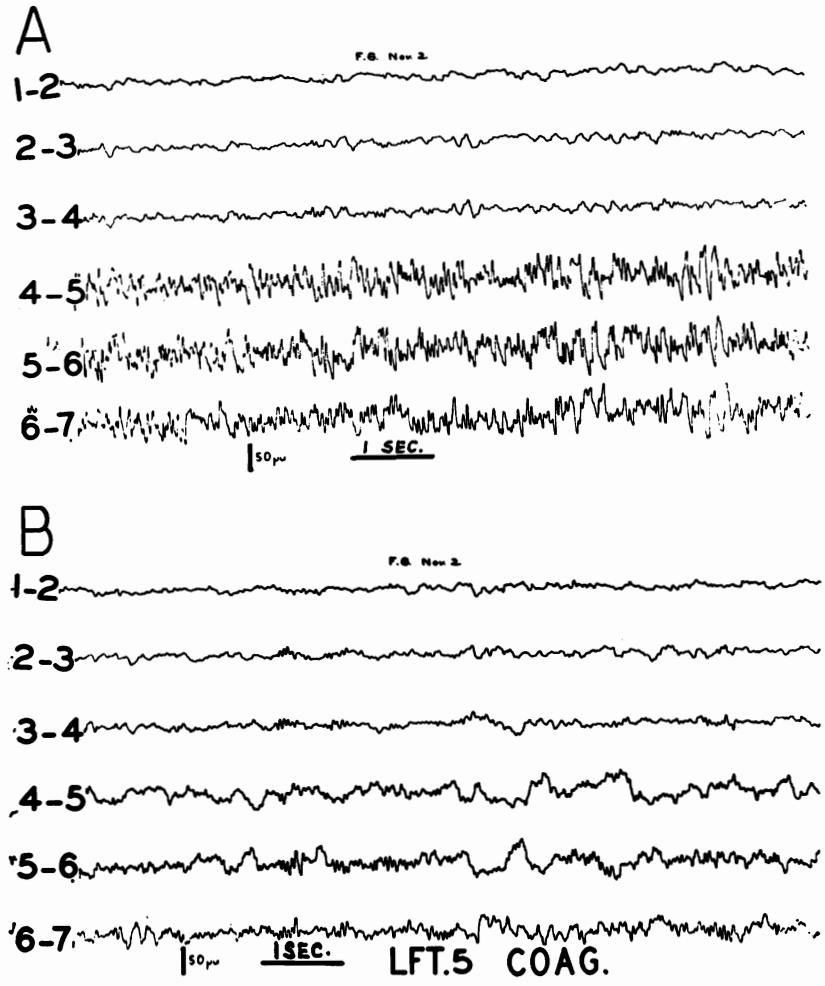

FIG. 5. *A*. Spontaneous electrical activity of the left frontal lobe before electrocoagulation.
B. General reduction in the spontaneous electrical activity of the left frontal lobe followed electrocoagulation of point 5 of the left needle electrode.

Electrocoagulation. The points to be electrocoagulated were selected after studying their spontaneous electrical activity and the results of electrical stimulation. It was done in the fully conscious patient while he was being interviewed. Recordings of electrical activity were made immediately before and after coagulation of each point. The patients were unaware that the final step was being taken and possible psychological factors were thus avoided. Six to ten points were routinely coagulated in each case and the following phenomena were observed:

(i) No change in the basic electrical activity of the frontal lobe.

(ii) General reduction in the amplitude of the spontaneous electrical activity of the homolateral frontal lobe (Fig. 5). The electrical activity of the other side was not altered until a similar contralateral point was electrocoagulated.

(iii) Slow waves and pulsation artefacts sometimes followed the destruction, lasting from several minutes to hours.

(iv) In two patients believed to be suffering from intractable pain, immediate but temporary improvement appeared to occur, which was coincidental with modification of electrical activity in the focal area of electrocoagulation.

DISCUSSION

In both cats and monkeys single shock stimulation of a cortical point may induce a localized electrical response at the corresponding point of the opposite hemisphere, according to Curtis and Bard.[3] In the same way local strychninization of a cortical point may fire the corresponding point in the opposite hemisphere, according to McCulloch.[15] Chang[2] also found in the cat a localized electrical response in a symmetrical point, contralateral to the stimulated cortex, especially in the suprasylvian cortex. In the present study single shocks applied within the frontal lobes in unanesthetized human patients evoked potentials which were recorded preferentially from leads located at a similar depth, as shown in Figures 2 and 3. These findings suggest that pathways in the explored area of the frontal lobes are not diffusely projected systems, and are oriented horizontally. In the ipsilateral recordings the evoked potentials could be caused by a spread of current from the stimulating leads to the area recorded, but even in this case the absence of diffuse responses would support the hypothesis of well organized pathways with delimited projections.

In contralateral recordings the initial sharp wave having a delay of a few milliseconds (Fig. 3) could be related to callosal transmission, and the slow wave having a delay of over 200 milliseconds to longer circuits with probable thalamic participation. It was interesting to observe that when intensity of stimulation was increased, the delay of the slow wave response was not modified and only the amplitude was greater.

When repeated stimulations of the frontal lobes evoked afterdischarges propagated to the premotor and motor areas, the onset and end of the

* The diagnosis of one patient was taboparesis and of the other, thalamic pain due to a stroke. Transient pain relief in these individuals following focal inferomedial electrocoagulation in the frontal lobe may simulate the more lasting improvement obtained in similar cases after uni- or bimedial lobotomy.

seizure activity were often independent in the two regions, with a rather slow propagation from one area to the other. This finding indicates that, at least in some cases, afterdischarges are dependent upon local activity and not upon a general pacemaker. Both frontal lobes could be involved in afterdischarges without apparent modification of the behavior of the patients, as contrasted to the loss of consciousness which accompanied similar afterdischarges of the motor areas. The pioneer work of Fulton and Jacobsen[11] and the considerable work accumulated afterwards (see bibliography in Greenblatt and Solomon[12]) proved that frontal lobes are not essential for consciousness but play an important rôle in behavior. However, according to our observations, disturbances of their electrical activity may not be registered in overt behavior.

The ipsilateral reduction of spontaneous electrical activity of the frontal lobes after electrocoagulation of some points seems to indicate (a) the independence of the origin of electrical activity in the two hemispheres, and (b) the importance of some points for the electrical activity of a wide area.

SUMMARY

Exploration and therapeutic electrocoagulation of discrete points in the frontal lobes was done by means of multilead electrodes implanted within the brains of nine patients for periods of one to four days. Potentials evoked by electrical stimulation were recorded at different depths of the ipsi- and contralateral frontal lobes. Conclusions follow:

1. Responses evoked by single shock stimulation consisted in a spike or sharp wave followed by one or more slow waves.

2. Evoked potentials were recorded mainly from contacts located at about the same depths as the stimulating points. This suggests that pathways within the frontal lobes are organized without diffuse projecting systems and are horizontally oriented.

3. Repetitive stimulation of the frontal lobes with appropriate parameters evoked afterdischarges which, depending upon the intensity of stimulation, were limited to one point, to one side, or to both sides of the frontal lobes.

4. The evoked electrical disturbance of the activity of the frontal lobes did not modify behavior, conversation, or motility of the patients except in the few cases in whom the evoked afterdischarges of the frontal lobes spread to the motor areas, producing a motor seizure with loss of consciousness.

5. Electrocoagulation of different points of the frontal lobes could produce the following effects upon its electrical activity: (a) no effect; (b) ipsilateral general reduction of amplitude; (c) slow waves.

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