Clinical Applications of Studies on Stereotactically Implanted Electrodes in Temporal-Lobe Epilepsy*

PAUL H. CRANDALL, M.D., RICHARD D. WALTER, M.D., AND ROBERT W. RAND, M.D.

Department of Surgery/Neurosurgery, University of California Medical Center, Los Angeles, California

The clinical manifestations of discharges of seizures now termed temporal-lobe epilepsy, have been recognized since the article of Jackson in 1888. That the origin is in the uncinate region was reported by Jackson and Colman in 1898. The development of electroencephalography was necessary to provide a confirmatory test and a reliable means to distinguish these states of seizures. Jasper and Kershman observed in 1941 that patients with psychomotor episodes usually had sharp waves and rhythms of 6 per sec., often synchronous bilaterally, and sometimes localized in the frontotemporal regions. It seemed clear to them from the nature of these disturbances that the temporal lobe and subjacent structures in the archipallium were the regions involved primarily. The first clear correlation of the clinical features and the foci of anterior-temporal spikes either unilaterally or bilaterally, as well as their detection by recording during sleep, came from Gibbs et al. in 1948.

With the identification of states of focal seizures in the temporal regions some afflicted patients who were not relieved by anticonvulsant medication were given surgical therapy by Penfield and Flanigin in 1950 and by Bailey and Gibbs in 1951. Subsequent long-term follow-up studies and confirmation of similar results by numerous other surgeons have established this method of treatment for clearly focal temporal epilepsy. The consensus of results is that at least two-thirds of patients have complete or very good relief from seizures and other disabilities caused by this condition. Improved surgical results, as well as a substantial contribution to the knowledge of the pathological lesions, were achieved by the en bloc resections developed by Falconer et al. in 1955.

It has been amply documented in all reported series that best results of surgical treatment are obtained in cases of clearly unilateral seizures. In the first large group of surgically treated cases Jasper et al. found 34 per cent of temporal epilepsy to be unilateral. Of 26 patients considered for surgical treatment at the University of California Medical Center in Los Angeles since 1956, after many scalp and basal electroencephalograms, only 4 with unilateral temporal epilepsy were found. The interpretation of bitemporal activity of several types of seizures is most important at present since bitemporal seizures are the great majority. Even though recurrences after temporal lobectomy are more common in bitemporal epilepsy, enough patients are benefited to lead one to suspect that more extensive diagnostic investigations might yield more successful courses of treatment.

The authors have been dissatisfied with the reliability of electroencephalographic techniques, necessary for the precise analysis of the complex subcortical epileptogenic activity in bitemporal epilepsy before surgical treatment. This report concerns our investigations with depth electrodes implanted stereotactically into the medial structures of the temporal lobes in selected patients. Frequent prolonged recordings were made in the normal alert state, asleep, with Metrazol activation, and with electrical stimulation of these structures.

Received for publication February 11, 1963.
Revision received August 15, 1963.
This investigation was supported by grants-in-aid from the United States Public Health Service (B 2508).

† Knoll Pharmaceutical Co., Orange, New Jersey.
Rationale for Direct Recordings with Depth Electrodes

The reasons for finally resorting to direct recordings from the epileptogenic structures are founded in our own experience and in that of others on the problems of lateralization and determination of number and characteristics of the foci of seizures.

Lateralizing Clinical Manifestations. The clinical features are very helpful in diagnosis of a condition as being of possible temporal origin, but seldom help to determine lateralization of the disorder.

The 26 patients with temporal-lobe epilepsy who underwent surgical intervention at the UCLA Medical Center since 1956 are representative of those seen in usual clinical practice. They were selected after many examinations, prolonged treatment with medications, and careful evaluation by the Neurology Clinic. There were 17 males and 9 females, 5 of whom were adolescents. The oldest patient was aged 52, the youngest, 14. There was only 1 patient with a psychiatric disorder severe enough to confine him temporarily to a mental hospital. The average duration of seizures before the surgical intervention was 12.1 years.

The patients in the group had one or more of the following symptoms, which are commonly attributable to temporal-lobe epilepsy. The frequency of the types of preceding auras were as follows: epigastric (6), visual or psychical illusions (5), gustatory (4), olfactory (2), auditory (2), vestibular sensations (1), fear (3), and palpitation (1). All of the patients had automatisms characterized by episodic lapses of awareness accompanied by staring (14), smacking, chewing, or swallowing (11), repetitive mumbling speech (8), semipurposeful movements (5), laughing spells (1), circling ambulation (3), midline cephalic sensations (4), unilateral numbness (2), wandering aimlessly (3), grimacing (2), and urination (1). There were 8 patients who also suffered from generalized convulsions in addition to the above attacks. There were 2 patients who had attacks of unilateral contraversive deviation with or without tonic or clonic movements. Ten patients had complete amnesia for their attacks, and probably more had amnesia for some of their attacks. Most of the patients were observed in spontaneous seizures or during a Metrazol-induced seizure, and their symptoms were recorded by a physician.

All of the above manifestations can be regarded as strong clinical evidence for a temporal origin of the seizures, but there is little of value for lateralization of the activity, with the exception of the unilateral contraversive attacks or unilateral distal numbness in the limbs, and they are definitive only if other than temporal origins for these attacks can be excluded. There were 3 patients who had defects of the superior homonymous sector or quadrant that were of lateralizing value. In our experience some neurological findings such as facial asymmetry or weakness, episodes of arrest of speech or transient aphasia were difficult to be certain of detection and liable to be misinterpreted. In the radiological examination there were 2 patients who had intracerebral calcification, 1 caused by hemangioma calcificans, and 1 by astrogliosis. Abnormalities were revealed at pneumoencephalography in 2 patients and at angiography in 1.

Lateralizing Pathological Changes. It has been shown by Meyer15 that a large proportion of epileptics with temporal-lobe seizures have pathological lesions. It has also been claimed that preoperative lateralization of the pathological process to indicate the side for lobectomy increases the chances of success for the operation. Pampiglione and Kerridge17 have used absence of the fast response to barbiturates found in connection with a generalized fast response in the electroencephalogram as indicative of the locale of the pathology. The reliability of this has not been confirmed yet. In our series, radiological studies were not too helpful in locating the pathological changes of these disorders. Although a large proportion of these patients have pathological lesions, focal, circumscribed pathological changes are in the minority and diffuse changes are more common. Of our 20 patients with en bloc temporal lobectomies who were examined systematically, there were 17 with pathological
changes. Twelve were diffuse changes scattered throughout the specimens such as scattered neuronal atrophy, astrogliosis, oligodendrogliosis, diffuse gliosis with cysts and calcifications, and sclerosis of the medial structures. There were 5 specimens with focal changes: 2 post-traumatic cicatrices, 1 hemangioma calcificans, 1 glial hamartoma, and 1 astrocytoma. There were 3 specimens with no pathological change. Neither the astrocytoma nor the glial hamartoma (measuring 4 mm. in width and 10 mm. in length) had been in evidence in the neuroradiological studies. However, 3 focal lesions and 2 of the diffuse lesions had been detected neuroradiologically. But in general, despite the high incidence of pathological changes, neuroradiological studies are not commonly lateralizing.

Electroencephalographic Studies. Electroencephalographic data derived from scalp and basal electrodes are an important confirmation of the diagnosis of temporal-lobe epilepsy, but are limited for the complete interpretation of the epileptogenic processes necessary for surgical decisions. Our classification is derived from the categories proposed by Jasper et al. It seems sound to interpret a unilateral temporal focus to be present in 2 groups if the same findings appear in a number of recordings. Group I, seizure activity localized consistently in one temporal region (4 patients); Group II, predominant spiking in one temporal region with intermittent immediate reflection of lesser amplitude in the opposite temporal region (5 patients). This bitemporal activity is commonly attributed to the homotopic cortical responses, but some doubt might exist since it could be a simultaneous temporal activation from a central pacemaker more evident on one side.

Completely independent bilateral activity of seizures was found in scalp and sphenoidal recordings in the remaining 17 patients. Although early in our series we decided to intervene surgically in 8 patients in whom the activity seemed stronger on one side, confidence in the decision was not great, and more recurrences did appear in this group. There were only 2 patients with bitemporal independent spiking activity whose clinical or radiological examinations yielded lateralizing findings to help in this decision. There was also uncertainty as to the presence of secondary foci, central, or multiple foci in these cases.

More recently in 6 cases of bilateral independent temporal spiking discharge, in 1 case of unilateral temporal discharges, and in 1 case of temporal-lobe epilepsy diagnosed by clinical evidence without confirmation by electroencephalographic data, we have undertaken to place electrodes directly by stereotactic surgery into the structures of the mesial temporal lobe for the following reasons:

1. To record the epileptiform activity over a long period of time and under circumstances of wakefulness and sleep.
2. To correlate the onset of activity of seizures in these structures during spontaneous clinical seizures, under Metrazol activation and by direct electrical stimulation.
3. To determine if these mesial structures are the site of foci of seizures by their electrographic characteristics, production of afterdischarges, and reproduction of the clinical seizure by stimulation. As will be seen, the procedure now is time-consuming but simpler methods may evolve.

The importance of correct assessment of the status of both temporal lobes is underlined by the reminder that if the wrong lobe is removed surgically the state of seizure is likely not to have been improved, and the patient is left with a severe defect of memory known to be the common sequel of extensive bilateral temporal-lobe damage.

Surgical Methods

The stereotactic method and atlas of Talairach et al. were used for placement of the electrodes. Teleradiography results in film images of negligible magnification, a great convenience in subsequent measurements and calculations. The use of double grids next to the film and telescopic sighting to center the roentgen-ray beam on the target area, eliminates errors caused by parallax. The low position of the frame permits both anteroposterior and lateral films and
temporal horn was filled with ethyl iodo-phenylundecylate.* All of our patients have had preceding diagnostic pneumoencephalography, so that it is known whether the temporal horns are symmetrical and equal beforehand.

The planes of reference are a horizontal axis (LT) along a line drawn from the tip of the temporal horn into the inferior margin of the ventricular trigone (Fig. 1).

The vertical axis (VA) is at the tip of the temporal horn at 90° with LT. The lateral positions are measured from the midsagittal plane. The 3 coordinate tables for our surgical targets are in millimeters related to these 3 axes.

The implanted depth electrodes are bipolar, slightly flexible, insulated stainless-steel wire. They are constructed of two parallel wires 0.010 mm. in diameter and enamel-coated with 5 additional coats of Epoxylite.† These are fused to a central strut that did not project to the tip so that the wires are 2 mm. apart. To avoid the effect of tines at the tip, the wires are placed diagonally with a connecting web of Epoxylite. The insulation is removed approximately 1.5 mm. from the tips. The combined diameter of each electrode is 2 mm. by 1 mm. In the patient the resistance determined by measuring flow of current at known voltage with 100 μsec. pulses (square wave) varied between 3,000 and 10,000 ohms.

Through the double grid of the Talairach apparatus twist-drill holes are made through the skull to the level of the dura mater and stainless-steel screws, each with a central channel, are fixed in place. These screws then are consolidated into an aggregate by applying Kadon cement externally to the scalp. The depth electrodes when inserted are also fixed to the screw heads by cement which insulates the lead connections. Stainless-steel screws are placed in standard electroencephalographic positions through the scalp and outer table of the skull and the scalp recordings are bipolar. These fixed electrodes have been very satisfactory in long-term function and well tolerated by the patients. All of the leads from the depth electrodes and scalp electrodes are gathered into plugs which are left outside the head dressing for convenient access in later recordings and stimulations. The final positions of the electrodes are measured from films of the contrast ventriculograms and electrodes in situ.

Daily testing for about 3 weeks has been carried out on each patient. Recordings of spontaneous activity awake and asleep, with and without anticonvulsant medications, and during various

---

* Pantopaque, General Electric Co.
† Epoxylite Corp., El Monte, California.
‡ L. D. Caulk Co., Milford, Delaware.
types of activities are possible. In some patients we have been fortunate to gather complete recordings of overt spontaneous clinical seizures. Pharmacological activation has been carried out with Metrazol administered intravenously in 100 mg. increments per min. and by monitoring the electroencephalograph in order to stop short of a major convolution. Electrical stimulations are made in the last phase of evaluation with a Grass type S4 stimulator with an A-578 A transformer delivering brief monophasic square-wave pulses (1–20 volts, 1–30 pulses per sec., 0.15–1.0 msec. in duration).

At the end of this period of evaluation, a decision is made as to the advisability of temporal lobectomy as surgical treatment. Before the depth electrodes are removed, small marker lesions are made on the side to be resected.

The extent of removal in all the anterior temporal lobectomies has been standardized. The operations are done under general anesthesia and with preliminary electrocorticograms of the lateral surface of the temporal lobe. The posterior limit of temporal lobe to be removed is measured from the cup of the middle fossa along the lateral surface, 4.5 to 5.0 cm. for a dominant lobe and 5.5 to 6.5 cm. for a nondominant lobe. The line of resection is inclined slightly inferiorly and medially to cross the temporal horn and through the body of the hippocampus. Superiorly the resection line is along the Sylvian fissure and bares the insula. It is carried across the limen insulae and along the tentorial edge and the pial margin bordering the cisterna ambiens. We have not considered it safe to have the resection medial to the pia mater, and thus we have not been able to identify and verify some of the sites of the electrodes in this manner.

Results

Although our experience to this time is with a group of only 8 patients, we have clarified some of the epileptogenic processes, which allows an interpretation of predominant lateralization in instances impossible before this. Three examples illustrate the possibilities.

I. Bitemporal independent temporal activity of seizures in surface recordings shown to be clearly lateralized when recording in the rhinencephalic structures.

Case 1. A.R., a 29-year-old man, had experienced 10 years of seizures, necessitating discharge from the Navy at the outset. Subsequently he was seen regularly at the University of California at Los Angeles Outpatient Neurology Clinic. He had had about 6 nocturnal generalized seizures and 10 to 12 psychomotor seizures per month under treatment with various combinations of Dilantin\(^*\), phenobarbital, Mysoline\(^*\), and Me-santoin\(^*\).

A typical seizure was described as preceded by *dèjà vu* phenomenon, which would last 3 to 4 min., and then the patient would be observed to be staring, raising his right arm and often smacking his lips. Afterwards the patient often reported feeling that he had been in a place that he had seen before, but sometimes would be amnesic for these attacks.

About January, 1961, after a series of severe attacks, he was admitted to the Brentwood Veterans Psychiatric Hospital because of combat, hostile behavior. He was transferred with his consent to the UCLA Neuropsychiatric Institute since many electroencephalograms over the past year had shown a left temporal spiking focus in addition to diffuse, slow, and paroxysmal activity.

No etiological factors in his past history were discovered. On examination a slight asymmetry in the cranium and face with widened right palpebral fissure was found. His gait was wide-based and slightly ataxic because of Dilantin intoxication. Laboratory examinations, plain roentgenograms, pneumoencephalograhic, and bilateral carotid angiographic findings were normal.

Scalp Recordings. Ten electroencephalograms recorded from the scalp showed left anterior temporofrontal spiking discharges with some less prominent independent spiking in the right temporal areas.

Sphenoidal Recordings. Four electroencephalograms with sphenoidal electrodes were made over a period of 5 days (Fig. 2a). Three revealed a spiking focus primarily from the right sphenoidal and right anterior temporal electrodes with less conspicuous spiking of lower amplitude from the left sphenoidal and anterior temporal leads.

In the remaining examination fairly frequent sharp-wave and spiking discharges in the left sphenoidal electrode were revealed with some reflection in the left temporal scalp. On more rare occasions there was the same activity independently in the right sphenoidal electrodes.

At this point the electroencephalographer considered that there was little consistent evidence of a persistent focus in that there were shifts from side to side, frequently at daily intervals.

On June 15, 1961, a positive-contrast right temporal ventriculogram was done and on August 11, bilateral monopolar depth electrodes were

* Parke, Davis & Co., Detroit, Michigan.
† Ayerst Laboratories, New York, New York.
‡ Sandoz Pharmaceuticals, Hanover, New Jersey.
implanted into the structures of the medial temporal lobe (Fig. 1c). The three coordinates of each site for stereotaxis are given in Table 1.

Depth Recordings. The implanted depth electrodes were left in place until August 19. All of the recordings from the depth electrodes during this time demonstrated conspicuous, frequent, and prominent series of single and polyphasic spiking discharges from the right hippocampal gyrus with much lower amplitude and independent spikes from the left. There was very little reflection into the scalp electrodes (Fig. 2b).

Electrical Stimulation Studies. (Left-side depth electrodes were removed prior to stimulations.) Prominent, long-lasting (10 to 20 sec.) after-discharges were obtained by stimulating the right hippocampal gyrus with 10 volt stimuli 0.5 msec. in duration, and 30 pulses per sec. (Fig. 3). This could be demonstrated repeatedly. The same parameters at the amygdala or pes hippocampi failed to elicit any after-discharges.

Electrocorticogram (Sept. 25, 1961). Focal spiking discharges were observed from the anterior aspects of the right midtemporal gyrus.

An en bloc resection of the right anterior temporal lobe, 6 cm. from its tip, was performed.

Serial sections of the ablated specimen were prepared with several stains including the ferriacyanide method (Gomori stain). Prior to removal of the electrodes, those on the right were marked with a small electrolytic lesion. The three sites of electrodes were identified on the sections as located in (a) lateral basal nuclei of the amygdala, (b) through the pes to entorhinal cortex, and (c) alveus of the pes hippocampi (Fig. 4).

Postoperatively the patient has been com-

![Fig. 2. Case 1. (a) Abnormal electroencephalogram with sphenoidal leads showing spiking discharges from the right sphenoidal and anterior frontal and temporal leads with independent left sphenoidal spiking discharges. (b) Tracing obtained from bilateral implanted and scalp electrodes showing single and polyphasic spiking discharges from the right hippocampal gyrus with very low amplitude but independent spikes from the left.]
Electrode Studies in Temporal-Lobe Epilepsy

 completely free of seizures and psychiatric disturbance to this time (18 months) and has returned to work. He has a postoperative left homonymous hemianopsia. Several postoperative electroencephalograms have been normal except for a rare low-amplitude spike in the anterior left hemisphere.

II. A hippocampal site may be found active in the beginning of spontaneous clinical seizures, and Metrazol-induced seizures and on electrical stimulation of this site there is reproduction of the exact clinical seizure.

Case 2. R.D., a 17-year-old male, had suffered a fracture of the skull at the age of 2 and the onset of seizures since the age of 5. The longest period free of seizures had been 8 months and he averaged 10 to 12 per month of three types of seizures.

He experienced brief spells preceded by a feeling of heaviness in the head and body and would be observed to stare fixedly for a few sec. In a second type for which he had amnesia of preceding events, he would often walk dazedly about and either clench his fists or hold anything in his hands very tightly. Often this walking would carry him into traffic or collision with objects without his being aware of them. On some occasions he would also slump to a crouching position. These spells lasted about 5 min. The third type was generalized convulsions.

An observed seizure was described as the patient suddenly becoming detached and unaware, staring with tearing from both eyes. Then he became very stiff, grasped hold of a leg of a table with his right hand, and remained generally stiff and rigid, sitting in his chair. He responded to any tactile stimulation with defensive movements and remained thus for nearly an hour.

Physical, neurological, and routine laboratory findings were normal. Plain roentgenograms and a pneumoencephalogram showed no abnormalities. One year of numerous attempts at control by medications had not given sufficient relief.

Scalp Electroencephalogram. On 6 recordings a greater amount of focal spiking was seen from the right anterior temporal area with some spread to the midtemporal region. There were also less prominent independent spikes appearing over the left temporal area. One recording was done during a spontaneous clinical seizure, but no focal findings were observed.

Sphenoidal Studies. Three sphenoidal record-

<table>
<thead>
<tr>
<th>Site</th>
<th>Distance from Midline (mm.)</th>
<th>Behind VA (mm.)</th>
<th>Above or Below LT (mm.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right side</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amygdala</td>
<td>25</td>
<td>+2</td>
<td>+9</td>
</tr>
<tr>
<td>Anterior hippocampal gyrus</td>
<td>23.5</td>
<td>+7</td>
<td>+2</td>
</tr>
<tr>
<td>Pes hippocampi anterior</td>
<td>30</td>
<td>+14</td>
<td>0</td>
</tr>
<tr>
<td>Left side</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amygdala</td>
<td>24</td>
<td>+1</td>
<td>+8</td>
</tr>
<tr>
<td>Anterior hippocampal gyrus</td>
<td>23</td>
<td>+7</td>
<td>0</td>
</tr>
<tr>
<td>Pes hippocampi</td>
<td>26</td>
<td>+14</td>
<td>+2</td>
</tr>
</tbody>
</table>

Fig. 3. Case 1. Separate electrical stimulations of each right depth site with recordings from the other two sites. Prominent, long-lasting after-discharges obtained by stimulation of right hippocampal gyrus.
TABLE 2
Stereotactic placement of electrodes in Case 2

<table>
<thead>
<tr>
<th>Site</th>
<th>Distance from Midline (mm.)</th>
<th>Behind Midline (mm.)</th>
<th>Above or Below LT (mm.)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Right side</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior commissure</td>
<td>24</td>
<td>+7</td>
<td>+13</td>
</tr>
<tr>
<td>Pes hippocampi</td>
<td>29</td>
<td>+16</td>
<td>+1</td>
</tr>
<tr>
<td>Medial hippocampal gyrus</td>
<td>23</td>
<td>+23</td>
<td>+3</td>
</tr>
<tr>
<td>Posterior hippocampal gyrus</td>
<td>22</td>
<td>+34</td>
<td>-3</td>
</tr>
<tr>
<td><strong>Left side</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amygdala</td>
<td>37</td>
<td>+7</td>
<td>+10</td>
</tr>
<tr>
<td>Pes hippocampi</td>
<td>27</td>
<td>+16</td>
<td>+1</td>
</tr>
<tr>
<td>Medial hippocampal gyrus</td>
<td>23</td>
<td>+23</td>
<td>-3</td>
</tr>
<tr>
<td>Posterior hippocampal gyrus</td>
<td>24</td>
<td>+34</td>
<td>-1</td>
</tr>
</tbody>
</table>

Right and left temporal leads all showed a greater amount of spiking from the right sphenoidal leads, less in the scalp, and rare, lower-amplitude independent spikes appeared in the left sphenoidal leads.

A right temporal positive-contrast ventriculogram was done on May 11, 1962, followed by implantation of four depth electrodes in each medial temporal lobe and screw electrodes in the calvarium in standard placements except for occipital leads on June 12, 1962. These electrodes were left in place until July 6, 1962. The three coordinates of each site for stereotaxis are given in Table 2.

**Depth-Electrode Recordings.** The major area of spiking activity was in the right posterior hippocampal gyrus, then the right pes hippocampi, and then the right midhippocampal gyrus, in that order. There was some spiking in the left hippocampal gyrus, but less prominent and less rhythmic.

**Metrazol Activation with Depth-Electrode Recording.** A typical temporal-lobe seizure corresponding to his spontaneous seizures was induced with the appearance of prominent spikes in the right midhippocampal gyrus initially and then spreading to the right pes hippocampi and 12 sec. later appearing in the left pes hippocampi (Fig. 5).

**Electrical Stimulation Studies.** From the preceding study of activation the site of electrode of special interest was the right midhippocampal gyrus. Since it was technically not possible both to record and to stimulate from the same electrode, the stimulation was delivered to an adjacent site, the right pes hippocampi. A typical psychomotor seizure corresponding to his spontaneous type was induced at 5 volts, -5 pulses per sec. (Fig. 6). The identical sequence of events occurred as in the Metrazol activation in that the right midhippocampal site and right posterior...
Fig. 5. Case 2. Metrazol-activation study. Note the small burst of discharges of seizure in the right midhippocampal gyrus just prior to the clinical manifestations and the same sinusoidal "seizure activity" later in the left pes hippocampi.

hippocampus to a lesser extent demonstrated low-amplitude rhythmic spiking activity and then rhythmic spiking discharges appeared in the left pes hippocampi about 30 sec. later. The entire sequence differs only in time.

In other stimulations induced seizures were obtained in stimulating the right midhippocampal gyrus. After-discharges seen in the right posterior hippocampal gyrus spread to the left amygdala.

With stimulation of the left pes hippocampi of 15 volts at 5 per sec. after-discharges were associated with complaints of bad taste and bad smell never experienced before. With 5-volt stimulation at 30 per sec. after-discharges occurred with chewing and swallowing movements not seen in patient's usual spontaneous seizures. Stimulation of the left posterior hippocampal gyrus of 5 volts at 30 per sec. evoked "memories" that stopped as stimulation ceased. With stimulation of the left amygdala there was no change.

After evaluation of the prominent electrographic changes on the right side, the appearance of spiking from the right side under activation with Metrazol, and the reproduction of his clinical seizure by electrical stimulation, right temporal lobectomy was carried out on Nov. 29, 1962. An electrocorticogram showed conspicuous discharges of seizure throughout the lateral surface from 2 to 8 cm. behind its tip. The posterior limit of the resection was made at 7 cm. behind the tip. The postoperative course was uneventful and the patient has been free of seizures in the short follow-up period. The patient has a left superior homonymous quadrantanopsia.

III. Detection of unilateral rhinencephalic activity of seizure in the absence of surface discharges.

Case 3. J.K., a 33-year-old male meatcutter, probably suffered injury at birth in a breech delivery and was semiconscious for 72 hours afterward. He was a small, inactive baby, began to walk at the age of 4, and later in school had trouble comprehending what he read. He had suffered from three types of seizures since age 12. The most minor was preceded by tinnitus; the patient could hear but could not speak and fell down if he was not sitting. A second variety occurred at least twice weekly. There was an aura of "going to sleep in both arms and legs" or a feeling of floating away. He often lost his voice before "passing out" and observed a moving micropsia of objects in front of him. This was followed by a brief period of unawareness lasting a minute or so that occurred with grimacing.

At examination he was discovered to be mildly deaf on the right side and to have a slightly flattened right nasolabial fold. He was left-handed for writing and for his occupation of meatcutting.

He was treated in the Neurology Clinic with 6 different anticonvulsants without improvement.

Scalp Electroencephalograms. Five electroencephalograms from 1957 to 1960 at the UCLA Medical Center failed to show any abnormality except occasional slow 5 to 7 c./sec. waves focally over the left anterior temporal region.

Ten electroencephalograms during hospitalization at another institute in April 1960 failed to show any surface activity of seizure despite the fact that the patient experienced 32 seizures in 6 weeks.
Sphenoidal Recordings. During hospitalization at the UCLA Medical Center in March 1962, a pneumoencephalogram was completely normal. Six recordings from March 26 to 31 with sphenoidal leads in place failed to disclose any activity of seizure beyond some sharp-wave activity observed in the right sphenoidal leads on one occasion. Metrazol caused some abruptly appearing generalized paroxysmal activity without focal features.

On June 21, 1962 a right temporal positive-contrast ventriculogram was performed.

On Oct. 15, 1962 bipolar depth electrodes were implanted in medial structures of both temporal lobes as well as screw electrodes in standard electroencephalographic positions in the calvarium (Fig. 7). The three coordinates at each site for stereotaxis are given in Table 3.

Six depth recordings from Oct. 16 to 20, 1962 all demonstrated spiking activity virtually limited to the left side and predominantly in the pes hippocampi and midhippocampal gyrus. Exceedingly rare spikes were seen sporadically in the right pes hippocampi (Fig. 8).

Activation with a large dose of Metrazol revealed only a generalized increase in amplitude of both depth and scalp electrographic patterns.

Electrical Stimulations. Stimulations were made with on-intervals of 42 msec., 10 stimuli per 20 sec., of 10 to 15 volts. All right-side sites gave no response. In the site of the left amygdala on 4 different days stimulation resulted either in an aura or a definite psychomotor seizure. The auras were described as a “sinking feeling like falling into a tunnel” and on one occasion they were followed by a poignant memory of an automobile accident in 1938 with vivid emotional reactions. The psychomotor seizure was manifested by searching, fumbling movements, grasping in air, chewing, swallowing, appearance of apprehension and failure to respond to questioning. There was amnesia for much of this episode. Early in the

Fig. 6. Case 2. Electrical stimulation of right pes hippocampi. Initially there are almost rhythmical spiking discharges but not in phase with artifacts of stimulus, then intermittent bursts in the right amygdala followed by a period of disorganized activity. The right mid- and posterior hippocampus then show very low-amplitude rhythmical activity changing to slightly higher-amplitude spikes in the right midhippocampus. Clinical manifestations of chewing and swallowing and automatism were seen when the muscle artifacts appeared in the scalp leads. Note the train of sinusoidal “seizure activity” in the left pes hippocampi about 20 sec. after the onset of the seizure.
course of this seizure, slow waves were apparent in the left midhippocampal gyrus which returned to normal while the clinical manifestations persisted. The paroxysmal activity in the amygdala died out about the same time that the clinical manifestations abated. These observations appeared to indicate a highly focal area of low epileptic threshold in the region of the left-amygdala electrode, which on stimulation reproduced the patient’s usual attacks.

Stimulation of the left pes hippocampi produced pulling of his lip to the right and a partial seizure. Stimulation of the left midhippocampal gyrus resulted in vague apprehension, whereas stimulation of the left posthippocampal gyrus produced no changes.

Left anterior temporal lobectomy was carried out on Dec. 27, 1962. Preliminary electrocortiogram of the lateral surface of the temporal lobe failed to show any activity of seizure. The posterior limit was 5.0 cm. Aside from transient disturbance of speech and several postoperative focal motor seizures, his course has been benign but the follow-up period is short.

**TABLE 3**

<table>
<thead>
<tr>
<th>Site</th>
<th>Distance from Midline</th>
<th>Behind VA</th>
<th>Above or Below LT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(mm.)</td>
<td>(mm.)</td>
<td>(mm.)</td>
</tr>
<tr>
<td>Right side</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amygdala</td>
<td>28</td>
<td>+2</td>
<td>+8</td>
</tr>
<tr>
<td>Pes hippocampi</td>
<td>28</td>
<td>+11</td>
<td>+1</td>
</tr>
<tr>
<td>Midhippocampal gyrus</td>
<td>27</td>
<td>+20</td>
<td>-3</td>
</tr>
<tr>
<td>Posterior hippocampal gyrus</td>
<td>23</td>
<td>+32</td>
<td>0</td>
</tr>
<tr>
<td>Left side</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amygdala</td>
<td>23</td>
<td>+2</td>
<td>+10</td>
</tr>
<tr>
<td>Pes hippocampi</td>
<td>31</td>
<td>+11</td>
<td>+3</td>
</tr>
<tr>
<td>Midhippocampal gyrus</td>
<td>23</td>
<td>+20</td>
<td>+2</td>
</tr>
<tr>
<td>Posterior hippocampal gyrus</td>
<td>22</td>
<td>+32</td>
<td>+2</td>
</tr>
</tbody>
</table>

**Discussion**

The safety of these operations takes precedence over most other considerations. The stereotactic diagnostic procedure has been well tolerated by the patients with only slight swelling of the scalp and transient stiff neck or soreness of movements of the jaw. The patients have been alert, oriented and without obvious additional mental impairment during the periods of observation. At operation and in the subsequent pathological specimens, the macroscopic cortical damage has consisted of several pits in the cortex at the sites of coagulation near the dura mater. In 1 patient even these were not seen. Beneath the cortical layer the tracts of the electrodes are microscopic and terminate in small electrolytic lesions purposely made only on the resected lobe. Considering the value to the patient of the information gained and that in 6 to 8 patients the procedure led to definitive treatment not possible otherwise, we feel that the minimal trauma inflicted is warranted. Further, the trauma is inflicted in already pathological states and intractable conditions.

The criteria used for the identification of the region responsible for the patient’s seizures are those that have accumulated over the years from many investigators’ findings. The use of these electrodes at these sites
permits most of these criteria to be tested at length and under physiological conditions. The spontaneous recorded activity in the depth sites has been quite different from surface recordings. In all of our patients the spontaneous discharges were frequent, high-potential, single and polyphasic spiking discharges appearing from one or more depth sites. Moreover the constancy of appearance day to day, week to week in the same sites contrasted strongly with the sporadic bursts and “jack-in-the-box” characteristics in surface recordings once described by McCulloch, and by Gastaut and Roger. Not only was this constant activity true from side to side but also from site to site on the same side. Epileptic neural pools have been characterized as susceptible to rhythmical, long-lasting, self-sustained activity in contrast to those that are recruited into epileptic discharge by excessive bombardment.

Spiking activity seen in the scalp leads did not appear in any instance independent of paroxysmal activity within the depth leads. On the other hand, there were frequent depth-seizure discharges, and hippocampal seizures in particular, not reflected in the scalp leads by visual inspection.

In every patient who has had a clinical psychomotor seizure, whether spontaneous or induced by electrical or pharmacological activation, there have been repetitive pseudorhythmical trains of spikes and slow waves in the hippocampus. However, we also have observed equally prominent but isolated hippocampal “seizure activity” that is not associated with any clinical manifestation, not reflected in the scalp leads, and not associated with any propagation to other depth sites.

During this type of isolated hippocampal trains of spikes, several patients tested during this existing activity performed complex visuomotor tasks with complete accuracy. We do not know the significance of this silent hippocampal “seizure” discharge.

The difference between these situations leads us to believe that the clinical manifestations are caused by propagation of the seizure into other systems but it is not clear why hippocampal discharges remain isolated in other instances.

Of the 8 patients who had this stereotactic investigation, we were confident in recommending unilateral temporal lobectomy in 6 because of the following characteristics:

![Fig. 8. Case 3. Depth recording demonstrates spiking discharges in the left pes hippocampi and midhippocampal gyrus without reflection in any apparent surface abnormality.](image)
(1) Marked disparity between the 2 sides, in that 1 site demonstrated the greatest amount of spiking activity with a greater amount of disorganization of the background frequencies also.

(2) The same site also displayed the lowest threshold for after-discharge on studies of electrical stimulation and frequently was the site of activation by Metrazol. Ralston\(^5\) has shown experimentally that the spiking after-discharge is a better index of the primary discharging focus than the presence of a spike alone. After-discharge usually consists of rhythmical, sinusoidal activity or rhythmical rapid, positive or negative spikes from 15 to 40 per sec. and with an amplitude one-third to two-thirds of that of the spike. These may appear as a result of electrical stimulation, during activation with Metrazol, and in some instances as spontaneous paroxysms and are one indication that the region is capable of self-sustained activity of seizure. Ajmone Marsan\(^1\) stated that after-discharges tend to be more discretely localized and often can be recorded only in close proximity to the "original" epileptic site.

(3) The same site demonstrated a lower threshold for the propagation of an induced focal seizure, i.e. that the hippocampal seizure would be apparent in the recordings from scalp or amygdala after first initiation.

(4) This same site when stimulated electrically reproduced part or the whole of the patients' spontaneous seizures which had been documented carefully in advance for this comparison. Stimulation of other sites sometimes produced subjective sensations but the patient could readily differentiate them as foreign to his customary pattern of seizure.

There were 2 patients in whom we were unable to make such a judgment, although the clinical pattern was much the same as in the remainder of the group. In 1 patient the recordings demonstrated sudden spike-and-wave complexes appearing simultaneously in all leads, and other spiking activity in the temporal depth electrodes appeared at nearly equal frequencies from both the right and left sides. In another patient spiking activity was independent and equally prominent from the two sides, and after-discharges were evoked by stimuli at equal parameters on either side.

Summary

Seizures of temporal-lobe origin may be associated with unilateral or bilateral discharges. In patients refractory to other treatment, temporal lobectomy has been quite successful for those with a unilateral origin. A much larger group of patients have bilateral temporal spiking discharges and few evidences of lateralization on consideration of the clinical and neuroradiological features. In a group of 8 patients with apparent independent bitemporal spiking activity and with seizures intractable to medical management there were placed stereotactically implanted electrodes in locations in amygdala, pes hippocampi, and hippocampal gyrus. In 6 patients 1 site demonstrated unmistakably greater spiking activity and disorganization of background frequencies as well as lowest threshold for after-discharges. Stimulation of the same site led to propagation of the discharges of seizure to other sites and frequently reproduced part or all of the characteristics of the patient's spontaneous seizures. Recommendations for temporal lobectomy were based on this evidence. Excellent precision in stereotactic placements has been verified in the 3 specimens that have been processed thus far. In 2 patients with bitemporal activity, no decision for lateralization could be made. In the course of investigation it has been found that several patients had intermittent trains of spiking discharges in the hippocampus which were isolated, non-propagating and silent clinically. Their significance is not apparent. Stereotactically implanted temporal electrodes in the amygdala and hippocampus have served as a useful technique in the further evaluation for surgical treatment of patients with bilaterally independent spiking activity but complete evaluation will require further experience and time.

Other investigations to gain new information by advanced techniques are conducted by W. Ross Adey, M.D., and M. A. B. Brazier, Ph.D. in
Anatomical and pathological studies are made by M.D. All of these persons have contributed in various ways to this study.

Kenneth Brinza, M.D., and W. Jann Brown, Ph.D. in behavioral and psychological studies.

840 Paul H. Crandall, Richard D. Walter and Robert W. Rand

References

1. AJMONE MARSAN, C. Electrographic aspects of “epileptic” neuronal aggregates. Épilepsia, 1961, 4 s. 2: 22–38.

Discussion

Dr. William H. Feindel: This excellent report describes a useful contribution to the investigation and selection for operation of that difficult group of patients who have bitemporal epileptic discharge. The technical approach that the authors have used, their anatomical control and their early surgical results are admirable. Methods now available for the evaluation of the lateralization of temporal-lobe discharge have included pharyngeal and multiple sphenoidal leads and special procedures of automation. Persistent use of these methods has given very satisfactory segregation and selection for cases for surgery.

Following the technique of Dr. Penfield, we have found that stimulation and recording during operation with the patient conscious provides valuable confirmation of both the pattern of the seizure and the distribution of electrographic abnormalities. Once the electrographic abnormality has been confirmed at operation a depth electrode can be placed in the periamygdaloid and hippocampal regions to enable stimulation and recording from these structures and correlation at the same time with the surface electrocorticogram. This has given evidence that electrographic discharge or stimulation in the periamygdaloid region is closely associated with automatism, pointing out the necessity for careful excision of this region during temporal lobectomy for seizures. It is also possible to outline the speech area at the time of surgery.

Despite these techniques and the one that the authors now have described so well, there still remains the problem of the patient who does in fact have independent bitemporal epileptic discharge. The stereotactic approach may well provide a means of placing small selective lesions in both temporal lobes without the catastrophic disturbance of memory which, in the light of our present knowledge, is likely to follow bilateral lobectomy.

Dr. Paul H. Crandall: I would just like to thank Dr. Feindel for commenting on this, and particularly in view of the large experience in Montreal Neurological Institute.