THE SURGERY OF EPILEPSY

LIMITATIONS OF THE CONCEPT OF THE CORTICO-ELECTROGRAPHIC "SPIKE" AS AN INDEX OF THE EPILEPTOGENIC FOCUS*

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Most neurosurgical procedures directed against epilepsy have been fashioned upon the generally accepted hypothesis that a hyper-irritable cortical focus ("epileptogenic focus," "firing point") is a prime factor in the pathogenesis of epileptic seizures. The hypothesis itself is based upon the pioneer work of Hughlings Jackson (1861–83), Fritsch and Hitzig (1870), Ferrier (1873), Munk (1880), Gowers (1881) and Talbert (1899), and from it follows logically the concept that the alleviation of epileptic seizures may be expected from (a) identification of the hyper-irritable focus and (b) its extirpation.

Unfortunately, the number of individuals who have obtained complete relief from epileptic attacks following surgical procedures does not conform closely to theoretic expectations. Even when grossly apparent lesions, such as cortico-meningeal scars, cysts of the cortex, and circumscribed atrophic areas are encountered at operation, only about one-fifth of patients subjected to operation can be freed of their seizures (Penfield and Erickson6). When, on the other hand, grossly apparent lesions are not in evidence and the surgeon is under the necessity of demonstrating the hypothetical firing point by physiologic means only, the results thus far have proven similarly disappointing.

This disparity between expected and actual clinical results is commonly accounted for by (a) citing the various practical difficulties encountered in identifying the cortical firing point; (b) assuming incomplete extirpation of the epileptogenic focus; (c) supposing the existence of more than one firing point; and/or (d) citing the inadvisability in certain instances of extirpating the cortical focus because of the likelihood of impairing crucial functions, such as speech and eupraxia. The fundamental concept of the cortical epileptogenic focus is, of course implicitly contained in all four of these accounts.

In consideration of the first three explanations (a, b and c above) the realization of better results would appear to reside in the improvement of methods for locating and precisely defining the limits of the cortical firing point. To this end, clinicians have striven toward more accurate observation and description of the convulsive seizure peculiar to each patient. Improved types of cortical stimulators have been designed, affording increasing control

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over voltage, amperage, wave form, frequency and pulse-duration for threshold determinations of cortical tissue. Roentgenography, including pneumoencephalography and cerebral angiography, has been extensively utilized and during the past 15 years electroencephalography has been employed to the same end. In connection with the latter diagnostic procedure, the concept has been evolved that the cortico-electrographic “spike” may be considered an indicator of the epileptogenous focus.

The assessment of spikes in the electroencephalograms of patients with convulsive disorders has been the particular object of several recent investigations (Jasper,2 Walker et al.,8,9 Penfield and Jasper7). The general viewpoint relative to post-traumatic epilepsy has been summarized by Walker et al.:9 “In post-traumatic epilepsy focal spikey* waves or spikes about the site of the injury indicate a convulsive diathesis.” In an extensive series of cases, Walker et al.9 showed that areas of after-discharge of spike and associated phenomena could be localized electrocortically following infraliminal sine-wave stimulation. Of these findings they say:

“These observations seem to indicate that certain cortical areas adjacent to cerebral scars may be excited by infraliminal stimuli producing a state of local epileptic hypersynchrony. Although these phenomena have many characteristics of cortical after-discharge, their lower threshold, more localized activity and longer duration suggest that they are different, at least in degree. That areas capable of such activity are potentially epileptogenic seems highly probable. That they are the foci, from which spontaneous epileptic attacks originate, lacks demonstration, but it seems a reasonable inference in those instances in which the electrocorticographic attack is associated with an aura identical to that in the spontaneous attacks. If the focus is some distance from the scar, another and perhaps primary focus may be located nearer the injury.”†

Inferentially, then, the spike per se is regarded as evidence of an epileptogenic focus, and from this it would follow that excision of the spike zone may be expected to have a salutary effect on the patient’s seizures.‡

Another view of “spikes” and “spikey” (or “sharp”) waves is given by Jasper.2 While he concurs in the notion that clean-cut spikes of brief duration are evidence of a focal zone of discharge, he considers that spike-like waves or “sharp” waves are the conducted end-result of spikes originating at a distance. The evidence supporting this view is convincing.

It is clear that caution must be exercised in differentiating between the two types of cortical potential change which may casually be included in the generic term “spiking.” In this connection, Jasper and Droogleever-Fortuyn,9 by stimulating midbrain and diencephalic structures, have demonstrated spikes formed with a dome simulating the familiar “petit mal” seizure pattern. These are, to be sure, not spikes in the sense that they are

* Italics ours.
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‡ This inference was made rather explicit by Quadfasel and Walker4 in a description of the delimitation of an epileptogenic focus. Their report was made relatively early after completion of an operative series and for this reason no statistical data were given. On the basis of clinical impression, however, the authors were inclined toward belief that the results were beneficial.
isolated. However, in some instances the dome can be absent, rhythmic spikes alone being apparent.

PROBLEM

The present investigation developed in the course of routine subcortical electrographic recording in a series of parkinsonian patients and non-parkinsonian "controls." Among the latter were 4 epileptic patients, 1 of whom represented an instance of post-traumatic epilepsy. The routine EEG examination in this subject revealed frequent clear-cut spikes over the right frontal lobe—the chief site of cicatization and gliosis following trauma. Following this, electrographic examination of the thalamic and striatal regions also revealed evidence of considerable spiking. The desirability of evaluating the incidence and behavior of cortical and subcortical spikes in epileptics thus suggested itself to us.

MATERIAL

Of the four epileptics examined, 1, a female of 23 years, failed to exhibit spikes (either cortical or subcortical) during the period of recording. The other 3 patients are reported upon. One of these was a 31-year-old male with post-traumatic epilepsy; another, a 10-year-old boy with a diagnosis of "idiopathic" epilepsy; and the third, a 36-year-old female with an "idiopathic" epilepsy since puberty and intractable pain of more recent origin in the left shoulder and arm due to Hodgkin’s disease.

METHOD

Routine EEGs were recorded by means of 8 to 12 scalp leads and 2 ear leads. Both monopolar (scalp-ear) and bipolar (scalp-scalp) recordings were employed. "Depth" records were made by means of needle electrodes of the type developed by Gibbs and Gibbs. One of these needles had 8 pickup rings, the other 4. The former was regularly used for recording from the striatum; the latter, from the thalamus. Both monopolar (ring-ear) and bipolar (ring-ring) records were routinely obtained. The needles were placed in accord with methods previously described. Immediately following electrographic recording in each patient, pneumoencephalography was carried out. By this means and the use of coronal brain sections cut on a grid, the approximate position of the ring leads was ascertained.

The recordings of the epileptic subjects thus obtained were compared with recordings similarly derived from 25 "controls," 13 of whom were patients having no known organic brain disease and 12 of whom were suffering from extrapyramidal disorders. None of these 25 cases exhibited spikes in either scalp or "depth" recordings.

RESULTS

Case 1. Male, aged 31 years, post-traumatic epilepsy. The position of the electrodes is shown in Fig. 1. The major results are presented in Figs. 2 and 3, each a 10-second strip of record (all bipolar) from the frontal scalp, striatum and thalamus.
Fig. 1. Case 1. Male, age 31, post-traumatic epilepsy. Positions of striatal (8-ring) and thalamic (4-ring) electrodes as revealed by A-P and lateral views in pneumoencephalogram.

Fig. 2. Case 1. Male, age 31, post-traumatic epilepsy. Evidence of independent spike activity in corpus striatum and thalamus, bipolar recording. For positions of deep electrodes, see Fig. 1 and text.
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Fig. 3. Case 1. Male, age 31, post-traumatic epilepsy. Evidence of independent spike activity in thalamic leads, bipolar recording. For positions of deep electrodes, see Fig. 1.

Fig. 4. Case 1. Male, age 31, post-traumatic epilepsy. Monopolar recording from thalamus and striatum, with greatest spike activity in Ring 1 of thalamus. For positions of deep electrodes, see Fig. 1.
In Fig. 2 there is evidence of focal spiking in the right frontotemporal area, in Ring 4 of the striatal lead, in Ring 6 of the striatal lead, in Ring 8 of the striatal lead and in Ring 3 of the thalamic lead. These foci are apparently quite independent. Fig. 3 shows further evidence of their independence, the scalp leads showing no clear instance of spiking, the thalamus a great deal, and the striatum a little spiking independent of that in the thalamus.

Monopolar deep leads are represented in Fig. 4. Here the thalamic leads are simultaneously active, the greatest amplitude apparently occurring in Ring 1 and the least in Ring 4. (All are negative with respect to the ear.) A little “spikey” activity appears in Rings 1, 3 and 8 of the striatal needle.

Case 2. Male, aged 10 years, “idiopathic” epilepsy. Evidence in Figs. 6 and 7 again shows that deeper structures may fire with a spike-like quality, independently of the surface, although in this case there is close following of certain striatal and thalamic leads. In Fig. 7, Rings 2–3 of the thalamic pickup show a considerable resemblance to Walker’s published data on post-stimulation saw-tooth spikes. (Simultaneous EKG in this record rules out pulse artifact.)

Case 3. Female, aged 36 years, “idiopathic” epilepsy; Hodgkin’s disease with intractable pain. In this patient, spikes were seen only with “activation” by intravenous sodium pentothal. The principal spike activity appeared only in striatal leads, referable chiefly to Ring 3 (Fig. 8). There was truncated spike-like activity, which may have been conducted by relay from a principal subcortical focus, apparent in the occipital lead; this was not at all times synchronized with the striatal spiking.

DISCUSSION

In a comprehensive discussion of the spread of epileptic activity in the cortex, McCulloch4 has recently observed:
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Fig. 6. Case 2. Male, age 10, “idiopathic” epilepsy. Evidence of “spikey” or spike-like activity in thalamic leads, bipolar recording. For positions of leads, see Fig. 5.

Fig. 7. Case 2. Male, age 10, “idiopathic” epilepsy. Evidence of thalamic “spikey” activity with striatal “following.” For positions of electrodes, see Fig. 5.
Fig. 8. Case 3. Female, age 86, “idiopathic” epilepsy, Hodgkin’s disease with intractable pain. Positions of striatal (8-ring) and thalamic (4-ring) electrodes shown in A-P and lateral views in pneumoencephalogram.

Fig. 9. Case 3. Female, age 86, “idiopathic” epilepsy, Hodgkin’s disease with intractable pain. Evidence of spike activity restricted within corpus striatum, after “activation” with pentothal sodium (bipolar recording). For positions of leads, see Fig. 8.
"...there is a ... method of spread of seizures which we cannot ignore. It is probably more common than we expect and of late has begun to come to the fore. There are seizures ... which may start in the cortex or in other structures,* but in which the seizures in the cortex play jack-in-the-box. You have them now at one place, and then they disappear out of the cortex, and then they reappear somewhere else in the cortex. ... If one has enough electrodes in the lower structures, one sees it as a seizure which disappears out of the cortex but persists in some lower structures and then from them reappears in the cortex."

These comments are based on evidence (Ward, McCulloch and Kopeloff10) that demonstrated spread from an experimental cortical focus to other cortical areas and to the cerebellum (but, interestingly, not to the hypothalamus). These investigators assert that spread will be restricted to centers that receive axons or collaterals from the primary focus. After initiation of such activity in a remote region, the primary focus may die out, but further spread from the secondary area may occur, returning perhaps to the initial (primary) region. Wycis et al.11 have also observed subcortical spiking, without concomitant cortical spikes, indicating that true subcortical foci, as we have described them, do exist.

We seem to have been in the box with "Jack," as well as outside, and so are in a position to make some comment about his unusual behavior.

In Case 1, there is every reason to believe that the seizures were on the basis of an epileptogenous zone in the vicinity of the demonstrable cicatrix. With its removal, clinical seizures (at least temporarily) have not recurred. Yet prior to operation, the ubiquitous "epileptogenic spike" appeared not only in this surface zone, but deeper in the cranial box. This deeper spiking was not restricted to one nuclear zone, but was distributed independently in at least two regions: the striatum and the thalamus. To analogize beyond McCulloch, the spike behaved like an ethereal Will-o'-the-wisp, its winking lamp leading us hither and yon, up and down: when we failed to see it, it may merely have been elsewhere, or it may not have been there at all.

In Case 2, the principal regions of spike-like activity were deep; scalp leads exhibited such "smoothing" as Jasper has attributed to conduction. (Actually, the raw data suggest smoothing in the sites studied, which would mean the primary focus might not have been tapped directly.)

Case 3 showed principally subcortical spiking, without primary cortical spiking, which, to use the analogies referred to above, suggests that Jack—or Jack's spring—was perhaps directly measured in his closed system.

Considering these cases together, spikes were derived from the thalamic and striatal leads in all 3 patients. They might appear during a particular time-interval in the thalamus alone, the striatum alone or in the surface leads alone. Combinations were also observed: thalamic spikes sometimes exhibited a "spread" to the striatum and/or cerebral surface, and in other instances striatal spikes sometimes exhibited a "spread" to the thalamus and/or cerebral surface. In still other instances, spikes apparently derived from the cerebral surface appeared to spread to the thalamic or striatal

* Italic commercially available
region. In no case was a surface spike observed spreading to both the thalamic and striatal regions simultaneously.

CONCLUSIONS

The surgical implications would seem to be that spiking per se cannot be considered evidence of an epileptogenic focus of a primary sort.* Rather, the full statement of Walker must be used in the neurosurgical assessment of the electrographic spike activity: "... spike about the site of the injury."† Yet, if subcortical spike genesis (Case 3, idiopathic epilepsy) is actually primary, "diathesis" may not always be consequent upon injury.

The present findings would seem to suggest that the concept of a cortical epileptogenic focus as the primary factor in the production of convulsive seizures stands in need of further evaluation. Even if this notion should ultimately prove tenable, we would still be under the necessity of critically inquiring whether the site of an epileptogenic focus is reliably revealed by the region(s) in which spike potentials happen to be recorded. Up to now, it has been tacitly assumed that this question is answerable in the affirmative. While the hypothesis has the appeal of engaging simplicity, there is a suggestion in the present data that "the epileptogenic firing point" is not invariably located in or just subjacent to the cerebral cortex, but that it may reside in deeper-lying nuclei, yet show corticpetal spread. This latter circumstance would explain the difficulty in identifying a cortical firing point responsible for convulsive seizures and account for the frequent failure of specific surgery directed against epilepsy.

REFERENCES


* This implication may also be drawn from the supporting evidence of the recent report of Wycis, Lee and Spiegel.
† Italics ours.