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Clinical Research

Ictal Spiking Patterns Recorded from Temporal Depth Electrodes Predict Good Outcome After Anterior Temporal Lobectomy

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Summary: *Purpose:* Investigators have shown that the presence of ictal spiking (IS) recorded from temporal depth electrodes is associated with mesial temporal sclerosis (MTS). We investigated the relation of IS to seizure control and pathology after anterior temporal lobectomy (ATL).

Methods: All patients undergoing intracranial ictal monitoring from a single institution since 1989 were identified. Those who did not undergo ATL or had postoperative follow-up of <1 year were excluded. All received at a minimum bilateral temporal depth electrodes. Ictal recordings were reviewed for the presence of IS, and the proportion of seizures with IS was determined for each patient. Outcome was determined by using Engel's classification. Surgical specimens were reviewed for pathology. Statistics used were χ^2, Fisher exact test, and Wilcoxon rank sum.

Results: Forty patients with 571 seizures were reviewed. In 292 seizures from 32 patients, IS was seen. Outcomes were 24 class I (22 with IS), five class II (four with IS), three class III (one with IS), seven class IV (four with IS), and one lost to follow-up (with IS). Pathologic review revealed 25 with MTS, 22 of whom had IS. The presence of IS was associated with class I outcomes ($p = 0.04$), but not MTS ($p = 0.06$). Patients with class I outcomes had a significantly greater proportion of seizures with IS (mean, 0.58 ± 0.3) compared with other outcomes (mean, 0.30 ± 0.3, $p = 0.02$).

Conclusions: The presence of IS and higher proportion of seizures with IS correlated with good seizure outcome after ATL. This information may be used in preoperative counseling.
Key Words: Temporal lobe epilepsy—EEG—Implanted electrodes—Seizure outcome—Mesial temporal sclerosis.

Several ictal patterns are observed in partial-onset seizures recorded by scalp EEG (1). Likewise, variable ictal patterns are seen in partial-onset seizures recorded intracranially: low-voltage fast activity, electrodecrement, periodic spiking, and rhythmic sustained activity of any frequency (2). Townsend and Engel (3) found that periodic spiking at seizure onset correlated with seizures of hippocampal and amygdalar onset and did not represent a propagation pattern, as had been previously proposed (3). Spencer et al. (4,5) found a correlation between ictal patterns recorded intracranially and surgical pathology with a low-voltage, fast-frequency discharge associated with mesial temporal sclerosis but not extratemporal pathology, and an ictal spiking (IS) pattern at onset associated with neuron loss in the CA1 region of the hippocampus. Other features of seizures recorded intracranially have been correlated with good surgical outcome after anterior temporal lobectomy (ATL) such as the presence of subclinical seizures (6) or prolonged interhemispheric propagation times (7). With the link to pathology established by other investigators, we sought to confirm and expand the findings of other investigators by examining the role of IS with respect to both surgical outcome and pathology after ATL.

METHODS

All patients undergoing intracranial ictal monitoring as part of their epilepsy surgery evaluation from the University of Michigan since 1989 were identified. All had medically intractable seizures, underwent a preoperative

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evaluation detailed elsewhere (8), and had suspected mesial temporal lobe onset epilepsy but conflicting localization data from noninvasive studies. For the time frame examined, by protocol, a patient could avoid intracranial ictal monitoring only if the ictal behaviors were consistent with mesiobasal limbic temporal lobe epilepsy, had ictal onsets localized to one anteromesial temporal region, had magnetic resonance imaging (MRI) findings consistent with ipsilateral mesial temporal sclerosis (MTS) and functional imaging (FDG-PET) abnormalities did not consist of contralateral temporal or exclusively extratemporal hypometabolism. Those who did not undergo ATL, had previous resective epilepsy surgery, or had postoperative follow-up of <1 year were excluded from analysis. Electrode placement was individualized but included at a minimum bilateral temporal depth electrodes and bilateral subdural temporal strip electrodes. The temporal depth electrodes were nonmagnetic eight- or 10-contact depth electrodes placed stereotactically from the occipital lobe and directed along the long axis of the hippocampus. Bilateral four- or six-contact temporal subdural strips were placed over subtemporal and anterolateral temporal neocortex from a temporal burr hole. Electrode placement was confirmed by MRI (9).

EEG was recorded continuously with a 64-channel Telefactor Beehive System. The ictal discharge was defined as a paroxysmal, focal, rhythmic discharge of any morphology sustained over a minimum of 10 s demonstrating frequency and/or spatial evolution, not attributed to a change in behavioral state. IS was defined as repetitive rhythmic or periodic spike discharges occurring at a frequency of <2 Hz with a typical duration of 5–100 s (Fig. 1) seen before subsequent sustained rhythmic discharges of any frequency demonstrating further evolution in space or frequency. Electrographic asymptomatic seizures were included in the analysis, and were differentiated from prolonged interictal bursts on the basis of absence of spatial or frequency evolution, a criterion of earlier studies (6). All seizures were reviewed by L.S., who was blinded to patient identity at the time of review. The presence of IS and the proportion of seizures with this pattern were determined for each patient. The only seizure-activation procedures used were anticonvulsant tapering and sleep deprivation. Nondominant temporal lobectomy included 6 cm of the superior, middle, and inferior temporal gyri, the occipitotemporal gyrus, and the lateral amygdala. The hippocampus and parahippocampal gyrus were resected posterior to the quadrigeminal cistern. Dominant temporal lobectomy was identical, but spared any cortex to which speech function was mapped, and extended only 4.5–5 cm. Seizure outcome was determined as of the latest follow-up (minimum, 1 year) by using Engel's classification (10). Good outcomes were defined as class I outcomes. Surgical specimens were analyzed for the presence of MTS or other pathology. All but one of the available specimens were analyzed by the same neuropathologist who examined coronally sectioned hippocampi, stained with hematoxylin and eosin. MTS was diagnosed when the CA1 region had apparent reduction in neuronal density by one half or more, and had apparent increase in glial density, with or without similar findings in the CA3–CA4 or dentate subfields. Cell counts were not obtained. The remaining specimen was analyzed in a similar fashion at Henry Ford Hospital where the ATL was performed.

Statistical analysis used χ^2, Fisher exact test, and Wilcoxon rank sum.

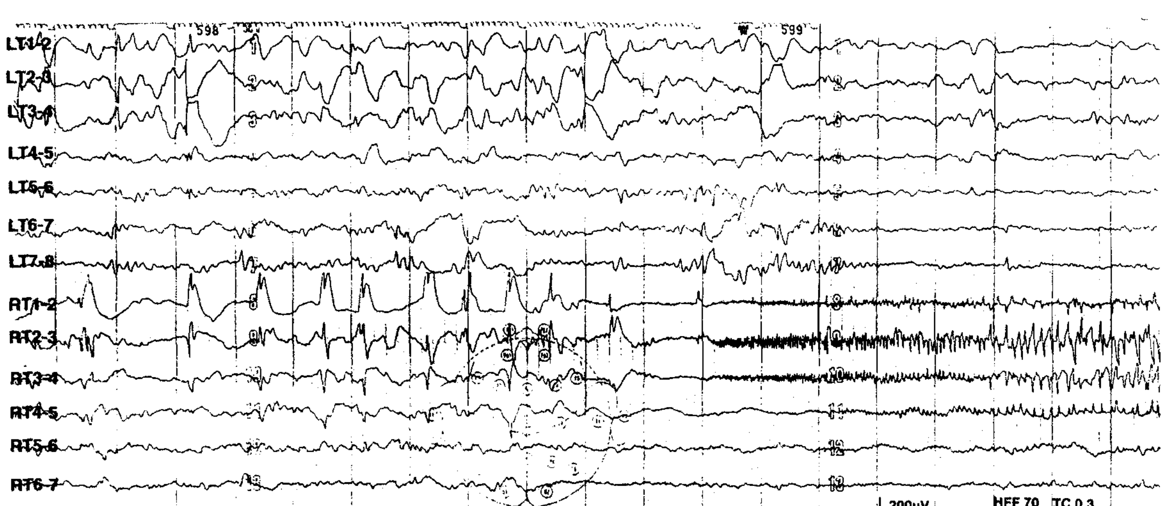

FIG. 1. Recording from bilateral temporal depth electrodes (temporal depth electrodes; LT, left; RT, right; electrode contacts 1–8, 1-amygdala). IS is characterized by repetitive ~1-Hz spike discharges seen in the right temporal depth electrode before the electrodecrement with beta/gamma frequency activity in the same location.

RESULTS

Between 1989 and June 1996, 64 patients underwent intracranial ictal monitoring. Forty patients, 20 men and 20 women, met inclusion criteria for this study. Of the 24 excluded, five underwent extratemporal resections, 11 had bilateral independent temporal ictal onsets without predominance and did not receive ATL, five patients experienced nonlocalized seizures, two had undergone previous resective epilepsy surgery and were being considered for repeated surgery, and one patient refused resection after intracranial monitoring. A total of 571 seizures was reviewed. The mean number of seizures reviewed for each patient was 15.3 ± 6.8, with a range of 4–34. IS was seen in 292 seizures from 32 patients. The proportion of seizures with IS ranged from 0 to 1.0, with a mean of 0.49 ± 0.35. Postoperative seizure outcomes were 24 class I, five class II, three class III, seven class IV, and one lost to follow-up. Of those with IS, 22 had class I outcomes, four class II, one class III, four class IV, and one was lost to follow-up. The presence of IS was statistically associated with class I outcomes after ATL ($p = 0.04$, Fisher's exact test). Of the 32 with IS, those with class I outcomes had a significantly greater proportion of seizures with IS (mean, 0.58 ± 0.3) compared with other outcomes (mean, 0.30 ± 0.3; $p = 0.02$, Wilcoxon rank sum).

Review of pathology revealed 25 with MTS, two with dysplastic lesions, one with a vascular lesion, six with no pathologic diagnosis, and six cases with insufficient tissue due to suction ablation of the hippocampus. Of the 32 with IS, 22 had MTS, five specimens were missing, three had no pathologic diagnosis, and two had an associated lesion (dysplasia, vascular anomaly). There was a trend between the presence of IS and MTS, but this did not reach statistical significance ($p = 0.06$, Fisher's exact test). Because of the large number of missing specimens in the IS pattern group, we reviewed the MRIs from the six patients with missing pathology specimens, and by including those having MRI-documented MTS with those having pathology-documented MTS, found a statistically significant correlation between IS and MTS ($p = 0.05$, Fisher's exact test). MRI performed preoperatively (1989–1996) revealed changes consistent with unilateral MTS in 10 of the 40 patients. In this selected group, MRI findings of MTS did not correlate with either good outcome ($p = 0.16$, χ^2) or MTS by pathology ($p = 0.42$, Fisher's exact test).

Our findings are not due to differences in length of follow-up between those with and those without IS (mean ± SD, 3.81 ± 1.52 vs. 3.57 ± 1.58 years, respectively). Likewise, these findings cannot be explained by differences in the likelihood of finding MRI evidence of MTS between the two groups ($p = 1.0$, Fisher's exact test). A separate analysis of low-voltage fast-frequency activity at onset revealed that this was a common pattern, seen in 24 of 40 patients, but this pattern did not have the same correlation with class I outcome ($p = 0.36$, χ^2).

DISCUSSION

Although in recent years, the use of temporal depth electrodes has diminished because of improvements in structural and functional brain imaging, better definition of the syndrome of mesial temporal lobe epilepsy, and increased use of temporal subdural strip electrodes exclusively, data acquired from temporal depth electrodes is useful and may lead to better understanding of the neurophysiology of mesial temporal lobe epilepsy. Williamson et al. (11) performed in vitro intracellular recordings of dentate granule cells in ATL specimens from patients with mesial temporal onset seizures and IS at ictal onset. They found that these patterns correlated with the loss of synaptically evoked inhibition, rather than enhanced inhibition akin to that seen in absence seizures, as had been widely believed before their investigations. Of course, with slice preparation, lateral inhibition may be lost, and in vivo correlation of this particular IS is, to our knowledge, unavailable.

Previous investigators found a link between ictal periodic spiking and MTS, and seizures of mesial temporal onset (3,5). Park et al. (12) reviewed initial ictal EEG patterns from temporal depth electrodes also confirming an association between IS and hippocampal sclerosis. Good surgical outcomes were seen in those with focal seizure onsets as opposed to regional ones, but no mention of an association between ictal pattern at onset and seizure outcome was made. Our findings of an association with good seizure outcomes after ATL in those with IS and greater proportions of seizures with this ictal pattern, is complementary and expands on the results of early investigators. Although we did not find a statistically significant association between IS and MTS by pathology, it is likely that this would not be the case if fewer pathology specimens were missing. This is suggested by MRI evidence of MTS in those with missing pathology specimens.

Alarcon et al. (13) also reviewed intracranial EEG patterns at seizure onset in those with presumed temporal lobe epilepsy, by using spectral analysis and visual analysis (13). Five patterns were recognized: electrodecrement, low-amplitude fast-activity, irregular sharp waves, regular spikes, and rhythmic activity of any frequency (typically <20 Hz). The patterns were not mutually exclusive; all early ictal patterns were included so that all or none might be present for any individual seizure. They found high-frequency activity was associated with a good surgical outcome. Direct comparison of our results with this study is again difficult, not only because we did not perform spectral analysis, but two of 15 patients did not receive surgery, and an additional two patients underwent extratemporal resections in the Alarcon study. Good outcomes also were defined differently between the two studies, with all except class IV outcomes considered good in the Alarcon study. Of the four patients in the Alarcon study with class I outcomes, all exhibited irregular sharp waves and three of four regular spiking at onset (both these groups appear to be equivalent to IS), but only two of four in this outcome class showed high-frequency activity initially. Schiller et al. (14) recently reviewed a series of consecutive patients undergoing intracranial monitoring, correlating initial ictal EEG patterns, and MRI findings with seizure outcome. They found no independent correlation between initial ictal discharge and seizure outcome after epilepsy surgery. It is difficult to compare the two studies because of study design. Our series was limited to ATL, whereas their study reviewed all undergoing intracranial monitoring including those with extratemporal epilepsy and those who did not undergo surgical resection.

We speculate that prolonged interhemispheric propagation and IS may represent the same phenomenon. We plan to investigate this in future studies.

In summary, the presence of IS recorded from temporal depth electrodes is correlated with good seizure outcome after ATL. A higher proportion of seizures with IS in individual patients also is correlated with good seizure outcome after ATL. This information may be used in preoperative counseling of patients.

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