



SHORT COMMUNICATION

Long term outcomes in patients with preoperative generalized interictal epileptiform abnormalities following amygdalohippocampectomy

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Summary We evaluated long term surgical outcomes in 21 patients with temporal lobe epilepsy and presurgical generalized interictal epileptiform discharges (IEDs). Following amygdalohippocampectomy, 12 patients (57.1%) were noted to have favorable outcomes (Engel classification of I–II). Favorable outcomes were significantly associated with a history of auras prior to seizure onset ($p=0.021$), the absence of generalized IEDs on postoperative EEG ($p=0.024$), and the presence of focal slowing on postoperative EEG ($p=0.045$).

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Introduction

Resection of mesial temporal lobe structures is an established therapy for select patients with medically refractory temporal lobe epilepsy (TLE) (Wiebe et al., 2001). The presence of focal interictal epileptiform discharges (IEDs) lateralized to the side of seizure onset has been identified as a favorable prognostic factor in these patients (Radhakrishnan et al., 1998). Conversely, it is often assumed that the presence of generalized IEDs precludes resective surgery. This assumption has been proven false in children with seizure types such as infantile spasms and continuous spike wave in slow wave sleep. Despite their generalized EEG appearances, the seizures in some of these children are

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secondary to focal pathology amenable to resections (Gupta et al., 2007; Wyllie et al., 2007; Loddenkemper et al., 2009; Chugani et al., 2010). However, surgical outcomes in adult patients with generalized IEDs and focal pathology has been less robustly explored. The purpose of our study was to determine the long term outcomes in patients with TLE and generalized IEDs on preoperative electroencephalograms (EEG) who underwent amygdalohippocampectomies.

Methods

We retrospectively reviewed the EEG reports of all 608 patients who underwent amygdalohippocampectomies for medically refractory TLE at our institution from 1989 to 2000. We selected those patients who demonstrated generalized IEDs on any preoperative scalp EEG for further analysis. Generalized IEDs were defined as the occurrence of generalized bilateral synchronous spike, or polyspike, and wave discharges on the interictal EEG. One patient also had a preoperative EEG showing modified hypsarrhythmia. We excluded patients with less than 6 months of postoperative follow up.

Preoperatively, all patients underwent brain MRI and video-EEG monitoring to confirm seizure localization. Patient demographics, presurgical epilepsy duration, seizure types, the presence or absence of aura or febrile seizures, MRI results, pre- and postoperative EEG findings, and seizure outcome were determined by review of the medical records. Outcomes were assessed at most recent follow up at our institution using the modified Engel classification (Engel, 1993). Favorable outcome was defined as an Engel classification of I–II; unfavorable outcome was defined as an Engel classification of III–IV.

All data entry and statistical analysis were performed using IBM SPSS Statistics 19 (SPSS Inc., Chicago, IL, USA). Correlations were examined using chi-square analysis (Fisher's exact test, 2-tailed) for categorical data and independent-samples Student's *t*-test (2 tailed) for continuous data. *p*-Values <0.05 were considered statistically significant.

This study was approved by the Institutional Review Board of Mayo Clinic, Rochester.

Results

Preoperative patient characteristics

Twenty one patients were identified using the criteria specified above; 11 (52.4%) were female. One patient had undergone a focal resection of a right temporal grade 1 ganglioglioma prior to amygdalohippocampectomy. The mean duration of epilepsy prior to amygdalohippocampectomy was 22.4 ± 13.8 years (range 2–52 years). The mean age at the time of surgery was 28.1 ± 12.3 years (range 10–54 years). The mean duration of postoperative follow up was 94.8 ± 55.3 months (range 24.3–244 months). Preoperative MRI revealed hippocampal atrophy and/or increased signal on T2-weighted/FLAIR images suggestive of mesial temporal sclerosis in 14/21 patients (66.7%). The remaining MRI findings are listed in Table 1.

Prior to amygdalohippocampectomy, all patients reported partial seizures. The majority (17/21, 81%)

reported auras prior to seizure onset. The minority (8/21, 38.1%) reported generalized tonic–clonic (GTC) seizures in addition to partial seizures. However, 5 of these patients (62.5%) had documented semiologies (e.g. aura prior, head/eye version, posturing, automatisms, and/or asymmetric clonic movements) suggestive of secondarily GTC seizures. Only 3 (14.3%) patients had preoperative histories suggestive of atypical absence seizures.

All patients had at least one or more types of interictal generalized IED on preoperative scalp EEG. These included atypical spike and wave (14/21 patients, 66.7%), slow spike and wave (2/21, 9.5%), polyspike and wave (4/21, 19%), generalized undifferentiated (7/21, 33.3%), and modified hypsarrhythmia (1/21, 4.8%, see Table 2). Focal features to the generalized IEDs (e.g. maximal in amplitude over a single hemisphere) were observed in 5/21 (23.8%) patients. All patients except one had partial seizures recorded on video EEG prior to amygdalohippocampectomy; the sole exception was a patient with a recorded atypical absence seizure. Another patient had a recorded generalized nonconvulsive seizure in addition to right temporal lobe seizures.

Postoperative outcomes

Of the 21 patients who underwent amygdalohippocampectomies, 12 (57.1%) had a favorable outcome (see Table 1). Five patients (23.8%) were able to successfully titrate off all antiepileptic drugs (AEDs) prior to last follow up. Favorable outcomes were significantly associated with reported aura prior to seizure onset (12/17 patients with aura had a favorable outcome versus 0/4 without aura, $p=0.021$). Favorable outcome was also significantly associated with lack of postoperative generalized IEDs (8/9 patients without such discharges had favorable outcomes versus 4/12 with such discharges, $p=0.024$) and postoperative EEG focal slowing (5/5 with focal slowing had favorable outcomes versus 7/16 without, $p=0.045$). Although there were trends towards improved outcomes in patients with preoperative MRI abnormalities ($p=0.27$) and lack of preoperative GTC seizures ($p=0.2$), these did not reach statistical significance. There was no correlation between the presence of preoperative generalized IEDs with focal features and outcome ($p=0.61$). There were also no correlations between outcomes and specific MRI abnormalities, pathology findings, or history of febrile seizures.

Conclusions

Our findings indicate that the presence of generalized IEDs in select patients with TLE being considered for amygdalohippocampectomy does not automatically portend a poor prognosis. The majority (57.1%) of patients in our cohort had favorable outcomes despite their preoperative generalized EEG findings. Seizure freedom was significantly associated with a history of aura prior to seizure onset and lack of generalized IEDs on postoperative EEG. Such data suggest that generalized IEDs in these cases likely had focal origins in cortical regions distant from surface electrodes, thus representing secondary bilateral synchrony (Tukel and Jasper, 1952). If these discharges truly represented concurrent idiopathic generalized epilepsy, the high rate of seizure freedom

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