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High frequency oscillations for lateralizing suspected bitemporal epilepsy

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ABSTRACT

Objective: In some cases of single focus epilepsy, conventional video electroencephalography (EEG) cannot reveal the epileptogenic focus even when intracranial electrodes are used. Here, we tested whether analyzing high frequency oscillations (HFOs) can be used to determine the ictal onset zone in suspected bitemporal epilepsy and improve seizure outcome.
Methods: We prospectively studied 13 patients with refractory temporal seizures who were treated over a 4-year period and underwent bilateral placement of intracranial electrodes. Subdural strips were used in all cases, and depth electrodes were implanted into mesial temporal lobes in 10 patients. The mean patient age was 30.92 years, and 30.7% of patients were male. Patients were monitored by conventional and wide-band frequency amplifiers.
Results: Conventional invasive EEG monitoring of interictal periods showed bilateral epileptiform abnormalities in 12 patients (92.3%) and unilateral epileptiform abnormalities in one (7.7%), and monitoring of ictal periods revealed unilateral seizure origins in nine patients (69.2%) and bilateral origins in four (30.8%). In contrast, high frequency invasive EEG monitoring of interictal periods showed bilateral HFOs in seven patients (53.8%) and unilateral HFOs in six (46.2%), and monitoring of ictal periods revealed unilateral HFOs in all 10 patients who were tested. Three patients were not monitored during ictal periods because of time limitations. All 13 patients subsequently underwent a standard unilateral temporal lobectomy and have been followed-up for a minimum of 12 months. Eleven (84%) had a Class I outcome, one (8%) a Class II outcome, and one a Class III outcome.
Significance: Bilateral placement of subdural strip and depth electrodes for seizure monitoring in patients with suspected bitemporal epilepsy is both safe and effective. Monitoring high frequency oscillations can help determine the laterality of the onset zone when localization using conventional EEG or brain MRI fails.

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1. Introduction

Antiepileptic medications fail to control seizures in more than 30% of patients with epilepsy (Kwan and Brodie, 2000). Resective brain surgery is then the most common treatment for medically intractable partial epilepsy. However, surgery sometimes fails because of incorrect localization, incomplete resection of the epileptogenic zone, or possibly, the development of new regions of epileptogenicity (Boongird et al., 2008). Bilateral temporal lobe epilepsy is a challenging issue, especially when the clinical symptoms recorded through scalp video-electroencephalography (vEEG) and magnetic resonance imaging (MRI) are nonlateralizing or discordant. In this situation, intracranial electrodes are often implanted to confirm the origin of the seizures. Subdural strip, grid and intraparenchymal depth electrodes represent the most accurate and definitive method for localizing epileptogenic cortex, and they overcome the limitations of scalp electrodes, namely signal

Abbreviations: EEG, electroencephalography; MRI, magnetic resonance imaging; MTLE, mesial temporal lobe epilepsy; HS, hippocampal sclerosis; SPECT, single-photon emission computed tomography; vEEG, video electroencephalography; iEEG, invasive electroencephalography; HFOs, high-frequency oscillations.

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attenuation from the intervening skin, bone, cerebrospinal fluid, and dura, as well as muscle artifacts (Diehl and Lüders, 2000; Nair et al., 2008). Yet, in some cases, even these electrocorticographs fail to identify the seizure laterality. A new biomarker for epileptogenic tissue has emerged, which promises to improve our understanding of epilepsy pathophysiology and to develop new clinical diagnostic methods. It consists of high-frequency oscillations (HFOs) above 80 Hz, which require the EEG to be sampled at a frequency above 2000 Hz. At present, HFOs are further sub-classified into ripples (80–250 Hz) and fast ripples (250–500 Hz) (Blanco et al., 2010; Staba et al., 2002). HFOs were explored through microelectrode recordings in epileptic rats and in human patients (Bragin et al., 1999b, 1999c), and studies expanded when they were found with clinical macroelectrodes (Jirsch et al., 2006; Urrestarazu et al., 2007). In epilepsy surgery, removal of tissue with HFOs seems to predict good surgical outcome, even better than removal of the ictal onset zone (Jacobs et al., 2010). This suggests that HFOs should be taken into account in clinical evaluations. Thus, we speculated that high frequency oscillations may help determine the laterality of the ictal onset zone in suspected bitemporal epilepsy and improve seizure outcome. We compared the laterality values obtained from 13 patients with suspected bitemporal epilepsy using either intracranial high frequency EEG or intracranial conventional EEG and brain MRI.

2. Patients and methods

2.1. Patients

Thirteen consecutive patients (four men, nine women; mean age: 30.92 ± 9.12 years) with suspected bitemporal epilepsy required bilateral implantation of electrodes at the Xuan Wu Hospital Comprehensive Epilepsy Center of Beijing between April 2012 and April 2014. This was a small fraction (10.7%) of the 109 patients who had anterior temporal lobe resection without electrodes implantation. The average duration of the seizure disorder was 14.92 years. Seizure frequency was 5.0–62 seizures/month. All patients had a comprehensive non-invasive evaluation prior to intracranial exploration (details see Table 1), including a detailed history and neurological examination, neuropsychological testing, brain MRI, and prolonged continuous scalp vEEG recordings (Adam et al., 1997). At least three habitual seizures were recorded. Several patients underwent additional diagnostic tests, including magnetoencephalography (n = 4) and single-photon emission computed tomography (n = 4). All patients gave their informed consent and procedures were approved by the Medical Research Ethics Committee at Xuan Wu Hospital of Capital Medical University.

2.2. MRI scan

Standard magnetic resonance imaging (MRI) was performed on Siemens Trio 3-T scanner (Siemens, Erlangen, Germany) with conventional axial and sagittal T1WI, axial T2WI, T2-FLAIR, and oblique coronal T2-FLAIR in epilepsy protocol. In addition, a whole brain volumetric series was acquired using a MPRAGE sequence (TR 1 900 ms, TE 2.2 ms, TI 900 ms, Flip angle 9°, FOV 256 mm × 256 mm, matrix 256 × 256, 176 slices, 1 mm × 1 mm × 1 mm). T2-FLAIR oblique coronal images perpendicular to the long axis of both hippocampi consisting of 20 slices was also obtained with 3 mm slice thickness, 0 mm interslice gap.

2.3. EEG criteria for lateralization

2.3.1. Interictal periods

All EEG data were obtained at least 2 h away from a seizure without artifact. We selected EEG data from two 30-min interictal periods, one while waking, and one while sleeping. Lateralization was classified as unilateral or bilateral according to the following criteria. Unilateral: If >80% of all epileptiform abnormalities (spikes or sharp waves) occurred in the same temporal lobe (sphenoid electrode). Bilateral (nonlateralized): If bilateral epileptiform abnormalities (spikes or sharp waves) appeared at similar amplitudes in both temporal lobes (sphenoid electrode) simultaneously or independently with <80% originating in the same temporal lobe. Sphenoidal electrode wires were inserted by the same physician using a 2.75-in., 22-gauge needle through the space formed by the zygomatic arch and the two rami of the mandible, aimed at the area of the foramen ovale (King et al., 1986), using sterile technique.

2.3.2. Ictal periods

All seizures recorded for each patient were visually identified and reviewed. The structures in which the earliest EEG changes appeared during seizure were defined as the seizure onset zone. The EEG pattern consisted of a low-voltage fast-frequency discharge, a periodic spike-and-wave complex, or rhythmic theta/delta activity. Lateralization was classified as unilateral or bilateral according to the following criteria. Unilateral: all seizure activity originated in the same temporal lobe (sphenoid electrode). Bilateral: seizure activity originated from both temporal lobes (sphenoid electrode) simultaneously or independently.

2.4. Indications for bilateral invasive electrophysiological monitoring

After collecting the diagnostic data (non-invasive information), we classified patients into four categories based on the indication for bilateral invasive monitoring (see Table 1). (1) In four patients (patient #8, #10, #3, and #2), the MRI scan was normal, the clinical semiology did not suggest lateralization, and the interictal events and ictal surface vEEG showed a bilateral pattern. (2) In six patients (#6, #9, #7, #5, #13, and #4), a unilateral lesion was visible in the MRI, but the clinical semiology, interictal events, and ictal surface vEEG all showed a bilateral pattern. Patient #4 had unilateral semiology but the EEG showed a bilateral pattern. (3) In two patients (#1 and #12), surface vEEG identified a unilateral pattern, but MRI results suggested contralateral abnormalities. (4) In one patient (#11), clinical semiology suggested laterality contralateral to the MRI abnormality. Thus, no laterality could be determined in groups 1 and 2, and contradictory laterality was seen in groups 3 and 4.

2.5. Intracranial electrodes implantation

Invasive intracranial electrodes were implanted when hemispheric laterality was not clear based on non-invasive data (i.e. the classification above: the data indicate a bilateral seizure onset or contradict each other). Bilateral strip electrodes were placed over the temporal pole and/or temporo-basal region in all 13 patients. Additional depth electrodes were placed stereotactically into the mesial temporal lobe structures in 10 patients (77%) via the occipito-temporal route (Blatt et al., 1997; Kral et al., 2002; Van Roost et al., 1998). Bilateral depth electrodes were inserted via frameless stereotactic guidance through burr holes over the occipital lobes at the level of the lambdoidal suture, approximately 2 cm from the midline and passing through the length of the hippocampus into the amygdala. Frameless stereotaxy has been shown to result in accurate placement of electrodes into the amygdala and hippocampus, with 98% of the electrodes providing informative recordings (Mehta et al., 2005). The depth electrode path was carefully chosen so as to avoid injury to critical vascular structures and to minimize entry into the ventricular system and the risk of tearing an ependymal vein. In some circumstances, ventricular entry was unavoidable in order to ensure adequate sampling of the mesial

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