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Clinical significance of ictal high frequency oscillations in medial temporal lobe epilepsy

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HIGHLIGHTS

- Ictal high frequency oscillations (HFO) were detected unilaterally.
- They were detected ipsilateral to the side of hippocampal sclerosis (HS).
- They were not propagated contralaterally except for one patient.
- In one case with bitemporal onset, ictal HFO were detected only on the side of HS.
- Ictal HFO in the medial temporal lobe is the electrophysiological signature of HS.

ABSTRACT

Objective: To clarify the clinical significance of ictal high frequency oscillations (HFO) in the medial temporal lobe.
Methods: This study included 19 patients who underwent intracranial electrode implantation in bilateral temporal lobes and had at least one seizure recorded at 1 kHz sampling rate. The characteristics of ictal HFO in the medial temporal lobe, and the relations between the presence of HFO, pathology, and postoperative seizure outcome were analyzed.
Results: Ictal HFO were detected from medial temporal structures in 11 patients with medial temporal lobe epilepsy (MTLE). Among eight patients without HFO, only three were diagnosed with MTLE. Ictal HFO were detected from unilateral medial temporal structures ipsilateral to the side of hippocampal sclerosis (HS). In one patient with bitemporal independent seizure onset, ictal HFO were detected only on the side of HS. HS was detected in all 11 patients with HFO, but in only one of four patients without HFO. Seizure outcome did not differ between patients with and without HFO.
Conclusions: Ictal HFO in the medial temporal lobe may be a specific marker for MTLE with HS.
Significance: Recording of ictal HFO in the medial temporal lobe may be useful for presurgical evaluation of MTLE.

1. Introduction

Electrophysiological studies in animals revealed that high frequency oscillations (HFO) with frequencies of 400–1000 Hz were recorded in the vicinity of epileptogenic foci (Gastaut and Fischer-Williams, 1959). Recently, HFO have attracted attention in epilepsy surgery. Previous studies have reported the characteristics of HFO in medial temporal lobe epilepsy (MTLE) as follows; (1) recorded from hippocampus or entorhinal cortex; (2) frequencies ranging from 170 to 400 Hz, usually with fast frequencies of 260–270 Hz [fast ripple: FR (Bragin et al., 1999), very high frequency band: VHF (Jirsch et al., 2006)]; (3) usually detected on the side of surgical resection; (4) not detected in the region of secondary propagation; (5) can be recorded ictally or interictally; (6) appear as clusters of short bursts with a duration of 6–53 ms; (7) usually associated with ictal spikes on conventional EEG; (8) detected by only 1–2 macroelectrode channels; and (9) low amplitudes of 5–30 μV (Bragin et al.,1999, 2002; Jirsch et al., 2006; Yamaguchi et al., 2008).

As for ictal HFO, Jirsch et al. (2006) reported ictal HFO in 10 patients with focal seizures, including four with medial temporal onset seizures. They used the EEG seizure onset as a surrogate for the epileptogenic area, and did not evaluate the postoperative seizure

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Table 1
Clinical characteristics of 19 patients.

Patient	Age (yrs)/sex	Age at onset (yrs)	Semiology	Interictal EEG	Ictal EEG
1	20/M	7	Automotor	Lt	Rt
2	21/F	1	Automotor	Bil (Lt predominant)	Rt
3	32/F	10	Dysmnestic aura → automotor	Rt	Rt
4	36/F	15	Aura → automotor	Rt	Lt
5	43/F	9	Dialeptic	Bil (Lt predominant)	Lt
6	34/F	1	Aura → automotor	Bil (Lt predominant)	Bil (Lt predominant)
7	30/F	4	Automotor	Rt	Lt
8	19/M	3	Abdominalaura → automotor	Bil (Lt predominant)	Bil (Rt predominant)
9	43/F	9	Aura → dialeptic	Rt	Lt
10	37/F	18	Automotor	Bil	Lt
11	39/M	10	Aura → automotor	Bil (Rt predominant)	Rt
12	36/M	27	Dialeptic	Bil	Lt
13	21/M	15	Abdominal aura → dialeptic	Rt	Rt
14	29/M	16	Aura → automotor	Bil	Lt
15	26/F	15	Automotor	Rt	Rt
16	26/M	5	Hypermotor	Bil	Bil
17	16/F	11	Automotor	Bil	Bil (Lt predominant)
18	31/F	11	Automotor	Lt	Bil (Lt predominant)
19	21/M	15	Aura → automotor	Bil	Lt

M: male; F: female; Rt: right; Lt: left; Bil: bilateral independent spikes on right and left.

outcome. Khosravani et al. (2009) also studied ictal HFO in seven TLE patients. However, the clinical significance of ictal HFO on surgical decision-making has not been fully examined.

To clarify the clinical relevance of ictal HFO, we analyzed their characteristics including the spatial distribution of ictal HFO in the medial temporal lobe, and compared the presence or absence of ictal HFO with hippocampal pathology and postoperative seizure outcome. We also demonstrated the clinical usefulness of detecting ictal HFO in surgical decision-making for bitemporal epilepsy.

2. Patients and methods

2.1. Patients

Previously, we proposed the following criteria for omitting intracranial EEG monitoring in patients with temporal lobe epilepsy; (1) appearance of focal epileptic discharges in unilateral sphenoidal lead during the phase of simple partial seizures, or unilateral discharges predominantly in the sphenoidal lead during the early phase of complex partial seizures; (2) interictal spikes on scalp-recorded EEGs localizing unilaterally in the anterior region of the temporal lobe, and if bilaterally independent, presenting with unilateral predominance in a ratio of greater than 4:1; (3) presence of autonomic signs in the initial phase of signal symptoms; and (4) neuroimaging findings in the mesial temporal region showing elongated T2 on MRI and HS, or a tumorous lesion (Mihara et al., 1992). Consequently, between May 2005 and May 2008, 19 patients underwent implantation of combined depth and subdural electrodes in bilateral temporal lobes (Mihara and Baba, 2001), and had at least one seizure recorded at 1 kHz sampling rate. These 19 patients were included in this study. Before intracranial video/EEG monitoring, all patients underwent noninvasive presurgical evaluations including history-taking, video/scalp sphenoidal EEG monitoring, neuroimagings, and neuropsychological tests. Brain MRI was performed at 1.5 tesla and 5-mm slice thickness, and axial, coronal, and sagittal T1-weighted, T2-weighted, and FLAIR images were acquired. The clinical characteristics of the 19 patients are shown in Table 1. Seizures were classified by the semiological seizure classification proposed by Lüders et al. (1998).

Depth electrodes (Unique Medical, Japan, 0.8 mm diameter, 1 mm length, either 5 or 10 mm center-to-center spacing) were placed in bilateral hippocampi and amygdala using MRI stereotaxy. Subdural electrodes (Ad-tech Medical Instrument, Racine, WI. 2.3 mm contact, effective area 4.15 mm^2, 10 mm spacing) were also placed over bilateral temporal regions including the basal and anterior aspects, and the adjacent parieto-occipital areas (Fig. 1). Reference electrodes were placed on the surface of the skull, with the contacts of the electrodes facing away from the skull to avoid the referential activation. Analyses were performed on referential montages. Antiepileptic medications were reduced, and EEG recording was started approximately 1 week after electrode placement and continued for approximately 2 weeks. The EEG signals were digitally recorded by EEG-1000 (Nihon Kohden) at a sampling rate of 200 Hz and a time constant of 10 s for conventional EEG analysis. For detection of HFO, EEG was low pass filtered at 300 Hz, recorded at a sampling rate of 1 kHz and a time constant of 10 s.

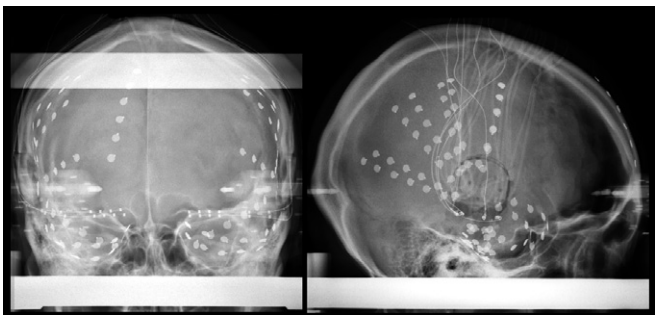

Fig. 1. Skull X ray showing the location of intracranial electrodes. Left: anteroposterior view. Right: lateral view. Two depth electrodes are inserted into the medial temporal structure on each side. RA and LA are aimed at amygdala, and RH and LH are at hippocampus. Basal temporal areas are covered by subdural electrodes.