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Ictal high-gamma oscillation (60–99 Hz) in intracranial electroencephalography and postoperative seizure outcome in neocortical epilepsy

Seong-Cheol Park [a], Sang Kun Lee [b], Huije Che [c], Chun Kee Chung [a,c,d,*]

[a] Department of Neurosurgery, Seoul National University College of Medicine, Seoul, Republic of Korea
[b] Department of Neurology, Seoul National University College of Medicine, Seoul, Republic of Korea
[c] Magnetoencephalography Center, Seoul National University Hospital, Seoul, Republic of Korea
[d] Neuroscience Research Institute, Seoul National University Medical Research Center, Seoul, Republic of Korea

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HIGHLIGHTS

- This study showed that the resection extents of neocortices containing ictal high-gamma oscillations (HGOs, 60–99 Hz) recorded during chronic intracranial electroencephalography were correlated with postoperative seizure-free outcome.
- The cluster epileptogenicity indices of 60–99 Hz bandwidth activities were effective in finding the centres of the ictal onset zones. In addition, the resection of areas with high-amplitude HGOs was correlated with a seizure-free outcome.
- This finding suggests that the 60–99 Hz bandwidth can provide clinically valuable information for defining epileptogenic zones.

ABSTRACT

Objective: High-gamma oscillations (HGOs) (60–99 Hz) have been suggested to correlate with seizure onset zones and seizure outcomes. We investigated the correlation between the extent of removal of ictal HGO generating areas and postoperative seizure outcome in neocortical epilepsy (NE).
Methods: Twenty three patients with medically intractable NE underwent chronic intracranial electroencephalography (iEEG) using subdural electrodes. Ictal HGOs and superimposed undersampled ripples within ±3 s of video-iEEG ictal onset were extracted by wavelet clustering and thresholding. Cluster epileptogenicity indices (CEIs) were calculated. The temporal analysis window was locked to the timing of the maximum CEI wavecluster. Root mean square amplitudes, cross-correlation synchronies and the local focus indices within the temporal window were calculated.
Results: Percentages of resected maximum CEI waveclusters and HGO zones with high standardised amplitudes (>3), high cross-correlation synchronies (>0.9) and high local focus indices (>2) were significantly higher in the seizure-free group compared to the not seizure-free group ($p = 0.036$, $p = 0.018$, and $p = 0.026$, respectively).
Conclusions: The automatic quantitative ictal HGO analysis may be effective in delineating the epileptogenic zone.
Significance: HGO analysis may be helpful for improving post-resection seizure outcome in NE in the future.

1. Introduction

Recently, clinical utility of high-gamma oscillations (HGOs) (60–99 Hz) in epilepsy is being revisited (Molaee-Ardekani et al., 2010; Rampp et al., 2010; Ayala et al., 2011; Uhlhaas et al., 2011). HGOs are the lower part of ripples and the higher part of fast activities. In extratemporal lobe epilepsy, ictal onset frequency was frequently in the gamma range (Lee et al., 2000). In addition, it was suggested that ictal ripples and gamma oscillations are augmented earlier than beta activities and fast ripples in paediatric Rolandic epilepsy patients (Nariai et al., 2011). These findings suggest that HGOs, investigated in our report, are probably a part of the most important bandwidth of ictal intracranial electroencephalography (iEEG) (Nariai et al., 2011; Zijlmans et al., 2011).

* Corresponding author. Address: Department of Neurosurgery, Seoul National University College of Medicine, 101 Daehangno, Jongno-gu, Seoul 110-744, Republic of Korea. Tel.: +82 2 2072 2352; fax: +82 2 744 8459.
E-mail address: chungc@snu.ac.kr (C.K. Chung).

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Both fast activities (12–99 Hz) and high-frequency oscillations (HFOs) (with a bandwidth usually over 80–100 Hz) have been suggested to be related to the epileptogenic zone in neocortical epilepsy (NE) and in mesial temporal lobe epilepsy (MTLE) as well (Fisher et al., 1992; Alarcon et al., 1995; Wendling et al., 2003; Ochi et al., 2007; Bartolomei et al., 2008, 2010; Wetjen et al., 2009; Andrade-Valenca et al., 2012; Blanco et al., 2011; Jacobs et al., 2011; Usui et al., 2011; Valderrama and Le Van Quyen, 2011; Zijlmans et al., 2011). Because HGOs is the overlapping bandwidth between fast activities and HFOs, both studies about fast activities and HFOs support the clinical efficacy of HGOs at least partially.

In the recent past, patients with a good outcome were reported to have a significantly larger proportion of interictal HFO or fast activity generating areas removed than patients with a poor outcome (Jacobs et al., 2010; Akiyama et al., 2012). With respect to ictal fast activities, a better seizure outcome could be expected in patients with focal fast activities ($\leqslant$4 channels, 20–100 Hz) compared to those with widespread fast activities in NE (Wetjen et al., 2009; Bartolomei et al., 2010). Proper resections of ictal fast activities or HFOs were recently suggested to be correlated with good seizure outcomes (Modur et al., 2011; Nariai et al., 2011).

On the other hand, ictal and preictal synchrony change may be complex and both synchronisation and desynchronisation were suggested to occur (Wendling et al., 2003; Bartolomei et al., 2004; Roopun et al., 2009; Jiruska et al., 2010a). In a few studies, ictal hypersynchronous clusters were suggested to be related to the epileptogenic zone and ictal onset (Roopun et al., 2009; Jiruska et al., 2010a). These studies predict that, in epilepsy surgery, resection of the region with high amplitude and hypersynchrony in HGO and HFO bandwidths will result in good seizure outcome. Thus, resection of ictal hypersynchronous cluster measured based on a local focus index (LFI) was also evaluated in this study (Roopun et al., 2009).

Another important consideration for the delineation of the epileptogenic zone is temporal relationship of iEEG activity with the ictal onset. Bartolomei has suggested that the epileptogenicity index, which is defined as the fast activity (12.4–96 Hz) energy divided by the lower frequency bandwidth energy and the delay from the ictal onset, is helpful in delineating the epileptogenic zone in temporal lobe epilepsy (Bartolomei et al., 2008, 2010). In addition, a correlation between seizure outcome and ictal iEEG activities within 3 s of ictal onset was identified whereas there was no correlation between iEEG activities up to 5 s of ictal onset and seizure outcome (Kim et al., 2010). Therefore, we concentrated on HGOs only within 3 s of ictal onset as determined by video-iEEG monitoring.

Here, we tried to test these hypotheses with respect to both seizure outcome and the extent of resection of ictal HGO generating areas in NE.

2. Methods

2.1. Subjects

From July 2005 to December 2008, 37 patients with medically intractable epilepsy, who were older than 16 years and who underwent subdural or depth electrode implantation for iEEG monitoring with subdural or depth electrodes at Seoul National University Hospital Epilepsy Center were registered for the study. All patients were followed up for more than 14 months postoperatively. This study was approved by the Seoul National University Hospital Institutional Review Board (No. C-1005-060-319).

Comprehensive preoperative studies including an epilepsy protocol magnetic resonance imaging (MRI 1.5T or 3.0T), video-iEEG monitoring, intracarotid amytal test, interictal with or without ictal single photon emission tomography, positron emission tomography, neuropsychological test, intracarotid amytal test and magnetoencephalography were done. The location of the ictal onset zone and the ictal time were determined by preoperative evaluations and video-iEEG monitoring (Lee et al., 2004). Antiepileptic medication was reduced or terminated during video-iEEG monitoring period.

Information about seizure type, MRI-positive lesion location and mesial hippocampal sclerosis, pathology, secondary generalisation, follow-up duration, the extent of the ictal onset zone, and the presence of adjacent eloquent cortex was identified (Lee et al., 2004).

Among 37 patients, 14 patients were found to have MTLE or MTLE plus NE. Hence, 23 patients with neocortical ictal onset zone in evaluations including video-iEEG monitoring were recruited for our study.

2.2. Ictal onset determination

In contrast to the statistical method (cumulative sum) used for the determination of ictal onset in the original epileptogenicity index, one epileptologist (S.L.) and one surgeon (C.C.) reviewed the patients' video-iEEG records and decided the ictal onset times, ictal onset zones, and irritative zones on the basis of conventional iEEG morphology analysis (Lee et al., 2004; Bartolomei et al., 2008, 2010). We did not quantify HGOs for the purpose of making clinical decisions and diagnoses, including determining the ictal onset time and surgical plan.

To determine the ictal onset time, the onset of clinical seizure was marked on the basis of videos showing the earliest identifiable abnormal behaviours, including unresponsiveness (Fisch and Spehlmann, 1999). The ictal onset time was determined by the earliest changes in the interictal activity preceding or accompanying the onset of clinical seizure (Modur et al., 2011). Low-voltage fast activity in the beta or gamma range rhythmic spikes in the alpha or theta range, rhythmic sinusoidal waves in the delta or theta range and semirhythmic delta activities were considered as the ictal onset rhythms (Fisch and Spehlmann, 1999; Lee et al., 2004; Kim et al., 2010). These ictal onset rhythms should be continuously shown during the clinical seizure with evolutions and propagations into the other channels (Blume et al., 1984; Modur et al., 2011). These ictal onset rhythms were traced retrospectively, and ictal onsets were selected as the earliest times that these activities with later evolutions could be distinguished from interictal rhythms by epileptologists (Lee et al., 2004; Kim et al., 2010).

2.3. Intracranial electroencephalography data collection and analysis

Subdural strips, grids and depth electrodes (Ad-Tech Medical Instrument Corporation, Racine, WI, USA) were used. Most electrodes used were subdural electrodes. Subdural electrodes were 4-mm-diameter stainless steel discs. Inter-electrode distances were 10 mm. Extra-operative video-iEEG was recorded using a Grass Beehive™ Horizon 128-channel LTM system with an AURA® 32-channel amplifier with 400-Hz sampling capacity and TWin® software (Grass Technologies, Astro-Med, Inc., West Warwick, RI, USA). The sampling rate was 200 Hz in TWin® software setting. A 60-Hz notch filter was used. No low-pass filter was used to prevent attenuation of HGO activities and to undersample superimposed aliases (60–99 Hz) of ripple (100–140 Hz) (Xia, 2000; Baker, 2005).

The peri-ictal period of ± 3 s was analyzed for HGOs. The frequency range between 60 and 99 Hz was evaluated statistically. The frequency range between 0 and 100 Hz was visualised on the spectrograms (Figs. 1–4). iEEG data in a text file format were exported by TWin software® in the average reference montage. Custom MATLAB® (Mathworks™, Natick, MA, USA) programs were