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Peri-ictal broadband electrocorticographic activities between 1 and 700 Hz and seizure onset zones in 18 patients

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HIGHLIGHTS

- Relationships between peri-ictal activities and seizure onset zones were analysed between 1–700 Hz and −15 to 5 s from the ictal onset.
- Maximum amplitude activities during the peri-ictal periods were significantly related to the seizure onset zones during −10 to 5 s from the ictal onset.
- Low-frequency activities, especially theta had significant relationships with seizure onset zones comparable to high-frequency activities.

ABSTRACT

Objective: We investigated the relationship between locations of broadband peri-ictal electrocorticographic activities determined by a semi-automatic detection method and seizure onset zones in medically intractable epilepsy patients.
Methods: We included 18 patients. Peri-ictal periods (−15 to +5 s from the ictal onset) were divided into 4 periods of 5 s duration each in bandwidth from 1 to 700 Hz divided into 11 bins. Thereafter, we calculated the mean overlapping percentage of the maximum amplitude activity electrodes with the seizure onset zone in the total number of seizures in each patient. Significance was considered at an adjusted *p*-value of 0.05.
Results: By the maximum amplitude method with the Bonferroni correction, only high-frequency activities (>60 Hz) during −5 to 0 s from the ictal onset were significantly related to seizure onset zones. In post hoc analyses, bands in 60–139 Hz and 4–7 Hz were significantly related to seizure onset zones in the Bonferroni correction. However, after the less conservative Benjamini–Yekutieli correction and with the epileptogenicity index, other bands and periods after −10 s from the ictal onset were also related with seizure onset zones.
Significance: Detailed bands, timings and analytic methods of peri-ictal activities with high relationships to seizure onset zones were identified.
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1. Introduction

Recently, high-frequency activities (HFAs, >60–100 Hz in previous studies) by electrocorticography (ECoG) have been recognised in seizure onset zones (SOZs) during ictal and interictal periods (Jacobs et al., 2009, 2010; Jirsch et al., 2006; Modur et al., 2011; Nariai et al., 2011; Pail et al., 2013; Zijlmans et al., 2011). HFAs have been suggested to be more specific to SOZs or seizure outcomes than low-frequency activities (LFAs < 60–100 Hz in

Abbreviations: CEI, cluster epileptogenicity index; FDR, false discovery rate; FR, fast ripple; HFA, high-frequency activity (60–700 Hz); HG, high-gamma; ECoG, electrocorticography; LFA, low-frequency activity (1–59 Hz); MAW, maximum amplitude wavecluster; MCW, maximum cluster epileptogenicity index wavecluster; MTLE, mesial temporal lobe epilepsy; NE, neocortical epilepsy; RP, ripple; SOZ, seizure onset zone.

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previous studies) in clinical macroelectrode recordings (Jacobs et al., 2010; Modur et al., 2011; Zijlmans et al., 2011). Peri-ictal HFAs were also suggested to precede LFAs (Khosravani et al., 2009; Nariai et al., 2011; Zijlmans et al., 2011). Main focuses of these previous studies were HFAs. Therefore, comparisons between HFAs and LFAs were at least partly unbalanced, i.e., the studies investigating LFAs excluded slow rhythms (<20 Hz), considered LFAs as a merged single band (1–100 Hz, for example) or evaluated spikes only (Khosravani et al., 2009; Modur et al., 2011; Nariai et al., 2011; Zijlmans et al., 2011). These methods might have underestimated LFAs' relationship to SOZs in comparison to HFAs. Furthermore, peri-ictal HFAs were also usually investigated only in two bands, ripples (RPs) and fast ripples (FRs) or up to 300 Hz (Modur et al., 2011; Nariai et al., 2011; Zijlmans et al., 2011). Thus, bands that are significantly related to SOZs have not been described in detail. However, a narrower band which is more important may exist (Tort et al., 2013; Weiss et al., 2013). The first comparison of this study is to compare peri-ictal HFAs vs. LFAs in multiple bands in relation to SOZs (Fig. 1).

In the present study, we selected 60 Hz as the boundary between HFAs and LFAs, as the alternating current frequency is 60 Hz in Korea and high-gamma (HG) is known to be potentially similar to RP in its electrophysiological mechanisms (Fig. 1) (Jefferys et al., 2012; Park et al., 2012).

Because ictal electrical activities in ECoG are much more capricious than interictal ones, most automatic detection algorithms for HFAs analyse the interictal activities (Blanco et al., 2011; Pail et al., 2013; Staba et al., 2002). Furthermore, most previous studies on peri-ictal activities employed visual analysis (Modur et al., 2011; Zijlmans et al., 2011). However, an automatic quantitative analysis has been suggested to be more objective and potentially fast. Recently automatic detection algorithms began to be applied to the ictal activities (Salami et al., 2012). In the present study, we investigated peri-ictal activities by our semiautomatic method based on the wavecluster amplitude (Park et al., 2012).

Recently, multiple *in vitro* and human studies have suggested that preictal discharges, including high amplitude spikes and HFAs preceding the ictal onset by a few seconds, are closely related to epileptogenesis and SOZs (Avoli et al., 2013; Huberfeld et al., 2011; Jiruska et al., 2010a; Khosravani et al., 2009; Levesque et al., 2013; Park et al., 2012; Zijlmans et al., 2011).

Several experimental studies have supported a concept of preictal discharge that is distinct in clinical implications and mechanisms. This type of preictal discharge (about −12 s from the ictal onset) was suggested to have high amplitudes (>approximately 180 ± 100 μV), frequent polyspike patterns, associations with HFAs and a glutamatergic mechanism, which is different from ordinary interictal spikes and direct epileptogenicity (Avoli et al., 2013; Huberfeld et al., 2011; Levesque et al., 2013). Previous studies investigating these preictal discharges in experimental models suggested that similar phenomena would occur in epilepsy patients (Avoli et al., 2013; Huberfeld et al., 2011). Clinical candidates of this special type of spike were exemplified and referred to as high-amplitude preictal discharges (HPDs) in this study. To analyse HPDs, an semiautomatic detector was designed to reveal high-amplitude activities specifically. Additionally, for HPD detection, an epileptogenic index that considers the time distance from the ictal onset may be more effective than indices that do not consider the time distance (Bartolomei et al., 2008, 2010; Park et al., 2012). Hence, the second comparison of this study is to compare two different electrical epileptogenic indices, one that considers only amplitudes (wavecluster amplitudes), and the other that considers

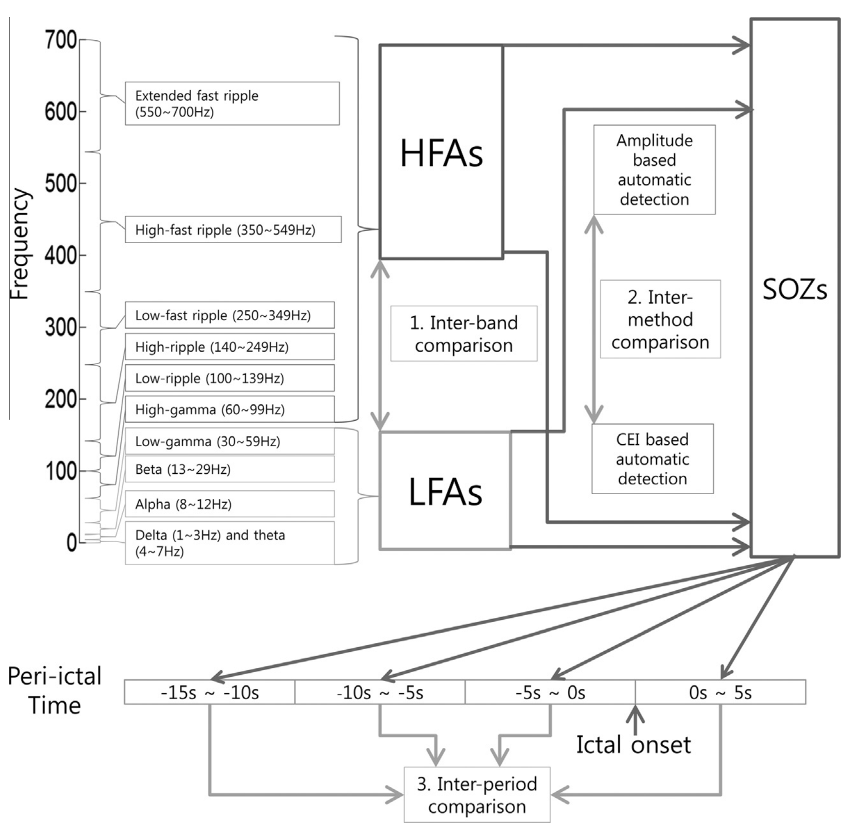

Fig. 1. Investigated bands, methods and periods in this study. Three types of comparisons were made. Frequency bands in the left vertical axis were used as 11 separate semiautomatic detection bins. Relationships to SOZs were compared between overlapping percentages of HFAs (⩾60 Hz) and LFAs (<60 Hz) (1. Inter-band comparison) and wavecluster amplitudes and wavecluster CEI (2. Inter-method comparison). Peri-ictal periods divided in 4 periods with 5 s durations were also compared (3. Inter-period comparison).

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