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Usefulness of interictal spike source localization in temporal lobe epilepsy: Electrocorticographic study

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Summary The success of epilepsy surgery depends on delineation of the suspected epileptogenic zone. The gold standard to delineate it is to use the ictal onset zone from an electrocorticography (ECoG). Although interictal spikes are also associated with the epileptogenic zone, their clinical significance has been under-evaluated. The aim of this study was to evaluate the source localization of interictal spikes in terms of the association with epileptogenic zone in surgical temporal lobe epilepsy patients. The proposition is that the resection volume in patients with favorable outcomes includes the epileptogenic zone. The association with the epileptogenic zone was assessed as follows: (1) how many of the interictal spike sources are within the resection volume in patients with favorable outcomes and (2) how many of the interictal spike sources are outside the resection volume in patients with unfavorable outcomes. Thirty-eight temporal lobe epilepsy (TLE) patients who underwent both ECoG monitoring and epilepsy surgery were recruited and their 10 min of ECoG recordings were analyzed. Six tumor-related TLE patients were excluded in the analysis. Of the remaining 32 patients, 20

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patients achieved favorable surgical outcomes (Engel I and II), while the surgical outcomes of 12 patients were unfavorable (Engel III and IV). In each patient, interictal spike sources were localized using sLORETA and co-registered into a reconstructed brain model. The correspondence rate with the resection volume was estimated by counting the percentage of interictal spike sources in the resection volume. The correspondence rate in patients with favorable outcomes was 72.8 ± 22.1, which was significantly higher than that (41.2 ± 28.8) of the patients with unfavorable outcomes ($p = 0.002$). Nine out of twelve patients (75%) with unfavorable outcomes had multiple interictal spike source clusters both interior and exterior to the resection volume, while 4 of the 20 patients with favorable outcomes (20%) had such multiple clusters ($p = 0.021$). In conclusion, interictal spike sources are highly associated with the epileptogenic zone. ECoG interictal spike source localization could help in the delineation of the potential resection volume.

Introduction

The epileptogenic zone is defined as a region of the cortex that can generate epileptic seizures. Complete removal of the epileptogenic zone is necessary and sufficient to be seizure-free and is the primary goal in epilepsy surgery (Luders and Awad, 1992; Luders et al., 1993). Of the various preoperative diagnostic modalities to approximate the epileptogenic zone, the ictal onset zone on the electrocorticography (ECoG) following subdural electrode placement has been considered as a gold standard in determining the resection area (Engel et al., 1981; Alarcon et al., 1997; Asano et al., 2005; Agirre-Arrizubieta et al., 2009; Cho et al., 2011). Incomplete resection of the ictal onset zone has been recognized as a risk for surgical failure (Jayakar et al., 2008; Asano et al., 2009; Kim et al., 2010a; Chang et al., 2011). However, visual inspection of ictal onset does not always result in the delineation of a potential epileptogenic zone because of fast propagation to the adjacent electrodes (Lee et al., 2000, 2005). Additionally, in some cases, the patients may have to undergo invasive monitoring for a prolonged period until a satisfactory number of habitual seizures occur increasing the risk of complications such as infection and neurologic deficit (Hamer et al., 2002).

On the other hand, interictal spikes recorded by ECoG can also be used to deduce the epileptogenic zone (Bautista et al., 1999; Hufnagel et al., 2000; Asano et al., 2003). However, the role of interictal spikes as an indicator to delineate the resection volume has not been clearly verified. Previously, conventional ECoG studies have been analyzed on a channel-level which determines the position of the electrodes on the cortical surface capturing the epileptic discharges. However, the accuracy of channel-level analysis depends on the inter-electrode distance. Moreover, it is difficult to localize interictal spikes arising from deep regions such as the sulcal fundi (Zhang et al., 2008). Those problems may be overcome by source-level analysis since it provides 3D source locations of epileptic discharges (Zhang et al., 2008; Kim et al., 2010b; Cho et al., 2011). Furthermore, source-level analysis could construct the resection volume instead of the resection area on which the culprit electrodes were placed. There have been several studies that evaluated the association between the interictal spike source location and the resection volume on the ECoG recordings (Zhang et al., 2008; Dumpelmann et al., 2009). However, one of the critical limitations of these previous studies is that they did not consider seizure outcome. One study conducted ECoG interictal spike source localization in 14 frontal lobe epilepsy (FLE) patients with focal cortical dysplasia (FCD) (Ramantani et al., 2013). They classified interictal spikes according to their affiliation with the seizure onset or irritative zone and each spike type was averaged before applying source localization. Although this technique may have increased the signal-to-noise ratio (SNR), the features of the individual spike were lost. In addition, insufficient consideration of patients with unfavorable outcomes seems to be another limitation of this study. We can only speculate that when the patient became seizure-free, it was because the epileptogenic zone must have been included in the resection volume (Rosenow and Luders, 2001). Therefore, in patients with favorable outcomes, how many of the interictal spike sources are included in the resection volume is important (sensitivity issue). Additionally, interictal spike sources in patients with unfavorable outcomes also need to be identified (specificity issue). The aim of the present study was to evaluate the source localization of interictal spikes in terms of the association with the epileptogenic zone in surgical temporal lobe epilepsy patients. We recruited 38 temporal lobe epilepsy (TLE) patients who underwent invasive monitoring and analyzed their 10-min ECoG recordings for interictal spike source localization.

Patients and methods

Patients profile

We included consecutive TLE patients who underwent invasive monitoring and respective surgery at the Comprehensive Epilepsy Center, Seoul National University Hospital, from 2006 to 2010. During this period, 66 TLE patients underwent both invasive monitoring and epilepsy surgery. However, 22 of the 66 patients' interictal ECoG recordings were not available for interictal spike source localization since only a short period of ECoG recordings followed by ictal activities were archived. Of the 44 patients whose interictal ECoG recordings were available, 6 patients were additionally excluded for one of the following reasons: (1) interictal spikes were not conspicuous compared to the background noise; (2) surgical outcome was unknown since the patient was lost on follow-up; and (3) interictal spikes were solely detected by depth electrodes. The present study focused on the source localization of interictal spikes detected on the ECoG. Additionally, we excluded 6 tumor-related TLE patients since tumor resection was emphasized more in