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Electrical source imaging of interictal spikes using multiple sparse volumetric priors for presurgical epileptogenic focus localization

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ABSTRACT

Electrical source imaging of interictal spikes observed in EEG recordings of patients with refractory epilepsy provides useful information to localize the epileptogenic focus during the presurgical evaluation. However, the selection of the time points or time epochs of the spikes in order to estimate the origin of the activity remains a challenge. In this study, we consider a Bayesian EEG source imaging technique for distributed sources, i.e. the multiple volumetric sparse priors (MSVP) approach. The approach allows to estimate the time courses of the intensity of the sources corresponding with a specific time epoch of the spike. Based on presurgical averaged interictal spikes in six patients who were successfully treated with surgery, we estimated the time courses of the source intensities for three different time epochs: (i) an epoch starting 50 ms before the spike peak and ending at 50% of the spike peak during the rising phase of the spike, (ii) an epoch starting 50 ms before the spike peak and ending at the spike peak and (iii) an epoch containing the full spike time period starting 50 ms before the spike peak and ending 230 ms after the spike peak. To identify the primary source of the spike activity, the source with the maximum energy from 50 ms before the spike peak till 50% of the spike peak was subsequently selected for each of the time windows. For comparison, the activity at the spike peaks and at 50% of the peaks was localized using the LORETA inversion technique and an ECD approach. Both patient-specific spherical forward models and patient-specific 5-layered finite difference models were considered to evaluate the influence of the forward model. Based on the resected zones in each of the patients, extracted from post-operative MR images, we compared the distances to the resection border of the estimated activity. Using the spherical models, the distances to the resection border for the MSVP approach and each of the different time epochs were in the same range as the LORETA and ECD techniques. We found distances smaller than 23 mm, with robust results for all the patients. For the finite difference models, we found that the distances to the resection border for the MSVP inversions of the full spike time epochs were generally smaller compared to the MSVP inversions of the time epochs before the spike peak. The results also suggest that the inversions using the finite difference models resulted in slightly smaller distances to the resection border compared to the spherical models. The results we obtained are promising because the MSVP approach allows to study the network of the estimated source-intensities and allows to characterize the spatial extent of the underlying sources.

1. Introduction

Approximately 30% of the patients with epilepsy suffer from refractory epilepsy, a condition in which epileptic seizures are not adequately controlled with anti-epileptic drugs. One of the treatments for refractory epilepsy patients is epilepsy surgery (Boon et al., 1999b). The suitability for a surgical procedure to treat the patient is assessed during the presurgical evaluation. During this evaluation, different anatomical and functional techniques, investigating various aspects of the patient's epilepsy, are combined in order to delineate the zone that is responsible

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for initiating the seizures. This is the so called epileptogenic zone (EZ), whose removal or disconnection is necessary for abolition of the seizures (Luders and Awad, 1992). The recording of the electroencephalogram (EEG) that measures the electrical brain activity non-invasively by means of electrode sensors placed on the patient's head, is one of the cornerstone techniques. EEG recordings allow to identify the seizure onset zone (SOZ), defined by the region in the brain generating the seizure onset discharges in the EEG, and the irritative zone (IZ) defined by the region in the brain generating interictal epileptiform discharges (IED) in the EEG in between the seizures (Rosenow and Lüders, 2001).

Interictal spikes are typical manifestations of IED in the EEG. They are characterized by a large amplitude rapid component lasting 50–100 ms that is usually followed by a slow wave, 200–500 ms in duration (de Curtis et al., 2012). Electrical source imaging (ESI) techniques allow to localize the generating sources of interictal spikes in order to delineate the IZ (Michel et al., 2004; Kaiboriboon et al., 2012; Michel and Murray, 2012). Several studies showed high positive predictive value of interictal spike ESI during the presurgical evaluation (Boon et al., 1997a, 1997b, 1999a; Michel et al., 1999; Plummer et al., 2007; Oliva et al., 2010; Brodbeck et al., 2010, 2011). However, the precise clinical value for epileptogenic focus localization is challenging because the IZ could be distant and, or completely separate from the SOZ and the EZ (Kaiboriboon et al., 2012). Moreover, the IZ is considered to be spatially more extensive than the SOZ (Carrette et al., 2011b).

The generation of interictal spikes is a complex phenomenon, and propagation of activity from the source to remote cortical regions can occur within milliseconds (Alarcon et al., 1994; Wennberg et al., 2011; Kaiboriboon et al., 2012). As a consequence, a common problem in the ESI procedure is the selection of the time points or time epochs of the spike in order to localize the primary sources of the activity and not the areas to which the epileptic activity is spreading. It has been shown in previous studies that the early component of the spike is likely to represent the location and field of the source, and the peak of the epileptiform discharge actually reflects propagated activity (Merlet et al., 1996; Lantz et al., 2003; Rose and Ebersole, 2009; Plummer et al., 2008; Aydin et al., 2015). As such, modeling of the spike peak could be misleading to delineate the IZ. However, the early component of the spike is of much smaller amplitude compared to the peak, so accurate modeling may be easily affected by noise contamination (Scherg et al., 1999).

The golden standard to assess the accuracy of ESI for interictal spikes is to compare the results of ESI with (simultaneously) recorded spikes from intracranial EEG. These kind of datasets are however restricted for validation to the locations where the intracranial electrodes are placed. Moreover, simultaneous recordings will affect the ESI results due to skull defects and the placement of the electrodes (Li et al., 2007; Lanfer et al., 2012, 2013; Lau et al., 2014). An alternative way is to evaluate presurgical EEG data with a high incidence of interictal spikes that were recorded in patients with good surgical outcome and who showed no interictal spike activity in postsurgical EEG registrations. Studies show that areas with high incidence of interictal spikes highly correlate with the EZ (Asano et al., 2003; Marsh et al., 2010) and the resection of the IZ, instead of the EZ provides good surgical outcome (Bautista et al., 1999). Moreover, a study using simultaneously recorded EEG/MEG and intracranial recordings showed that the very early components of interictal spike activity were not yet subject to propagation and were found within the SOZ (Aydin et al., 2015). By including these kinds of patients and retrospectively analyzing interictal epileptiform spikes, the ESI activity can be correlated to the resected zone (Mégevand et al., 2014). This relies on the assumption that the very early components of the interictal spike activity in these patients, which are not necessarily visible in the EEG, were part of the EZ.

In this paper we evaluate an ESI technique that allows to estimate the activity of sources distributed in the brain of the patient corresponding with a specific time epoch of the interictal spike activity. It is an application of our previous work in which we suggested to use multiple sparse volumetric priors (MSVP) for ESI using the hierarchical Bayesian framework implemented in the statistical parametric mapping software[1] (Strobbe et al., 2014a, 2014b). Compared to the more traditional approaches, where the sources are typically estimated that correspond to the spike peak, or to 50% of the spike peak during the rising phase of the spike (Boon et al., 1997a, 1999a; Brodbeck et al., 2011; Birot et al., 2014), the choice of the time epoch in order to localize the origin of the activity using the MSVP method is not clear. In the Ossa et al. (2015) study, the authors already suggested to use the approach by limiting the inversion procedure to a specific time epoch before the spike. In this study, three different time epochs were chosen for inversion: (i) a window starting 50 ms before the spike peak and ending at 50% of the spike peak during the rising phase of the spike, (ii) a window starting 50 ms before the spike peak and ending at the spike peak and (iii) a window starting 50 ms before the spike peak and ending 230 ms after the spike peak. For each of the time windows, the time courses of the intensity of the distributed sources in the brain of the patients were estimated. Subsequently, the primary sources generating the interictal spikes were identified as the sources with the maximum energy corresponding to the beginning of the spike till 50% of the peak during the rising phase of the spike.

For verification, we compared the performance of the MSVP approach with the results obtained with the LORETA approach and an equivalent current dipole (ECD) approach. For these more traditional approaches we estimated the sources at the spike peak and at 50% of the spike peak during the rising phase of the spike. Based on interictal spikes recorded in six patients that were rendered seizure free after surgery and that showed no interictal spikes in post-operative routine EEG recordings, we were able to evaluate the considered approaches by comparing the distances of the estimated activity to the border of the resected area.

2. Patient data

We retrospectively selected interictal spike data in six patients with refractory partial temporal lobe epilepsy who underwent resective surgery using the following inclusion criteria: (i) the patient was seizure free (i.e. Engel class I) after surgery, with minimum follow-up of 1.5 years, (ii) the electrode positions were known, (iii) the seizures and the majority of interictal spikes showed the same lateralization in the EEG recordings, i.e. over the left or right hemisphere and (iv) there were no spikes observed in routine EEG registrations of 0.5 h, 6 months after resection. An overview of the patient data is given in Tables 1 and 2.

Three patients had 27 channel EEG recordings and 3 patients had 64 channel EEG recordings. The recorded interictal EEG data was first filtered between 0.5 and 40 Hz with a Butterworth zero phase filter and a 50 Hz notch filter implemented in the Brain Vision Analyzer software (Brainproducts, Munich). Spike selection was visually performed by one expert electrophysiologist (AM or EC) experienced in reading clinical EEG. All patients had one dominant spike type with an invariable morphology and maximal amplitude at the same electrode. For patient 2 both anterior and posterior spikes were observed over the left hemisphere. The majority of spikes were anterior and selected for analysis. For the patients that showed bilateral interictal activity, i.e. patients 3 and 5, we only selected the dominant side for analysis because more than 90% of the spikes originated from that side. The spikes were marked at the time point with the highest amplitude, i.e. the peak of the spike, on the same channel. The spikes were subsequently segmented from −50 ms to 230 ms around the peak, in order to include the large amplitude rapid component followed by a slow wave for inversion. The spikes were subsequently averaged. Some electrodes were removed in the analysis due to bad signal quality. In Figs. 1 and 2, the averaged spikes for the 64 channel and 27 channel recordings are shown, respectively. The electrode for spike selection and the number

[1] A MATLAB (The MathWorks Inc., Natick, USA) toolbox for the analysis of EEG, MEG, PET, SPECT and fMRI data.