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Ictal EEG source imaging in presurgical evaluation: High agreement between analysis methods

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ABSTRACT

Purpose: To determine the agreement between five different methods of ictal EEG source imaging, and to assess their accuracy in presurgical evaluation of patients with focal epilepsy. It was hypothesized that high agreement between methods was associated with higher localization-accuracy.
Methods: EEGs were recorded with a 64-electrode array. Thirty-eight seizures from 22 patients were analyzed using five different methods phase mapping, dipole fitting, CLARA, cortical-CLARA and minimum norm. Localization accuracy was determined at sub-lobar level. Reference standard was the final decision of the multidisciplinary epilepsy surgery team, and, for the operated patients, outcome one year after surgery.
Results: Agreement between all methods was obtained in 13 patients (59%) and between all but one methods in additional six patients (27%). There was a trend for minimum norm being less accurate than phase mapping, but none of the comparisons reached significance. Source imaging in cases with agreement between all methods was not more accurate than in the other cases. Ictal source imaging achieved an accuracy of 73% (for operated patients: 86%).
Conclusion: There was good agreement between different methods of ictal source imaging. However, good inter-method agreement did not necessarily imply accurate source localization, since all methods faced the limitations of the inverse solution.

1. Introduction

There is compelling evidence for the role of electric source imaging (ESI) in the localization of interictal epileptiform discharges [1–5]. However, the irritative zone generating the interictal EEG discharges might not necessarily coincide with the seizure-onset zone [6]. Ictal source imaging faces additional technical challenges (artifacts occurring during seizure, absence of ictal EEG correlate in scalp recordings, propagation of ictal activity), and it has received less attention compared to interictal analysis [5].

Several methods of ictal source imaging have been previously described and validated in clinical practice [7–13]. However, it is not known to what extent the different methods lead to the same source location, and which is the best approach for localizing ictal sources. It was hypothesized that concordance between different methods/inverse solution was associated with a higher localization-accuracy [14].

The objectives of this study were: to investigate the agreement between different analysis strategies of ictal source imaging, to assess their accuracy in the presurgical evaluation of patients with epilepsy, and to test the hypothesis that higher inter-method agreement was associated with higher localization-accuracy.

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2. Methods

2.1. Patients and recordings

Thirty-eight seizures from 22 consecutive patients (10 females) who met the inclusion criteria, were analyzed. The age of the patients was between 17 and 49 years (mean: 33.8 years). The mean duration of epilepsy, from the onset to the Long Term Monitoring was 17 years (median: 12.5, range: 2–48 years). Inclusion criteria were: patients who undergone long-term video-EEG monitoring for presurgical evaluation, who had had at least one seizure recorded, and for whom the multidisciplinary epilepsy surgery team was able to decide on the localization of the epileptogenic zone. Exclusion criteria was the absence of identifiable ictal EEG activity.

Patients gave their informed consent prior to the admission to the epilepsy monitoring unit (EMU). EEGs were recorded using 64 scalp electrodes according to the 10–10 setting.

Seventeen patients (77%) had epileptogenic lesion on the MRI. Supporting document 1 in the online version at DOI: 10.1016/j.seizure.2016.09.017 shows demographic and clinical information (including neuroimaging and electrophysiology) for all patients.

2.2. Ictal source imaging

Anonymized ictal EEG recordings were retrospectively analyzed, blinded to all clinical data, using BESA Research 6.1 software. Five different source analysis methods were applied: phase-mapping (PM), dipole fitting, CLARA, cortical-CLARA and minimum norm estimation (MN). The analysis methods are described in detail elsewhere [12,13]. Briefly:

2.2.1. Phase mapping

The first detectable oscillatory pattern at seizure-onset was marked and the spectral peak was determined using FFT. By combining the real and imaginary peak FFT coefficients at different phase angles, phase maps were calculated, i.e., voltage maps at various relative latencies by transforming phase into time [13,15].

2.2.2. Averaging of seizure onset waveforms and source imaging

The alternative approach to PM was based on averaging the ictal onset waveforms [12]. The averaged signals were analyzed using various inverse methods: discrete multiple dipole fitting to analyze onset and peak [16,17], a distributed source model in the brain volume, i.e., classical LORETA analysis recursively applied (CLARA), a similar distributed source model, but constrained to the cortex (cortical CLARA), and a cortex-constrained minimum norm estimation [18,19].

Iterative application of LORETA in the brain volume as used in CLARA [20,21] is a well-known and widely used method [22,23]. Here, two iterations were performed. The initial image was regularized using a SVD cutoff of 0.005%; the two iterations were regularized with a cutoff of 0.01%.

Cortical CLARA was applied as a modification of the volume CLARA algorithm by constraining the source space to the cortical surface. For this, a graph Laplacian operator [24] was used that smooths along the cortical surface in contrast to the volume CLARA where the Laplacian smooths in all three dimensions [25]. The initial cortical CLARA image and the 10 following iterations used a SVD cutoff of 0.005%.

Thus, dipole fitting and CLARA provided equivalent centers of activation in the brain volume, whereas cortical CLARA and MN provided equivalent centers of activation along the cortical folds.

The cortex-constrained minimum norm was applied on the averaged data with depth and spatio-temporal weighting based on the signal subspace correlation measure [26]. Noise was estimated from the baseline interval. For each channel, separate noise weights were used for the diagonal noise covariance matrix.

2.2.3. Head model

The new standard head model of BESA Research 6.1 for adults (age 20–24) was used [27]. This is based on a head template created by non-linear morphing and averaging of 10 adult heads into one standard head with the goal to render the cortical folds optimally. Currently, this standard template is the only one having sufficiently good rendering of all tissues needed for the computation of the forward, finite-elements model (FEM) in BESA MRI [28,29]. The full set of standard 10–10 electrodes was warped onto the head template according to the rules of the 10–10 system how to place electrodes relative to the landmarks, i.e., nasion, inion, and pre-auricular points. These landmarks could be identified on the reconstructed standard head surface. Thus, standard electrode coordinates and FEM lead fields vectors were available to compute the forward model for the 64 electrodes used in this study.

2.3. Reference standard (“gold standard”)

We compared the source images with two sets of reference standards. For all patients, source images were compared with the final decision of the multidisciplinary epilepsy surgery team. In addition, for the 20 patients who underwent respective epilepsy surgery, we also compared the centers of the source images with the resected areas and the surgical outcome one year after the operation [30]. Patients were considered seizure-free if they were in Engel class I.

2.4. Evaluation of the source models

The source images were evaluated by one of the authors (IR) who was blinded both for the clinical and for the raw-EEG data. Center source locations were scored at sub-lobar level [31]. In temporal lobe cases, we considered a source as mesial temporal if it localized to the mesial, basal or antero-polar part of the temporal lobe; other temporal localizations were scored as lateral-neocortical in concordance with previous studies, using simultaneous scalp and intracranial recordings [7,32–35].

The scored sub-lobar source locations were compared with the reference standard, and classified as concordant, partially concordant or discordant. A full match at sub-lobar level between the source locations and the gold standard was considered concordant. When the source images involved several sub-lobar structures, including the one in the reference standard, or, in patients with several seizures when at least one seizure was concordant and the other(s) were not, source location was considered partially concordant. All other cases were considered discordant.

Nine patients had two or more seizures with identifiable ictal EEG correlate. We analyzed each seizure separately in these patients; when all seizures in a patient were concordant with the reference standard, the patient was considered “concordant”; when only a part of the seizures were concordant with the reference standard, the patient was scored as “partially concordant”; when all seizures were discordant with the reference standard, the patient was considered “discordant”.

We compared the incidence of concordant cases among the five methods using Fisher’s exact test [36].

3. Results

Figs. 1 and 2 show source imaging results in patients with a temporal and a frontal focus. Supporting document 1 in the online version at DOI: 10.1016/j.seizure.2016.09.017 contains clinical data