Clinical Neurophysiology 129 (2018) 1291–1299

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Automatic ictal onset source localization in presurgical epilepsy evaluation

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ARTICLE INFO

Article history:
Accepted 24 March 2018
Available online 6 April 2018

Keywords:
Ictal
Source localization
Electric source imaging
EpiSource
Epilepsy surgery

HIGHLIGHTS

- Ictal onset source localization (IOSL) showed high diagnostic accuracy during presurgical evaluation.
- IOSL contributes to a correct localization of the seizure onset zone on a sublobar level.
- IOSL can be obtained within 5 minutes per seizure and used in standard epilepsy monitoring settings.

ABSTRACT

Objective: To test the diagnostic accuracy of a new automatic algorithm for ictal onset source localization (IOSL) during routine presurgical epilepsy evaluation following STARD (Standards for Reporting of Diagnostic Accuracy) criteria.
Methods: We included 28 consecutive patients with refractory focal epilepsy (25 patients with temporal lobe epilepsy (TLE) and 3 with extratemporal epilepsy) who underwent resective epilepsy surgery. Ictal EEG patterns were analyzed with a novel automatic IOSL algorithm. IOSL source localizations on a sublobar level were validated by comparison with actual resection sites and seizure free outcome 2 years after surgery.
Results: Sensitivity of IOSL was 92.3% (TLE: 92.3%); specificity 60% (TLE: 50%); positive predictive value 66.7% (TLE: 66.7%); and negative predictive value 90% (TLE: 85.7%). The likelihood ratio was more than ten times higher for concordant IOSL results as compared to discordant results ($p = 0.013$).
Conclusions: We demonstrated the clinical feasibility of our IOSL approach yielding reasonable high performance measures on a sublobar level.
Significance: Our IOSL method may contribute to a correct localization of the seizure onset zone in temporal lobe epilepsy and can readily be used in standard epilepsy monitoring settings. Further studies are needed for validation in extratemporal epilepsy.

1. Introduction

Epilepsy surgery is a valuable treatment option for patients with medically refractory epilepsy (Rosenow and Luders, 2001). Successful surgical treatment depends on a thorough presurgical evaluation localizing the epileptogenic zone and essential brain regions in each individual patient (Rosenow and Luders, 2001). Video-EEG monitoring is one of the cornerstones of each presurgical evaluation with interictal EEG providing information on the

Abbreviations: amTLR, anteromesial temporal lobe resection; ESI, electrical source imaging; IOSL, ictal onset source localization; LAURA, local autoregressive average; LORETA, low resolution electromagnetic tomography; MRI, magnetic resonance imaging; MUSIC, multiple signal classification; sAHE, selective amygdala-hippocampectomy; sLORETA, standardized low resolution electromagnetic tomography; SMAC, spherical model with anatomical constraints; SNR, signal-to-noise ratio,; SOZ, seizure onset zone; SPECT, single-photon emission computed tomography; TLE, temporal lobe epilepsy; mTLE, mesial temporal lobe epilepsy; TLR, temporal lobe resection; vEEG, video electroencephalography.

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https://doi.org/10.1016/j.clinph.2018.03.020
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irritative zone and ictal EEG localizing the seizure onset zone (SOZ). While routine clinical practice still relies on visual analysis of EEG data, electrical source imaging (ESI) facilitates attribution of epileptiform EEG discharges to the three-dimensional intracerebral location of their neuronal generators and thus significantly increases the localizing information of EEG (Brodbeck et al., 2011). Most studies on ESI concentrated on interictal EEG data and thus on better delineation of the irritative zone because spike averaging improves signal-to-noise ratio and therefore robustness of source modeling (Bast et al., 2006; Leijten and Huiskamp, 2008; Brodbeck et al., 2011; Scherg et al., 2012; Megevand et al., 2014). However, accurate localization of the SOZ by ESI of ictal EEG data (ictal onset source localization – IOSL) seems even more important for surgical planning (Merlet and Gotman, 2001). So far several studies using different ictal source localization techniques have reported concordance between 37.5% and 100% with the actual SOZ (Assaf and Ebersole, 1997; Blanke et al., 2000; Lantz et al., 2001; Jung et al., 2009; Lee et al., 2009; Stern et al., 2009; Holmes et al., 2010; Yang et al., 2011; Lu et al., 2012; Beniczky et al., 2013; Breedlove et al., 2014; Akdeniz 2016). Various reference standards for IOSL confirmation were used: interictal EEG (Boon and D'Have, 1995; Koutroumanidis et al., 2004; Valentin et al., 2014), intracranial EEG (Assaf and Ebersole, 1997; Lantz et al., 2001; Merlet and Gotman, 2001; Koessler et al., 2010), postsurgical outcome (Assaf and Ebersole, 1999; Lantz et al., 1999; Blanke et al., 2000; Jung et al., 2009; Lee et al., 2009; Lu et al., 2012; Breedlove et al., 2014), MRI (Worrell et al., 2000), ictal SPECT (Beniczky et al., 2006; Habib et al., 2016), decision of the multidisciplinary epilepsy surgery team (Beniczky et al., 2013) or a combination thereof (Boon et al., 2002; Ding et al., 2007; Stern et al., 2009; Holmes et al., 2010; Yang et al., 2011). Only one recent publication using a distributed source model (LAURA) to localize ictal activity reported precise performance measures (sensitivity of 70%, specificity of 76% and PPV of 92%) (Beniczky et al., 2013).

Several drawbacks and difficulties regarding ictal source localization analysis of scalp EEG recordings have to be considered: possible low signal-to-noise ratio, lack of ictal EEG correlates in scalp recordings during seizure onset, rapid propagation or already propagated ictal patterns in scalp EEGs and artifacts obscuring EEG seizure patterns (Pacia and Ebersole, 1997; Alarcon et al., 2001; Foldvary et al., 2001; Rosenow and Luders, 2001; Boon et al., 2002; Beniczky et al., 2013). Most important no standard method of IOSL has been established so far (dipole modeling, LORETA, sLORETA, MUSIC, LAURA, etc.) and most methods require highly interactive analysis of ictal EEG patterns including individual parameter adjustments which complicates the use of IOSL in clinical practice (Koessler et al., 2010).

We developed a new automatic algorithm which requires only visual selection of the EEG pattern at ictal onset. The algorithm then automatically performs source localization without further interactions and parameter adjustments by the user, making IOSL results easy to obtain, reproducible and objective. Solutions can be obtained within five minutes per seizure. Therefore the algorithm can be used in everyday clinical practice in the epilepsy monitoring unit. We tested the algorithm's diagnostic accuracy in a standard long-term video-EEG monitoring setting following STARD (Standards for Reporting of Diagnostic Accuracy) criteria. Postoperative outcome two years after resective epilepsy surgery was used as reference standard. We hypothesized that IOSL results correctly localized the SOZ if IOSL matched the actual resection site on a sublobar level and patients were seizure free after epilepsy surgery.

2. Methods

2.1. Patient selection

We searched our database for patients with refractory focal epilepsy who were admitted for presurgical evaluation in our center and subsequently underwent resective epilepsy surgery. We included all patients for whom raw EEG data was available and identified in this way 30 consecutive operated patients. All patients gave their informed consent prior to being admitted to long-term video EEG (vEEG) monitoring. The local ethics committee approved the study.

2.2. EEG data

Long-term vEEGs were recorded from 23 electrodes placed according to the Extended International 10–20-system (including additional 'true' anterior temporal electrodes FT9/FT10) and TP9/TP10 at a 256 Hz sampling rate using a Micromed EEG recording system (SystemPlus Evolution, Veneto, Italy). Patients' EEG recordings were visually analyzed by board certified electroencephalographers (JK, SP and CB). We visually determined time, location and frequency of the EEG pattern at onset of every seizure defined according to criteria previously published (Foldvary et al., 2001). We excluded seizures obscured by artifacts from further analysis. All included seizures were anonymized and randomized. IOSL was applied to the pattern at onset of these seizures by an independent reviewer (GG) who was blinded to all clinical data.

2.3. Visual EEG seizure onset localization

We systematically localized seizure onset zones visually according to criteria proposed by Foldvary et al. (2001). Specifically we distinguished between the following seizure onset localizations: 1. Generalized seizure onset: activity involving multiple electrodes over both hemispheres having a less than 2:1 amplitude predominance over one hemisphere; 2. Lateralized seizure onset: activity involving multiple electrodes over multiple lobes of a single hemisphere having a 2:1 or greater amplitude predominance over this hemisphere; 3. Regional or lobar seizure onset: activity involving electrodes overlying a single lobe having a 2:1 or greater amplitude predominance than that seen over other regions of the same hemisphere; 4. Focal or sublobar seizure onset: activity with a maximum at a single electrode with no more than 2 contiguous electrodes within 80% to 100% of the maximum amplitude (Foldvary et al., 2001). In temporal lobe seizures, we assigned a medio-basal seizure onset localization if ictal activity fulfilled these criteria with a maximum at electrodes FT9 or FT10, respectively and a lateral temporal seizure onset localization if ictal activity fulfilled these criteria with a maximum at electrodes T7 or T8, respectively.

2.4. Ictal onset source localization

The core idea of our ictal onset source localization (IOSL) technique was to automatically determine the most dominant rhythmic EEG pattern within the earliest ictal activity, i.e. the first change in EEG time–frequency plots. Next, we implemented a frequency dependent time window which had to contain at least eight ictal waves or discharges (e.g. 4 Hz ictal activity = time window of 2 s; 8 Hz ictal activity = time window of 1 s) to the selected ictal activity. The spatial distribution of this rhythmic activity over all EEG electrodes was the basis for our source localization method, leading to an automatic localization approach. The inverse method used in our study was a frequency domain version of the minimum