Clinical Neurophysiology 125 (2014) 1095–1103

Contents lists available at ScienceDirect

Clinical Neurophysiology

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

Automatic detection of prominent interictal spikes in intracranial EEG: Validation of an algorithm and relationsip to the seizure onset zone

Nicolas Gaspard *, Rafeed Alkawadri, Pue Farooque, Irina I. Goncharova, Hitten P. Zaveri

Comprehensive Epilepsy Center and Computational Neurophysiology Laboratory, Dept. of Neurology, School of Medicine, Yale University, Yale-New Haven Hospital, New Haven, CT, USA

ARTICLE INFO

Article history:
Accepted 27 October 2013
Available online 5 November 2013

Keywords:
Interictal spike detection
Intracranial EEG
Automatic detection
Mahalanobis distance
General extreme value statistics
Localization of the seizure onset zone

HIGHLIGHTS

- Individual interictal spikes can be described by their time–frequency characteristics.
- An automated algorithm can detect and rank spikes by order of prominence.
- Most prominent spikes are accurately identify the lobe of the seizure onset.
- They occur within 2 cm of the seizure onset zone in half of the cases.

ABSTRACT

Objective: To develop an algorithm for the automatic quantitative description and detection of spikes in the intracranial EEG and quantify the relationship between prominent spikes and the seizure onset zone.
Methods: An algorithm was developed for the quantification of time–frequency properties of spikes (upslope, instantaneous energy, downslope) and their statistical representation in a univariate generalized extreme value distribution. Its performance was evaluated in comparison to expert detection of spikes in intracranial EEG recordings from 10 patients. It was subsequently used in 18 patients to detect prominent spikes and quantify their spatial relationship to the seizure onset area.
Results: The algorithm displayed an average sensitivity of 63.4% with a false detection rate of 3.2 per minute for the detection of individual spikes and an average sensitivity of 88.6% with a false detection rate of 1.4% for the detection of intracranial EEG contacts containing the most prominent spikes. Prominent spikes occurred closer to the seizure onset area than less prominent spikes but they overlapped with it only in a minority of cases (3/18).
Conclusions: Automatic detection and quantification of the morphology of spikes increases their utility to localize the seizure onset area. Prominent spikes tend to originate mostly from contacts located in the close vicinity of the seizure onset area rather than from within it.
Significance: Quantitative analysis of time–frequency characteristics and spatial distribution of intracranial spikes provides complementary information that may be useful for the localization of the seizure-onset zone.

1. Introduction

Automatic spike detection has been a longstanding issue (Gotman and Gloor, 1976) (and see the extensive review by Wilson and Emerson (2002)). However, algorithms developed specifically for intracranial EEG have focused on the detection of spikes and the calculation of their frequency (Dümpelmann and Elger, 1999; Valenti et al., 2006; Brown et al., 2007; Barkmeier et al., 2012). Spike frequency and the global spatial distribution of spikes are only partially informative of the localization of the seizure onset zone (Hufnagel et al., 2000; Asano et al., 2003; Goncharova et al., 2009; Marsh et al., 2010) and other attributes of spikes may provide crucial additional information (Hufnagel et al., 2000; Asano et al., 2003).

Intracranial spikes exhibit considerable variability in their morphology at the inter-individual, intra-individual and even intra-electrode levels. The quantitative analysis of their morphology may assist in the surgical planning and possibly improve surgical outcomes, although data on the relationship between spike

* Corresponding author. Address: Comprehensive Epilepsy Center and Computational Neurophysiology Laboratory, Yale University, 15 York Street LLCI 700, New Haven, CT 06520, USA. Tel.: +1 203 785 4836; fax: +1 203 737 2799.
E-mail address: nicolas.gaspard@yale.edu (N. Gaspard).

1388-2457/$36.00
http://dx.doi.org/10.1016/j.clinph.2013.10.021

amplitude and the seizure onset zone are contradictory (Hufnagel et al., 2000; Asano et al., 2003, 2008). The clinical implementation of these methods is currently limited by the lack of automated algorithms for the quantitative analysis of spike characteristics, requiring quantitative analysis to be performed manually, which is time consuming.

We thus aimed to develop an algorithm that would quantify the morphology of spikes so that their detection and the analysis of their temporal and spatial distribution could be performed based on the quantitative measure of inherent spike characteristics. In a first step, we aimed to validate the accuracy of the algorithm by comparing it to detections made by expert EEG readers. We then aimed to demonstrate its ability to focus the detections to spikes of increasing prominence. In a third step, we applied this algorithm to detect spikes of increasing prominence and study the relationship between the prominence of spikes and their spatial distribution relative to the seizure onset zone.

2. Methods

2.1. Selection of patients and intracranial EEG segments

This study was approved by the Yale University Human Investigation Committee. Intracranial EEG recordings obtained from 18 adult patients undergoing routine epilepsy surgical evaluation for epilepsy surgery at the Yale-New Haven Hospital between September 2004 and April 2005 were included (see Table 1 for clinical details). One hour of icEEG recording was selected during an artifact-free period of daytime (from noon to 4 pm) obtained from days 2 to 5 of the monitoring. The recordings were removed from clinical seizures by at least 6 h.

2.2. Intracranial EEG recordings

Intracranial EEG was recorded with commercially available 128-channel long-term icEEG monitoring equipment (Natus/Bio-logic Systems Incorporated, San Carlos, CA). The icEEG was sampled at 256 Hz and archived for subsequent review and analysis. The icEEG was recorded with reference to a peg electrode implanted in the diploic space of the skull at a distance from the icEEG electrodes.

Macroelectrode contacts (Ad-Tech Medical Instrument Corp., Racine, WI) were used in this study. The icEEG electrode placements typically included several subdural strip electrodes with 8–12 contacts and a grid electrode of dimension 8×8 contacts. Some patients also received depth electrodes.

Subdural electrodes and depth electrodes were as described previously. (Goncharova et al., 2009) Briefly, intracranial electrode contacts were located from a postimplantation computed tomography (CT) image. The postimplantation CT was then coregistered, first, with a postimplantation magnetic resonance (MR) image using a linear coregistration procedure, and then with a preimplantation MR image using both a linear and nonlinear coregistration procedure.

2.3. Development of the automated detector and validation of its performance

The automated detection algorithm was developed in MATLAB (The MathWorks, Natick, MA, USA) and is summarized in Fig. 1.

The approach employed sought to express detection candidate spikes with a single numerical value that reflects its likelihood of being an exemplar spike. In the absence of a consensus definition of intracranial spikes, we decided to base our detection on the time–frequency description of a spike. In the time–frequency plane, a spike corresponds to an edge with power at frequencies greater than 14 Hz (Zaveri et al., 1992). Mindful that a full time–frequency analysis of the multichannel icEEG is computationally intensive, we sought surrogates for this time–frequency description of the spike.

In the initial step of the algorithm, the icEEG is band-pass filtered between 10 and 70 Hz using a zero-phase lag Butterworth filter of order 8. This frequency band has been shown to contain most of the icEEG power of a spike (Zaveri et al., 1992).

Then the Teager energy is computed for each sample point using a 8 ms (−4 to +4 ms; or more precisely a 7.8 ms window defined by the interval between 3 consecutive sample points) window. Teager energy, also known as the Teager-Kaiser energy oper-

Table 1
Patient characteristics.

Patient #	Seizure onset	Pathology	Follow-up (years)	Outcome (Engel class)	Nb of clinical seizures	Nb of subcliniclal seizures	Nb of SOZ contacts	Seizure onset type
1	R Medial Temporal	Hippocampal sclerosis	4	4	13	5	1	LVFA/RS
2	R Inferior Temporal	Hippocampal sclerosis	1	2	5	0	3	LVFA
3	R Inferior Temporal	Hippocampal sclerosis	3	4	34	0	2	LVFA/RS
4	R Anterior Superior Lateral Temporal	Reactive gliosis	4	3	5	0	6	RS
5	L Medial Temporal	Hippocampal sclerosis	3	1	5	0	2	LVFA
6	L Medial Temporal	Hippocampal sclerosis	3	1	3	0	11	RS
7	L Parieto-Occipital	Unknown	NA	NA	3	1	3	RS
8	L Medial Temporal	Unknown	NA	NA	3	1	1	RS
9	R Inf Post Temporo-Occipital	Unknown	NA	NA	3	2	3	RS
10	R Parietal	Neuronal loss and reactive gliosis	3	1	7	0	5	RS
11	L Medial Occipital	Unknown	NA	NA	3	0	4	LVFA
12	L Superior Parietal	Unknown	NA	NA	8	0	2	LVFA
13	R Parietal	Gliosis	3	1	4	0	3	LVFA
14	L Medial Temporal	Hippocampal sclerosis	4	1	13	0	1	LVFA
15	L Anterior Medial Frontal	Unknown	3	1	10	0	4	LVFA
16	L Post Inf Temporal	Hippocampal sclerosis	2	1	3	0	2	LVFA
17	L MT	Hippocampal sclerosis	4	3	2	2	1	RD/LVFA
18	R Medial Temporal	Heterotopic neurons and reactive gliosis	3	3	3	2	3	LVFA/RS

Abbreviations: L = left; R = right; LVFA = low voltage fast activity; RS = repetitive spiking; RD = rhythmic delta; NA = not applicable.