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Automatic detection of fast ripples

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HIGHLIGHTS

- We propose a novel method for automatically detecting fast ripples (FRs, 250–600 Hz)
- The signal energy in low and high frequency bands is used to classify EEG events as FRs, interictal epileptic spikes or artifacts.
- The sensitivity and the specificity of this method is high enough to avoid "false ripples" caused by sharp transients.

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ABSTRACT

Objective: We propose a new method for automatic detection of fast ripples (FRs) which have been identified as a potential biomarker of epileptogenic processes.
Methods: This method is based on a two-stage procedure: (i) global detection of events of interest (EOIs, defined as transient signals accompanied with an energy increase in the frequency band of interest 250–600 Hz) and (ii) local energy vs. frequency analysis of detected EOIs for classification as FRs, interictal epileptic spikes or artifacts. For this second stage, two variants were implemented based either on Fourier or wavelet transform. The method was evaluated on simulated and real depth-EEG signals (human, animal). The performance criterion was based on receiving operator characteristics.
Results: The proposed detector showed high performance in terms of sensitivity and specificity.
Conclusions: As designed to specifically detect FRs, the method outperforms any method simply based on the detection of energy changes in high-pass filtered signals and avoids spurious detections caused by sharp transient events often present in raw signals.
Significance: In most of epilepsy surgery units, huge data sets are generated during pre-surgical evaluation. We think that the proposed detection method can dramatically decrease the workload in assessing the presence of FRs in intracranial EEGs.

1. Introduction

High frequency oscillations (HFOs) have been a topic of increasing interest in neuroscience over the past decade. They now constitute a novel trend in neurophysiology (Jefferys et al., 2012) that has been made possible with the development of digital EEG equipments allowing for high sampling rates and with the identification of oscillations at up to 600 Hz in animals (Buzsaki and Lopes da Silva, 2012). Among the wide diversity of HFOs which dominant frequency can vary from 30 Hz to 600 Hz, fast ripples (FRs) are particular transient oscillations (a few tens of ms) occurring in the frequency band ranging from 250 Hz to 600 Hz. In the normal brain (monkey), FRs have been associated with cortical spike bursts (Baker et al., 2003). In the epileptic brain, FRs were shown to be related to abnormal modifications in the excitability of underlying neuronal systems (Demont-Guignard et al., 2012). Epileptic FRs have first been observed in animal models (Bragin et al., 1999b) as well as in patients with drug-resistant partial epilepsy (Bragin et al., 1999a). A number of studies then confirmed the existence of interictal HFOs in brain structures involved at the onset of seizures (Bragin et al., 2002; Jacobs et al., 2008; Worrell et al., 2004) and the potential value of FRs as a marker of the degree of epileptogenicity (Engel et al., 2009; Jacobs et al., 2009; Worrell and Gotman, 2011).

In this context, the accurate detection of FRs in depth-EEG signals recorded in patients candidate to surgery could considerably improve the identification and delineation of the epileptogenic zone which is an essential step in planning the best therapeutic strategy (Bartolomei et al., 2002). However, this detection is far

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from being a trivial problem. In most of aforementioned studies, the detection of FRs was performed visually by inspecting either the raw signals or the filtered signals in the frequency band of interest (beyond 80 Hz). However, on the one hand, the visual inspection of EEG signals remains fastidious. Indeed, the number of events of interest (EOIs) occurring during interictal periods can be potentially high. In addition, the review of EEGs must be performed with an appropriate time scale (strongly magnified w.r.t. those classically used) in order to visually assess the actual presence (or absence) of transient oscillations associated with EOIs. The detection of FRs can also be helped by the use of simple signal processing algorithms like, in particular, the filtering of depth-EEG signals in the frequency band of interest (typically beyond 250 Hz). However, on the other hand, as shown in (Benar et al., 2010), any high-pass filtering technique has one major pitfall: the lack of specificity due to sharp transients present in depth-EEG signals. Indeed, in this study, authors could verify that some “pulse-like” events (typically, the spike component of interictal epileptic spikes – IES) are associated with an abrupt increase of the signal energy in the higher frequency bands, exactly as in the case of actual FRs. A typical example is provided in Fig. 1A. As a consequence, the oscillations generated in the filtered signal that are related to the features of the impulse response of the high-pass filter can be confounded with actual FRs, leading the authors to denote them as “false ripples” (Fig. 1B).

In this context, the demand is high for automatic detection procedures with increased specificity, while maintaining a good sensitivity. In this paper, we propose a novel detection method for automatically identifying FRs occurring in depth-EEG signals. To our knowledge, very few methods have been proposed so far to achieve this goal. A few years ago, band-pass filtering techniques were combined with a thresholding procedure of the energy of sub-band signals to automatically detect HFOs (Crepon et al., 2010; Gardner et al., 2007; Staba et al., 2002). Very recently, Zelmann et al. (2012) proposed a new method (referred to as the MNI detector) and compared it to the three aforementioned ones. The initial step of their method was also based on a band-pass filter (80–450 Hz) but included a baseline analysis (based on wavelet entropy) to differentiate channels with transient HFOs from those with continuous HF activity. The decision (presence/absence of a HFO) was based on a threshold. While these methods offer a good sensibility they exhibit poor specificity due to sharp IES or artifacts often present in raw signals. The method proposed in Blanco et al. (2010) makes use of the result of the Staba’s method as a first step and then automatically classifies the resulting candidate events using a data mining algorithm. The method could separate actual HFOs (including ripples and FRs) from artifacts in a very large data set but the issue of spurious detections due to IES was not addressed.

In contrast, our detection method was designed to exclusively recognize FRs and to avoid false detections caused by sharp transient events (typically IES). It is based on a two-stage procedure: (i) global detection of EOIs, defined as transient signals accompanied with an energy increase in the frequency band of interest (250–600 Hz) and (ii) local energy vs. frequency analysis of detected EOIs for classification as FRs, IESs or artifacts. For this second stage of the detection procedure, two variants were implemented based either on Fourier or wavelet transform. Performance was first evaluated on real depth-EEG data recorded in human (temporal lobe epilepsy – TLE) as well as in an experimental in vivo model of TLE (mouse kainate). It was also evaluated on simulated signals which consisted of real FRs and IESs (assessed by the expert) inserted at known occurrence times in an EEG background activity generated with a realistic computational model of hippocampal activity (Wendling et al., 2005). We also provided how to calculate the optimal threshold that allows the discrimination of FRs from IESs in the method. Results showed that the proposed detection method can achieve good performance with relatively few parameters to adjust. As an important finding, best results were obtained when the energy ratio between oscillations in the FR band vs. gamma band was used as a discriminant factor in the second stage of the detection procedure.

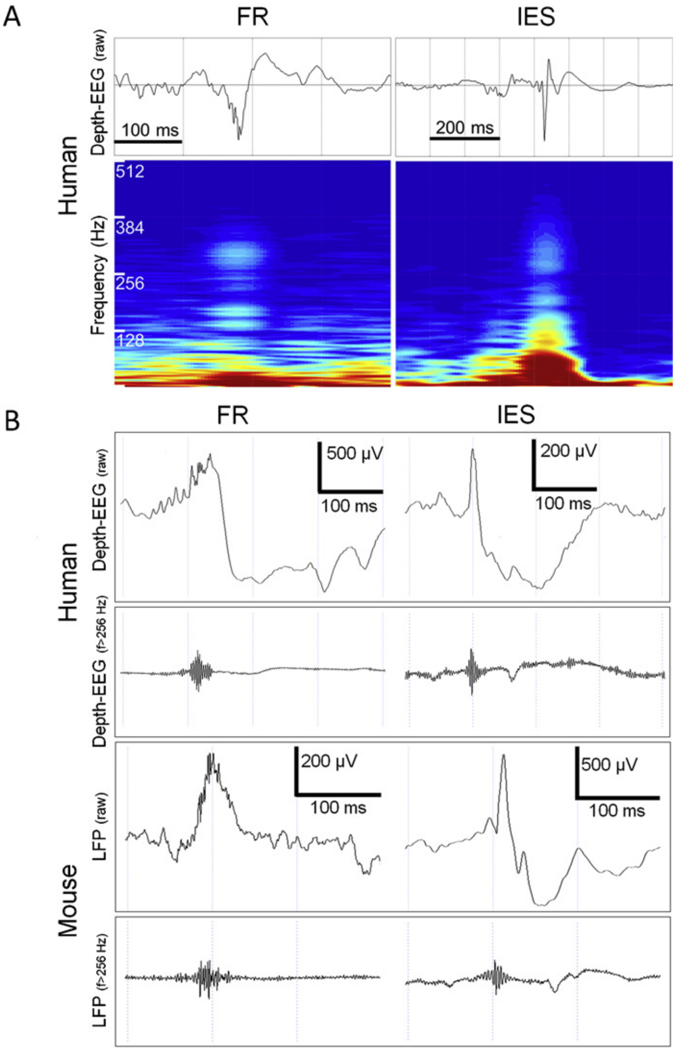

Fig. 1. Typical FRs and IESs recorded from hippocampus in human (TLE) and in an animal model of epilepsy (mouse, kainate model). (A) Human FRs and IESs (depth-EEG signals) with corresponding spectrograms. Note that both EOIs (the FR and the IES) exhibit energy in the 250–600 Hz. (B) FRs and IESs recorded from hippocampus using macro-electrodes (human: depth-EEG, mouse: LFPs). Upper plots: raw signals. Lower plots: filtered signals (high-pass cutoff frequency = 256 Hz). Note that the two types of epileptic events can hardly be discriminated using a simple high-pass filtering procedure.

2. Materials and methods

2.1. Problem formulation and notations

The depth-EEG signal on which the detection is performed is denoted by $\{s[n]\}$. This signal mainly contains background (denoted by $\{\mathrm{BKG}[n]\}$) activity in which some transient events may appear randomly. These transient events include (i) events of interest (EOIs) characterized by significant energy (compared to BKG) in the frequency band of interest, typically ranging from 250 to 600 Hz (rounded to 256–512 Hz in our case for methodological reason) and (ii) some other events of non-interest (EONI) exhibiting energy at lower frequencies. The occurrence time of the pth EOI is denoted by t_p. Each EOI is assumed to have a finite time support of length