NeuroImage: Clinical 17 (2018) 865–872

Contents lists available at ScienceDirect

NeuroImage: Clinical

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

Spectral bandwidth of interictal fast epileptic activity characterizes the seizure onset zone

Marcel Heers[a,b,c,*], Moritz Helias[d], Tanguy Hedrich[e], Matthias Dümpelmann[a,c], Andreas Schulze-Bonhage[a,c], Tonio Ball[a,b,c]

[a] Epilepsy Center, Department of Neurosurgery, Medical Center — University of Freiburg, Faculty of Medicine, University of Freiburg, Germany
[b] Translational Neurotechnology Lab, Department of Neurosurgery, Medical Center — University of Freiburg, Faculty of Medicine, University of Freiburg, Germany
[c] Cluster of Excellence BrainLinks-BrainTools, University of Freiburg, Germany
[d] Institute of Neuroscience and Medicine (INM-6) and Institute for Advanced Simulations (IAS-6), Jülich Research Centre and JARA, Jülich, Germany
[e] Multimodal Functional Imaging Lab, Biomedical Engineering Department, McGill University, Montreal, Québec, Canada

ARTICLE INFO

Keywords:
Intracranial EEG
Fast epileptic activity (FEA)
Focal epilepsy
Focal cortical dysplasia (FCD)
Harmonic oscillator
Spectral bandwidth
Hopf bifurcation

ABSTRACT

The foremost aim of presurgical epilepsy evaluation is the delineation of the seizure onset zone (SOZ). There is increasing evidence that fast epileptic activity (FEA, 14–250 Hz) occurring interictally, i.e. between seizures, is predominantly localized within the SOZ. Currently it is unknown, which frequency band of FEA performs best in identifying the SOZ, although prior studies suggest highest concordance of spectral changes with the SOZ for high frequency changes. We suspected that FEA reflects dampened oscillations in local cortical excitatory-inhibitory neural networks, and that interictal FEA in the SOZ is a consequence of reduced oscillatory damping. We therefore predict a narrowing of the spectral bandwidth alongside increased amplitudes of spectral peaks during interictal FEA events. To test this hypothesis, we evaluated spectral changes during interictal FEA in invasive EEG (iEEG) recordings of 13 patients with focal epilepsy. In relative spectra of beta and gamma band changes (14–250 Hz) during FEA, we found that spectral peaks within the SOZ indeed were significantly more narrow-banded and their power changes were significantly higher than outside the SOZ. In contrast, the peak frequency did not differ within and outside the SOZ. Our results show that bandwidth and power changes of spectral modulations during FEA both help localizing the SOZ. We propose the spectral bandwidth as new source of information for the evaluation of EEG data.

1. Introduction

Epilepsy is one of the most common neurological disorders that affects 70 million people worldwide (Ngugi et al., 2010). It consists of recurrent seizures that presumably occur as a result of disturbed synaptic excitation and inhibition (Jiruska et al., 2013). Approximately 60% of all epilepsy patients suffer from focal epilepsy (Zarrelli et al., 1999) and drug resistant focal epilepsy accounts for 30% of all focal epilepsies (Schuele and Lüders, 2008). In these patients it is hence one of the main aims to localize and characterize the SOZ. In some but not all patients the SOZ spatially correlates closely with structural cerebral abnormalities or with epileptic activity in between epileptic seizures, i.e. interictal activity (Rosenow and Lüders, 2001). Pathological changes related to epilepsy that are interictally observed in electrophysiological recordings are usually more extended than the SOZ. Apart from epileptic spikes these changes include fast oscillatory patterns in the β, γ and high γ band > 14 Hz (fast epileptic activity (FEA); de Curtis et al., 2012). Recently, there is an increased interest in interictal FEA as it may help in the definition of the SOZ for the planning of epilepsy surgery (Bartolomei et al., 2008; Engel et al., 2009; Ren et al., 2015).

Previous studies have focused on a number of parameters characterizing interictal FEA, such as the number of events per time, their co-occurrence with epileptic spikes, and the frequency range of oscillations; for example the distinction of high frequency oscillations (HFOs) between ripple or fast ripple bands from 80 to 250 and 250 to 500 Hz, respectively (Zijlmans et al., 2012). However, a basic parameter of FEA has so far been neglected: its spectral bandwidth, i.e., the width of the peaks reflecting FEA in the spectral domain. Spectral bandwidth may be important as it closely relates to the damping of an oscillation, which describes how quickly an oscillation decays in amplitude. Spectral bandwidth may thus be informative with respect to epilepsy-related oscillations. Specifically, reduced bandwidth together with increased peak amplitude would indicate reduced damping of the

* Corresponding author at: Epilepsy Center, Department of Neurosurgery, University Medical Center Freiburg, Breisacher Str. 64, D-79106 Freiburg, Germany.
E-mail address: marcel.heers@uniklinik-freiburg.de (M. Heers).

https://doi.org/10.1016/j.nicl.2017.11.021
Received 17 September 2017; Received in revised form 4 November 2017; Accepted 22 November 2017
Available online 26 November 2017

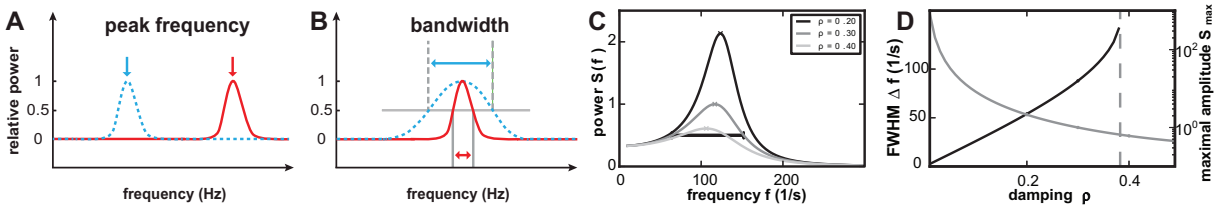

Fig. 1. Concept of spectral bandwidth changes. Generally, spectral changes may differ with respect to the peak frequency of the responses (A). However, even if responses have the same peak frequency, they may differ with respect to their spectral bandwidth (blue and red curves in B). Gray lines indicate the full width at half maximum (FWHM): the width at which the amplitude decays to half its maximum value. (C) Power spectrum of a harmonic oscillator for different values of the damping, normalized to the peak value for damping constant $\rho = 0.3$. The FWHM is indicated for the curve of $\rho = 0.3$. (D) Inverse Q factor (black) as a function of the damping constant ρ. Peak value of the power spectrum as a function of the damping (gray). The dashed vertical line indicates the limit for which a FWHM can be defined. Beyond this line, the power does not decay below half the peak value at small frequencies. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

underlying oscillation (Fig. 1). Reduced damping has been described in evoked cortical responses in generalized epilepsy (Lee et al., 1980). Also theoretical models describe seizure generation as a process during which cortical network dynamics approach a critical point which is a phase transition from interictal to seizure activity (Breakspear, 2005; Izhikevich, 2000; Jirsa et al., 2014). Interictal FEA in the SOZ may therefore be characterized by reduced damping, but a quantitative analysis of corresponding signatures in the spectral properties of FEA is so far lacking.

Intracranial EEG (iEEG) recordings during presurgical evaluation of epilepsy patients allow us to assess bandwidth and power changes associated with FEA events recorded directly from the cortical surface both in and outside of the SOZ. To quantify bandwidth changes in conjunction with other spectral parameters, we analyzed FEA-related relative spectral power modulations and mapped those relative to the SOZ. We show that bandwidth and spectral power changes differ between SOZ and non-SOZ contacts, whereas the peak frequency is not informative about the SOZ. Thus, FEA in the SOZ carries the predicted spectral signatures of reduced oscillatory damping. We argue that damping-related spectral changes not only shed new light on epilepsy-related oscillations, but may be relevant for pathological oscillatory activity in a broad range of neurological and possibly also psychiatric diseases that involve a cortical disbalance of synaptic excitation and inhibition.

2. Patients and methods

2.1. Patient selection

All 13 patients included in the analysis underwent elaborated clinical iEEG evaluation for drug resistant focal epilepsy at the University Epilepsy Center Freiburg between 2006 and 2009. Initially we screened data of 22 epilepsy patients with at least one 64-contacts electrode grid implanted for presurgical epilepsy evaluation. These extended cortical recordings with high spatial resolution allow us to map the spatial distribution of spectral changes accurately. A secondary aim of our study is to develop parameters that can be used in future studies to objectify the clinical performance, e.g., of novel grid electrodes of the same size with high contact density.

The ethics committee of the University Medical Center Freiburg approved this study and all patients gave their written informed consent to the scientific use of their clinical data recorded during their presurgical evaluation at the University Epilepsy Freiburg. Eight of 22 patients were excluded, because no FEA was detected on the 64-contacts grid electrode. One of 22 patients was excluded, because no habitual seizures occurred during iEEG acquisition and thus the SOZ could not be defined.

For each of the 13 patients included, we compared the bandwidth analysis to clinical findings from their presurgical evaluation. For the comparison of spectral changes, we defined SOZ positive contacts concordant to the clinical reports. When different seizure types were reported, all contacts involved at seizure onset were counted as SOZ-positive contacts. Surgical resection of the epileptic focus was performed in 12/13 patients included in our study. Histological analysis of the resected specimens in those 12 patients who underwent surgical resection revealed focal cortical dysplasia (FCD) type I in 5/12 patients and FCD type II in 6/12 patients according to the classification of FCDs (Palmini et al., 2004). In 1/12 patient no histological assignment of the resected specimen was possible (Table 1).

The average follow-up for postsurgical outcome was 3.8 years (range 1–8 years). The postsurgical outcome was Engel 1 in six, Engel 2 in two, Engel 3 in three, and Engel 4 in 1 patient (Table 1) (Engel et al.,

Table 1
Clinical characteristics of included patients.

ID	Age	Seizure types	Location of implanted electrodes	SOZ	Histological specimens	No trials FEA	Hours of raw data	Postsurgical outcome
1	17	FS, FDS	G: RFP	RF	FCD 1B	709	2	1a (2)
2	23	FDS, sGTCS	G: RFP; RiH, RFL, RFB strips	RF	FCD 2A	862	6	1a (3)
3	51	FS, FDS, sGTCS	G: LF; LFL, LFP, LiH strips	LF	FCD 1B	174	4	2b (1)
4	40	FDS, sGTCS	G: LF; LFP, LiH strips	LF	FCD 2A	286	4	1a (5)
5	38	FS, FDS, sGTCS	G: LFP; LFB, LFL, LiH strips	LF	FCD 1A	1060	1	3a (4)
6	14	FDS, sGTCS	G: LTPO; LTB, LOPM, LOPL strips	LOP	FCD 2A	1339	1	4a (2)
7	27	FS	G: LFP; LiH strips, 2 DE: LIn	LF	FCD 1B	373	5	1a (5)
8	57	FDS, sGTCS	G: LFTPO; FP, TB, TL, POL, OM strips, DE: LH	LO	N/A	2512	1	3a (8)
9	34	FS, FDS, sGTCS	G: RFTP; RiH strips	RP	N/A	2242	1	N/A
10	58	FS, FDS, sGTCS	G: RTPO, RTL, RTB strips, DE: RH	RO	FCD 1A	149	6	1c (4)
11	42	FS, FDS, sGTCS	G: RFP	RF	FCD 2B	1077	1	1a (1)
12	21	FS	G: LF	LF	FCD 2A	1181	5	2a (5)
13	17	FS, FDS, sGTCS	G: RFP; RFB, RFL, RiH strips	RF	FCD 2A	553	3	3a (5)

Patient data and clinical findings, implanted electrodes, histological findings, hours of raw data visually evaluated for FEA (fast epileptic activity) and baselines, postsurgical outcomes according to the Engel classification and follow up time (in years): DE: depth electrode, FB: fronto-basal, FCD: focal cortical dysplasia, FP: frontopolar, FDS: focal dyscognitive seizures, FL: fronto-lateral, FS: focal seizures, G: 8 × 8 contacts quadratic subdural grid electrode, H: hippocampus, iH: inter-hemispheric, In: insula, L: left, R: right, M: mesial, N/A: not available, O: occipital lobe, P: parietal lobe; sGTCS: secondarily generalized tonic-clonic seizures, T: temporal lobe.