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Identifying seizure onset zone from electrocorticographic recordings: A machine learning approach based on phase locking value

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ABSTRACT

Purpose: Using a novel technique based on phase locking value (PLV), we investigated the potential for features extracted from electrocorticographic (ECoG) recordings to serve as biomarkers to identify the seizure onset zone (SOZ).
Methods: We computed the PLV between the phase of the amplitude of high gamma activity (80–150 Hz) and the phase of lower frequency rhythms (4–30 Hz) from ECoG recordings obtained from 10 patients with epilepsy (21 seizures). We extracted five features from the PLV and used a machine learning approach based on logistic regression to build a model that classifies electrodes as SOZ or non-SOZ.
Results: More than 96% of electrodes identified as the SOZ by our algorithm were within the resected area in six seizure-free patients. In four non-seizure-free patients, more than 31% of the identified SOZ electrodes by our algorithm were outside the resected area. In addition, we observed that the seizure outcome in non-seizure-free patients correlated with the number of non-resected SOZ electrodes identified by our algorithm.
Conclusion: This machine learning approach, based on features extracted from the PLV, effectively identified electrodes within the SOZ. The approach has the potential to assist clinicians in surgical decision-making when pre-surgical intracranial recordings are utilized.

1. Introduction

Surgical resection of the seizure focus is an effective treatment for patients with medically intractable focal epilepsy. Success of the surgery depends on the precise localization and complete resection of the epileptogenic seizure onset zone (SOZ). Accurate localization of the SOZ is crucial for both clinical management and understanding the mechanism of epilepsy. Currently, localization of seizure onset relies on the visual analysis of scalp electroencephalographic (EEG) or intracranial electrocorticographic (ECoG) recordings in low frequency bands.

Patients with focal lesions identified by magnetic resonance imaging (MRI) of the brain often can undergo surgery following favorable scalp EEG findings without intracranial EEG recordings [1]. However, scalp EEG recordings may be inadequate for precise localization of the SOZ in many patients and intracranial recordings are then necessary. The intracranial ictal EEG recordings provide information about seizure onset and propagation. Epileptologist typically inspect the ictal ECoG recordings visually, and look for signatures (e.g., low-voltage fast activity and rhythmic spiking) from individual electrodes at the time of seizure onset to determine the SOZ [2]. Considering the large number of implanted electrodes (typically 50 to 100 contacts), identifying the seizure onset by visual inspection of the ictal ECoG recordings is often time consuming and requires expertise [3,4]. Furthermore, visual inspection of the ictal ECoG recordings to identify the SOZ can result in poor surgical outcome [3]. A study involving 414 patients who underwent intracranial electrode placement reported that visual inspection of the ictal ECoG recordings resulted in complete seizure freedom in 61%, 47%, and 42% of patients at one, three, and ten years after surgery, respectively [3].

There is a need to identify reliable biomarkers that can accurately localize the extent of the ictal epileptogenic zone, thus

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assisting and improving visual identification of the SOZ. Recently, high frequency oscillation (HFO; gamma: 40–100 Hz, ripples: 100–200 Hz, and fast ripples: 250–500 Hz) of neural activities has been proposed as an indicator of seizure-generating sites [5–9]. It has also been demonstrated that HFO carries information distinct from that provided by low-frequency discharges [5–9]. Ripples have been found to coexist with various background EEG patterns [10]. Surgical resection of the areas generating ripples and fast ripples coexisting with flat background EEG activity has been found to significantly correlate with a seizure-free outcome [11]. Moreover, resection of areas generating ripples with a continuously oscillating background EEG pattern showed no positive correlation with post-surgical outcome [11]. It has been shown that HFOs are also present in intracranial EEG recording from normal brain regions and even in non-epileptic subjects [12]. The presence of theses physiologic events complicates the use of HFOs as biomarkers in epilepsy.

In light of these limitations, some studies have looked at the interactions between different rhythms to localize the seizure onset. Specifically, cross frequency coupling (CFC) in the form of modulation has been explored as predictive feature of seizures [13,14]. Phase-amplitude coupling (PAC) occurs when the amplitude of a faster rhythm is coupled to the phase of a slower rhythm. Phase locking value (PLV) has been used to calculate the phase synchrony between two frequency bands [15]. Recently, CFC of ictal ECoG recordings was shown to characterize SOZ successfully [16–18]. In particular, it has been shown that PAC between the phase of low-frequency and amplitude of high frequency oscillations was more useful for localization of an epileptic focus than the amplitude of high gamma alone [16]. By employing microelectrode array recording, Weiss et al. [16] calculated PLV and phase locking high gamma (PLHG) measures to identify the SOZ. By adapting a threshold on PLHG, Weiss et al. could differentiate the core seizure territory (SOZ) from the surrounding penumbra.

The main aim of the this study was to develop and evaluate a method for identification of the SOZ using a machine learning approach based on biomarkers extracted from PLV of ictal ECoG recordings obtained using standard intracranial electrode arrays. We hypothesized that PAC between the amplitude of high frequency (80–150 Hz) and phase of low frequency (4–30 Hz), recorded from ECoG data immediately before and also after seizure onset, could be used as a biomarker to identify SOZ. We demonstrated that features extracted from the PLV could automatically classify the SOZ and non-SOZ electrodes.

2. Methods

2.1. Patient population

This was a retrospective study of 18 patients with epilepsy who underwent a Phase II epilepsy surgery evaluation with intracranial electrodes at Le Bonheur Children's Hospital. The patients were evaluated between August 2013 and July 2015 (Table 1). Eight patients who had no resection after their Phase II evaluation or had less than six months follow up were excluded, leaving 10 patients (7 males, ages 23.0 ± 9.0 (mean $\pm$ SD) years) (Table 1). All patients had a diagnosis of medically intractable epilepsy and underwent pre-surgical evaluation including scalp video-EEG monitoring and MRI of the brain. Seven patients had temporal lobe seizures and three patients had extra-temporal epileptogenicity. Four patients with the temporal lobe epilepsy underwent Phase II evaluation as they had normal MRI of the brain. Three patients with possible mesial temporal sclerosis (i.e. Patients 1, 4, and 5) needed a Phase II evaluation for localization of the seizure focus. Patient 4 had left mesial temporal sclerosis in addition to left thalamic and generalized white matter volume loss. MRI of the brain in patients 1 and 5 showed reduced hippocampal size without associated increased signal and their scalp EEG features didn't reveal a clear temporal lobe onset of seizures. Three patients with extra-temporal lobe epilepsy (Patients 2, 9, and 10) also had findings necessitating a Phase II evaluation. Patient 2 had a suspected non-lesional dominant frontal lobe focus, Patient 9 had tuberous sclerosis complex with multiple tubers, and Patient 10 had a prior resection in addition to seizure origin being close to visual cortex.

Table 1
The demographics of the patients along with characteristics of their epilepsy, pathology, MRI findings, and outcome.

Patient	Age (year)/ Gender	Pathology	MRI	Duration of epilepsy	Seizure type	Seizure focus	Seizure instances	Num. Elec. (Grid/ Strip)	Follow up (months)	Engel Class
1	27/F	Hippocampal sclerosis and microdysgenesis of amygdala	Decreased volume of the left hippocampus	10 years	CPS	Left TL	1	48/16	13	I
2	27/M	FCD, Type 1A	Normal	21 years	CPS	Left FL	2	80/18	8	I
3	20/M	FCD and microdysgenesis	Normal	13 years	CPS	Left TL	2	40/20	14	I
4	40/M	Hippocampal sclerosis	Left thalamic and hippocampal volume loss, and white matter volume loss	36 years	CPS	Left TL	2	40/14	16	I
5	19/F	Hippocampal sclerosis	Left hippocampal volume loss	6 years	CPS	Left TL	3	48/12	5	I
6	21/M	FCD, Type 2A	Normal	10 years	CPS	Right TL	1	32/24	26	I
7	27/M	Gliosis, chronic inflammation, reactive changes	Normal	8 years	CPS	Left TL	3	41/30	14	IV
8	20/F	FCD, Type 2A	Normal	3 years	CPS	Left TL	3	32/20	28	IV
9	5/M	Cortical dysplasia/tuber	Multiple cortical tubers	2.6 years	CPS and myoclonic tonic seizures	Right PL	1	32	6	III
10	17/M	FCD	Prior right occipital resection	15 years	Simple partial seizures and CPS	Right OL	3	32/24	9	IV

CPS: Complex partial seizures; FCD: focal cortical dysplasia; FL: frontal lobe; PL: parietal lobe; TL: temporal lobe; OL: occipital lobe.
Engel class (I): seizure-free since surgery, Engle class (III): Worthwhile improvement, Engel class (IV): no worthwhile improvement, Seizure instances: Number of seizure episodes used in this study.