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moviEEG: An animation toolbox for visualization of intracranial electroencephalography synchronization dynamics

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HIGHLIGHTS

- We present an open source MATLAB-based toolbox for spatiotemporal mapping of network synchronization dynamics in intracranial electroencephalography data.
- Connectivity dynamics including seizure network coalescence and fractioning are visualized and overlaid over operating room images of the electrode grid.
- Two case studies provide preliminary evidence for application of the toolbox in mapping epileptogenic cortex.

ABSTRACT

Objective: We introduce and describe the functions of moviEEG (Multiple Overlay Visualizations for Intracranial ElectroEncephaloGraphy), a novel MATLAB-based toolbox for spatiotemporal mapping of network synchronization dynamics in intracranial electroencephalography (iEEG) data.
Methods: The toolbox integrates visualizations of inter-electrode phase-locking relationships in peri-ictal epileptogenic networks with signal spectral properties and graph-theoretical network measures overlaid upon operating room images of the electrode grid. Functional connectivity between every electrode pair is evaluated over a sliding window indexed by phase synchrony.
Results: Two case studies are presented to provide preliminary evidence for the application of the toolbox to guide network-based mapping of epileptogenic cortex and to distinguish these regions from eloquent brain networks. In both cases, epileptogenic cortex was visually distinct.
Conclusion: We introduce moviEEG, a novel toolbox for animation of oscillatory network dynamics in iEEG data, and provide two case studies showing preliminary evidence for utility of the toolbox in delineating the epileptogenic zone.
Significance: Despite evidence that atypical network synchronization has shown to be altered in epileptogenic brain regions, network based techniques have yet to be incorporated into clinical pre-surgical mapping. moviEEG provides a set of functions to enable easy visualization with network based techniques.

1. Introduction

Epilepsy has long been thought of as a disorder of neural synchronization. Initially, seizures were thought to involve hypersynchronization based on visual inspection of raw EEG waveforms.

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More recently, computational approaches to the study of synchronization have emerged, including network analysis of frequency specific synchronization (i.e. Wendling et al., 2010; Schindler et al., 2008; Wilke et al., 2010; Ponten et al., 2009; Van Dellen et al., 2009). Application of such techniques to recordings of epileptic brain activity measured using intracranial electroencephalography (iEEG) have yielded a more complex account of the relationship between epilepsy and neural synchrony. Several studies have indicated that the seizure onset zone (SOZ) is functionally disconnected (Warren et al., 2010; Ibrahim et al., 2013), and the fragmentation and recoalescence of network connectivity has been associated with the evolution and cessation of seizures (Kramer et al., 2010). Altered network properties have been shown to be concentrated in the SOZ, and postsurgical normalization of network synchrony patterns has been associated with seizure freedom (Wilke et al., 2010). iEEG metrics for mapping epileptogenic brain areas which incorporate phase synchrony have been shown to be associated with good post-surgical outcome (Weiss et al., 2015). Such findings suggest that mapping large-scale neural synchronization may provide useful complementary information for localizing epileptogenic cortex, but the clinical utility of such methods to guide surgery in individual patients remains largely unknown.

Although presurgical mapping based on synchronization of neural oscillations has not yet been clinically implemented, presurgical planning is increasingly performed on the basis of the spectral properties of locally-expressed neural oscillations (Ochi et al., 2007; Akiyama et al., 2011). In particular, pathological high frequency oscillations (pHFOs; >80 Hz) are increasingly accepted as biomarkers of epileptogenicity (see Jacobs et al., 2012 for review). Recently, epileptogenic pHFOs have been shown to be associated with frequency-specific alterations in inter-regional phase-locking synchrony (Cotic et al., 2015; Ibrahim et al., 2013), and recent research has exploited this concordance to develop new approaches to seizure mapping (Weiss et al., 2015). Neural oscillations are understood to reflect fluctuations in neural excitability constrain spiking in space and time (Fries, 2005), and further evidence for the relationship between pHFOs and oscillatory phase comes from observations that cross frequency phase-amplitude coupling involving high frequencies corresponds to ictal activity topographically (Ibrahim et al., 2014) and corresponds to the evolution of ictal activity (Cotic et al., 2010).

The utility of pHFOs for presurgical mapping also depends an accurate analysis of their evolution in both space and time (Ochi et al., 2007). Similarly, conventional methods for visual identification of epileptogenic brain areas equally rely on accurate timing information regarding regions of early seizure propagation in iEEG recordings. One potential barrier to the translation of network connectivity mapping to presurgical planning for drug resistant focal epilepsy is the ability to map network topologies at sufficient temporal resolution, as prior studies have tended to analyze synchronization across the entire seizures, or in smaller segments which still fall short of the temporal resolution garnered using other presurgical mapping techniques (i.e. Wendling et al., 2010; Schindler et al., 2008; Wilke et al., 2010; Ponten et al., 2009; Van Dellen et al., 2009; Ibrahim et al., 2013; Kramer et al., 2010).

Presently, we introduce moviEEG (Multiple Overlay Visualizations for Intracranial ElectroEncephaloGraphy), a freely available and open source, MATLAB-based toolbox for animating inter-regional synchronization and cross-frequency interactions in iEEG data. The goal of this toolbox is to provide easily interpretable depiction of time-resolved network synchronization dynamics in with the goal of identifying new means for mapping epileptogenic cortex. Detailed explanation of the toolbox and its usage will be provided. We will also present data from two illustrative cases of children with medically-refractory focal epilepsy undergoing invasive monitoring at the Hospital for Sick Children (HSC). These cases outline the potential clinical utility of these mapping approaches.

2. Methods

2.1. Data recording and preprocessing

The following will serve as an overview of representative network connectivity dynamic analysis enabled by the toolbox, which will form the basis of demonstrations using individual case data. Analysis was performed on two patients undergoing invasive monitoring for drug resistant focal epilepsy at HSC. This involved surgical implantation of grids of electrodes in a silicone elastomer sheet (see Benia et al., 2009). The electrodes had a diameter of 4 mm and pitch (interelectrode separation) between 8 and 10 mm. In addition, strip and depth electrodes were implanted according individual patient mapping needs based on non-invasive assessments. During electrode implantation, photographs were taken to record the placement of electrode placement on the patient's brain using a handheld digital camera. Data were recorded over a period of several days in order to capture typical seizures for each patient, and extra-operative mapping of language and motor functions was also performed (see Benia et al., 2009). iEEG data were recorded using a Stellate Harmonie system (Montreal, Canada) and digitized at 2 kHz with a low-pass Butterworth antialiasing filter at 600 Hz prior to sampling. Data were referenced to an electrode chosen by clinical electrophysiologists in an electrographically silent area. The HSC Research Ethics Board approved this use and analysis of the selected clinical iEEG recordings.

Once the peri-ictal periods were identified, the iEEG recordings were epoched from 60 s before seizure onset to the end of the seizure. Interictal epochs of 60 s in length were also selected from the iEEG recordings. The interictal epochs were removed from ictal events by at least one hour, whenever possible, and were selected in a period with as few interictal discharges, and in a neurological state as similar as possible to the analyzed seizures. Thus, for example, for the analysis of a seizure occurring while the patient is awake and previously lying still, baseline interictal data was selected from a period where the patient is awake and lying still, and at least one hour removed from any ictal events. The interictal epochs were used to establish baseline connectivity measurements, to which we compare the ictal connectivity measurements to determine increases and decreases in connectivity leading up to, and during seizure.

2.2. Filtering and extraction of instantaneous phase

Each individual electrode waveform was filtered at 7 frequency bands known to be relevant for childhood epilepsy (delta, 1–4 Hz; theta, 4–7 Hz; alpha, 8–12 Hz; beta, 13–32 Hz; gamma, 40–80 Hz; pHFO1 (lower ripple), 80–150 Hz; pHFO2 (upper ripple) 150–200 Hz) using a digital FIR filter. Filters were designed using the MATLAB Filter Design and Analysis toolbox. The analytic signal from the Hilbert transformation of the filtered recordings provided time series of instantaneous phase and amplitude values for each electrode at each frequency, and used in the subsequent calculation of inter-electrode phase locking and cross-frequency phase-amplitude modulation. We have previously described similar methods for network analysis of EEG and MEG data (Ibrahim et al., 2013; Ibrahim et al., 2014).

2.3. Inter-electrode phase locking and network analysis

The functional connectivity between every pair of electrodes at each frequency band was indexed using the phase-locking value