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Regional and network relationship in the intracranial EEG second spectrum

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HIGHLIGHTS

- We examined relationships in the intracranial EEG band power time-series (second spectrum).
- Second spectrum coherence was low except at short distances and decreased with increasing frequency.
- Default mode network-specific analysis did not show enhanced connectivity in the second spectrum.

ABSTRACT

Objective: We examined low-frequency amplitude modulations of band power time-series, i.e. the second spectrum, of the intracranial EEG (icEEG) for evidence of support for spatial relationships between different parts of the brain and within the default mode network (DMN).
Methods: We estimated magnitude-squared coherence (MSC) of the running power in the delta, theta, alpha, beta, and gamma frequency bands for one-hour background icEEG epochs recorded from 9 patients. We isolated two test areas within the DMN and one control area outside it. We tested if the relationship between DMN areas was stronger than the relationship between each of these areas and the control location, and between all intrahemispheric contact pairs with similar intercontact distance.
Results: We observed very low values of second spectrum relationship between different parts of the brain, except at very short distances. These relationships are strongest in the delta band and decrease with increasing frequency, with gamma band relationships being the weakest. Our DMN-specific analysis showed no enhanced connectivity in the second spectrum in DMN locations in any frequency band.
Conclusions: Though we observed significantly nonzero relationships in lower frequency bands, second spectrum relationships are consistently very low across the entire brain in every frequency band.
Significance: This study suggests a lack of support for the DMN in the icEEG second spectrum.

1. Introduction

There is considerable interest in understanding the correlation in activity between different brain regions. Several fMRI studies have described a number of resting state networks (RSNs), distant brain areas that show relatively high correlation in blood-oxygen-level dependent (BOLD) signal while the patient is in a resting state (Biswal et al., 1995). A resting state network (RSN) that is of particular interest is the default mode network (DMN), which has been linked in fMRI studies to cognitive processes during "rest." The DMN is proposed to include the medial prefrontal cortex (MPFC), posterior cingulate cortex (PCC), and retrosplenial cortex (RCC) (Raichle et al., 2001). There is still uncertainty regarding the existence of these RSNs, and the underlying electrophysiology is not yet well understood. We know that the correlation and coherence of the intracranial EEG (icEEG) diminishes with distance, making the icEEG an unlikely candidate to explain the long-distance correlation observed in the BOLD time-series. Indeed, it has been shown

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previously by our group that the icEEG relationship within the DMN was not significantly greater than the relationships between DMN locations and a control location, indicating a lack of support for the DMN in the icEEG (Duncan et al., 2013). An argument has been made that the low-frequency changes in blood flow may be better reflected in synchronous amplitude modulation of band power time-series, i.e. the second spectrum, of the icEEG (Nir et al., 2008; Ko et al., 2011; Palva and Palva, 2012). Recent literature from magnetoencephalography (MEG) studies support this view, suggesting that there may be brain-wide correlation structure in the low-frequency modulating activity in the band power time-series, the so-called second spectrum (Hipp et al., 2012). It would be of value to determine whether similar relationships in the second spectrum are observed in icEEG recordings, a modality which can provide direct measurements of neuronal activity in specific brain regions with high spatial and temporal resolution. In particular, it has been proposed that RSNs may manifest in electrophysiological measures as synchronous modulation in the second spectrum of the theta and alpha bands (de Pasquale et al., 2010; Brookes et al., 2011; Hipp et al., 2012; Wens et al., 2014).

We studied icEEG data from patients being monitored for epilepsy surgery. Electrode contacts were available from all major lobes, as well as DMN areas. We examined icEEG second spectrum relationships between different areas of the brain and further analyzed the second spectrum for evidence of support for the DMN.

2. Methods

2.1. Subjects

We studied icEEG data collected from 9 epilepsy patients who were undergoing surgical evaluation and seizure localization at Yale-New Haven Hospital between 2003 and 2006 and had icEEG electrodes placed in areas of interest for the study. For the DMN analysis, we used the data studied previously by Duncan and coauthors (Duncan et al., 2013). Additional information about individual patients may be found in Table 1. The patients provided written informed consent for analyses of their records.

2.2. Intracranial EEG acquisition and selection of epochs for analysis

Macro depth, strip, and grid intracranial electrodes (Ad-Tech Medical Instrument Corporation, Racine, WI) were placed in a manner tailored to the individual patient. Intracranial EEG and simultaneous video were recorded with commercially available 128-channel long-term video-icEEG monitoring equipment (Natus/Bio-logic Systems Incorporated, San Carlos, CA). The icEEG signals were sampled at 256 Hz and 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.

For each patient, we selected a one-hour epoch at least 6 h removed from a seizure, when the patient appeared to be resting quietly with eyes open at night prior to sleep. Importantly, this was a retrospective analysis and patients were not specifically asked to rest quietly. Patient state was evaluated from the video and icEEG record, and segments of data when the patients were interacting with staff, eating, or performing other activities were removed. Noise segments and other artifacts were also visually identified and removed (Duncan et al., 2013). We analyzed an average of 51.88 min of data for each patient, ranging from 37.38 to 59.91 min in the different patients.

2.3. Second spectrum connectivity between lobes and DMN-specific analysis

For each icEEG epoch, we calculated the running power, at a one-second resolution, in different frequency bands (delta [0–4 Hz], theta [4–8 Hz], alpha [8–13 Hz], beta [13–25 Hz], and gamma [25–55 Hz]). These running power time-series were examined for evidence of relationship between different regions of the brain in the following manner. We first estimated magnitude-squared coherence (MSC) for all possible electrode contact pairs for each one-hour band power time-series (3600 samples), using 3-min windows (180 samples) with 50% overlap, with a mean deletion performed on each segment. As we were interested in quantifying low-frequency modulations of the band power time-series, we subsequently averaged the MSC of the second spectrum for frequencies less than 0.15 Hz to give a single MSC value for each contact pair. An example of the second spectrum MSC of the gamma band power time-series was included in the study by Duncan et al., but a mean deletion was not performed for that estimation (see Fig. 4 in Duncan et al., 2013). In this study, a mean deletion was performed. We provide both a corrected spectrum and an example of the gamma band MSC spectrum between 0 and 0.2 Hz of those data in Supplementary Figs. S1 and S2. We aggregated MSC estimates for all patients, and examined how relationships in the second spectrum vary with distance and frequency. We considered all contact pairs, as well as all combinations with interhemispheric pairs omitted. A total of 59,959 contact pairs were analyzed across 9 patients, of which 46,370 were intrahemispheric and 13,589 pairs were interhemispheric. We then examined relationships within and between different lobes of the brain (left frontal, left medial temporal, left temporal, left parietal, left occipital, right frontal, right medial temporal, right temporal, right parietal, right occipital). All icEEG electrode contacts were localized from a postimplantation CT and visualized on a preimplantation MRI based on a procedure described previously (Papademetris et al., 2006; Goncharova et al., 2009). There were a small number of contacts that could not be localized exclusively to one lobe; these were not included in our analysis. The total number of pairs analyzed within and between lobes was 58,580.

To examine second spectrum relationships in DMN locations, we analyzed the same data studied by Duncan et al. (2013). The DMN-specific data were a subset of the data used in the analysis

Table 1
Patient information.

Patient	Gender	Age	Seizure onset area	Number of contacts studied (T1, T2, C)	Duration of data studied (min)
1	F	19	Right occipital pole	2,3,5	59.92
2	M	20	Left anterior and medial frontal	7,1,3	56.40
3	F	40	Left medial temporal	2,5,8	38.45
4	F	24	Right posterior fronto-parietal	9,8,4	50.15
5	F	18	Right anterior lateral and inferior temporal	2,2,3	37.53
6	F	39	Left medial temporal	4,5,7	56.23
7	M	12	Right medial fronto-parietal	4,7,2	57.88
8	F	27	Right medial temporal	8,3,3	59.95
9	M	35	Left fronto-parietal-occipital	8,4,2	50.90