EEG correlates of time-varying BOLD functional connectivity

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Target Audience: Researchers interested in resting-state fMRI, functional connectivity, or EEG-fMRI

Purpose: A growing number of studies are focusing on the dynamic properties of resting-state functional connectivity (FC), where it has been observed that brain connectivity patterns inferred from correlational relationships between regions can exhibit substantial variations across a several-minute scan. For example, an anti-correlated relationship between two important networks, the default-mode network (DMN) and dorsal attention network (DAN), appears to occur in occasional, transient epochs[1,2]. However, the basis and importance of such network connectivity fluctuations are largely unknown; while this phenomenon may reflect neuronal dynamics and brain state, it may to some degree result from physiological noise or random fluctuation. Here, we examine the electrophysiological correlates of within-scan FC variations during eyes-closed rest. A sliding window analysis of simultaneous EEG-fMRI data was performed to examine whether temporal variations in FC between three major networks (DMN, DAN, and salience network; SN) are associated with temporal variations in mental state, as assessed from the power of alpha and theta oscillations in the EEG. Resting-state EEG rhythms have ongoing fluctuations in amplitude that track shifts in vigilance and cognitive state, and may therefore be used as marker of state change with which to query changes in FC over time[3].

Methods: Ten subjects underwent simultaneous EEG-fMRI at 3T (eyes-closed rest, TR = 2s, voxel size 3.4x3.4x4mm^3, scan durations 9.75-12.24 min). Network regions were defined from a functional atlas[4], and an aggregate measure of FC between networks was computed in temporal sliding windows (width 40s, overlap 50%) across each scan. For each sliding window, the aggregate FC between networks *i* and *j* was determined by computing the pairwise correlation coefficient between each node of network *i* and each node of network *j*, followed by averaging the resulting Fisher-z transformed correlation coefficients. The EEG power in posterior alpha and frontal theta bands were computed in identical sliding windows, and were simultaneously regressed against the sliding-window FC between each network pair to determine whether changes in FC over time have a spectral signature. We also examined whether the degree of anti-correlation between DMN and DAN across sliding windows was predicted by alpha and theta power, where an anti-correlation index was defined as the fraction of negatively correlated voxel pairs between the networks.

Results: A significant degree of temporal variation in FC can be explained by the combination of alpha and theta power variations (Fig. 1). Alpha power had a significant inverse relationship with the strength of connectivity between DMN and DAN ($p<0.003$ corrected). This inverse relationship remained significant across a range of sliding window sizes (30-60 s), as well as when global (rather than posterior and frontal) measures of alpha and theta were used. Theta power showed a trend for positive but insignificant correlation with FC within and between all pairs of networks. Importantly, both alpha and theta power covaried with the spatial extent of *anti-correlation* between DMN and DAN (Fig. 2), with higher alpha power associated with larger anti-correlation extent ($p = 0.009$) and higher theta power associated with smaller anti-correlation extent ($p=0.049$). In addition, the thalamus and anterior insula nodes of SN showed a trend toward increased coupling as a function of increased alpha power.

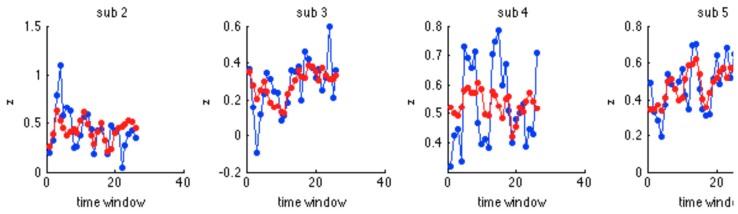

Fig. 1 Time course of DMN-DAN functional connectivity (blue), superimposed on the time course of functional connectivity that is predicted from a linear combination of EEG alpha and theta bands (red), shown for 4 subjects.

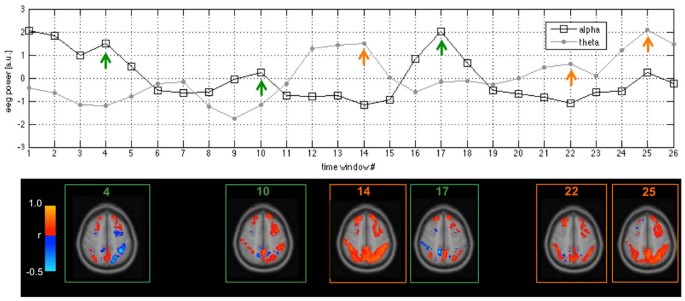

Fig. 2 Illustration of relationship between anti-correlations and EEG power, for one subject. *Top*: Normalized sliding-window time series of alpha and theta power. *Bottom*: Seed-based FC maps (seeded in the posterior cingulate cortex) shown at the indicated time windows (arrows in upper graph). Greater anti-correlations are apparent in windows of higher relative alpha power, whereas greater positive correlations are apparent in windows of higher relative theta power.

Discussion: Fluctuations in alpha power were associated with fluctuations in DMN-DAN connectivity as well as in the spatial extent of DMN-DAN anti-correlation. These results suggest an electrophysiological signature and potential state dependence of time-varying DMN-DAN connectivity. The observed relationship may arise in part from fluctuations in vigilance and arousal; previous studies have shown that EEG alpha and theta power are modulated as a function of vigilance, with drowsiness characterized by diminished alpha power and increased theta and delta power[5]. Consistent with our findings, states of alertness and improved performance have been linked with greater DMN-DAN anti-correlations[6] and, separately, increased alpha power[7]. Our observation that DMN-DAN anti-correlation has an EEG signature is of note since the existence and functional significance of network anti-correlation has been under debate[8].

Conclusions: Dynamic changes in resting-state DMN-DAN functional connectivity were found to correlate with fluctuations in alpha band power. Simultaneous measurement of EEG during resting-state scans may therefore provide a greater understanding of variance in functional connectivity, and potentially allow one to attribute certain variations to arousal or attentional states.

References: [1] Chang et al., Neuroimage 50:81-98 (2010). [2] Popa et al., J Neurosci 29:1191-1201 (2009). [3] Laufs, HBM 29:762-769 (2008) [4] Shirer et al. Cer Cor 22:158-165 (2012). [5] Klimesch, Brain Res Rev (1999). [6] Thompson et al. HBM (2012) [7] Sadaghiani et al., J Neurosci 30:10243-10250 (2010).[8] Fox et al., J Neurophysiol 101:3270-3283 (2009).