## SIMULTANEOUS FMRI AND EEG STUDY OF NEVER RESTING BRAIN: SPATIAL AND TEMPORAL SIMILARITY OF EEG MICROSTATES CORTICAL REPRESENTATION AND BOLD RESTING STATE NETWORKS

Han Yuan<sup>1</sup>, Lei Ding<sup>2,3</sup>, Min Zhu<sup>2</sup>, and Jerzy Bodurka<sup>1,4</sup> <sup>1</sup>Laureate Institute for Brain Research, Tulsa, OK, United States, <sup>2</sup>School of Electrical and Computer Engineering, University of Oklahoma, Norman, OK, United States, <sup>3</sup>Bioengineering Center, University of Oklahoma, Norman, OK, United States, <sup>4</sup>College of Engineering, University of Oklahoma, Norman, OK, United States

Target audience: Researchers and clinicians utilizing fMRI and/or EEG to study spatiotemporal patterns of the resting human brain in healthy and diseased states. Purpose: Neuroimaging research suggests that in the awake, resting behavioral state, cerebral function is driven by patterns of neuronal activity in large-scale functional networks. The BOLD fMRI studies of brain at rest reveal spontaneous, large-amplitude, low-frequency (<0.1Hz) fluctuations that are temporally correlated and spatially organized into several functional networks referred to collectively as resting state networks (RSNs). However, the neurophysiological basis of these BOLD RSNs is not fully understood. Recently, the electroencephalography (EEG) microstates have been suggested to correlate with the temporal dynamics of various RSNs<sup>1</sup>. However, the spatial characteristics of the RSN-related EEG microstates (EEG-ms) have not been investigated. In this study we combined electrophysiological source imaging and independent component analysis to obtained cortical sources of EEG microstates and compared them to the resting state networks independently derived from simultaneously measured BOLD fMRI. This novel approach results in EEG-ms-derived RSNs with significant similarity in spatial structure as well as high correlation in temporal dynamics as compared with RSNs independently derived using simultaneously acquired BOLD fMRI.

Methods: Simultaneous resting-state EEG and fMRI data were acquired from nine healthy human subjects (age  $33 \pm 10$  years; one female). The experiments were performed on a General Electric Discovery MR750 3T MRI scanner with an 8-channel receive-only head array coil. For the whole brain fMRI, a single shot gradient

echo EPI sequence with Sensitivity Encoding (SENSE) and FOV/slice thickness/gap=220/2.9/0.2mm was used (TR/TE=2000/30ms, acceleration=2, image matrix 64×64, flip=30°, 34 axial slices). Structural MRI T1-weighted images were obtained with an MPRAGE sequence. High-density EEG signals from 126 channels were simultaneously recorded with BOLD fMRI scans using MRI-compatible BrainAmp MR Plus amplifiers (in 0.016-250 Hz band with 0.1 µV resolution and 5000 Hz sampling rate). Three closed-eye resting scans, each lasting six minutes and ten seconds, were acquired for each subject. A pneumatic respiration belt and a photoplethysmograph were used to obtain respiration and pulse oximetry measurements, respectively. A new method was developed to analyze EEG-ms using electrophysiological source imaging (ESI) and independent component analysis (ICA). After MRI and cardioballistic artifacts correction, ESI analysis was employed on the EEG topographies at the local peaks of global field power (defined as EEG-ms<sup>4</sup>) to estimate cortical source activity. We modeled the sources for electrical potentials as current dipoles evenly distributed over the cortical surface. The volume conductor was modeled by a three-shell boundary element model with three different conductive tissues (the scalp, skull, and brain, with conductivities of 0.33 [S/m], 0.0165 [S/m], and 0.33 [S/m], respectively). Structural MRIs were segmented to build the realistic geometric models. The inverse problem was solved using minimum norm estimate<sup>5</sup> with the Tikhonov regularization<sup>6</sup>. The sources of EEG-ms were then subject to temporal ICA and decomposed into independent components (ICs), which are considered as the main microstates. A back-projection was performed to obtain source maps



Fig. 1 Maps of RSNs obtained using EEG microstates source analysis.

associated with each IC. Thus for each IC, the source map corresponds to the spatial topology of a specific type of microstate, i.e. the main microstate, and the intensity of the main microstate is reflected in the temporal trace of the IC, which is maximally independent from others. The same decomposition matrix was applied to the sources of continuous EEG, resulting in IC time courses for the entire recording. At each time point, a dominant main microstate was selected based on which IC has the maximum absolute intensity value. The time courses of main microstates were convolved with a canonical hemodynamic response function and down-sampled to TR. Thus we have identified cortical representation of EEG-ms or EEG-ms-derived RSNs and their corresponding time courses. The preprocessed fMRI data were subject to group spatial ICA in order to extract BOLD RSNs. The source maps of EEG-ms were compared to the spatial maps of RSNs independently derived from BOLD fMRI and the correlation of their time courses were assessed.

Results: Five representative networks were selected from BOLD fMRI RSNs, i.e. the default mode, sensorimotor, attention, auditory, and visual networks<sup>3</sup>. Their corresponding RSNs derived from EEG-ms sources were identified by choosing those with highest spatial correlations with BOLD fMRI RSNs. The maps of EEG-msderived RSNs are displayed in Fig. 1. The default mode, sensorimotor, attention, and auditory networks show high spatial similarity between EEG-ms RSNs and BOLD fMRI RSNs. Note that the three EEG-ms-derived RSNs of the visual cortex were identified to be similar to the visual BOLD fMRI RSNs: two of them consist of left or right primary visual cortex alone, and the third one is more extensive, including left and right visual cortex and part of the parietal cortex. The time courses of these EEG-ms RSNs were all significantly correlated with the time courses of corresponding BOLD fMRI RSNs (p<0.001).

Discussion & Conclusion: We describe a method to obtain RSNs from EEG-ms and report that the EEG-ms-derived RSNs are of both high spatial similarity and temporal correlation with RSNs independently derived from BOLD fMRI. Previous studies showed that RSNs can be measured from MEG and they are of high spatial similarity with BOLD fMRI RSNs<sup>2</sup>. However, the temporal relationship between MEG derived RSN and BOLD fMRI was not clear since it is not technically feasible to simultaneously measure MEG and fMRI. The temporal aspect of BOLD fMRI RSNs has been shown to be correlated with band-limited EEG power<sup>3</sup> and temporal independent EEG microstates<sup>1</sup> from simultaneous EEG and fMRI recordings. However, our study for the first time localized the cortical sources of EEG-ms RSNs and demonstrated their spatial similarity with BOLD fMRI RSNs. Although EEG-ms RSNs and BOLD fMRI RSNs are spatially similar, it is also worthwhile to note that the visual network was found split into three EEG-ms RSNs that are temporally independent from each other.

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