Contribution of A Brain-state Specific Neurophysiological Event to Large-scale fMRI Signal Fluctuations

Xiao Liu[1], Toru Yanagawa[2], David A Leopold[3], Marieke Schölvinck[4], Catie Chang[1], Hiroaki Ishida[5], Naotaka Fujji[2], and Jeff H. Duyn[1]
[1]*AMRI, LFMI, NINDS, NIH, Bethesda, MD, United States,* [2]*BSI, RIKEN, Saitama, Japan,* [3]*Laboratory of Neuropsychology, NIMH, NIH, Bethesda, MD, United States,* [4]*Ernst Strüngmann Institute for Neuroscience, Frankfurt, Hessen, Germany,* [5]*Tokyo Metropolitan Institute of Medical Science, Tokyo, Japan*

Target Audience Neuroscientists, fMRI Researchers

Purpose Resting-state fMRI (rsfMRI) studies have shown a brain-wide ("global") increase in signal fluctuations under conditions of reduced alertness during light sleep[1] or eyes-closed conditions[2]. Similarly, caffeine has been found to reduce the level of such global fluctuations in the rsfMRI signal[2], whereas hypnotic drugs increase them[3-4]. While a neurophysiological contribution to this phenomenon has been identified in the form of changes in gamma-band power of concurrent local field potentials (LFPs)[5], its detailed characteristics and behavioral relevance remain unclear. Temporal decomposition of rsfMRI data has suggested that global signal changes often occur as discrete events that are preferentially associated with activation of sensory networks[6]. Guided by this, we examined electrocorticography (ECoG) data sampled from extensive cortical areas for global, state-sensitive neural events and then confirmed their relationship to rsfMRI signals by examining concurrent LFP-fMRI data from a different study.

Methods ECoG signals were recorded from 4 macaques using subdural electrode grids (128 channels) implanted over almost the entire left hemispheric surface (an example shown in Fig 1C)[7]. The animals were studied during waking eyes-opened (EO), eyes-closed (EC) conditions, and sleep. A time-frequency transform was applied to the raw signals of each electrode to derive spectrograms, after which power level was normalized across frequencies. Electrode signals were then averaged to generate a global mean spectrogram. Band-limited power signals (BLPs) were also extracted by averaging the spectrograms within the low- (< 4 Hz), middle- (9–21 Hz), and high-frequency (42–87 Hz) bands. Cross-correlation functions of BLPs were calculated on 300-sec time segments. Concurrent fMRI (CBV-based) and LFP data was acquired from awake macaques in a previous study[5], and here we focused on a dataset with two 16-channel depth electrodes in the frontal and parietal regions, respectively.

Results The global mean spectrogram of ECoG signals from sleep sessions typically revealed a repetitive, stereotypical event characterized by sequential power changes in three distinct bands (Fig. 1A): Low-frequency power increases, attributed to K-complexes and slow waves, were generally preceded by both a sudden decline in mid-frequency power and an increase in high-frequency power. The averaged patterns of such sequential spectral transitions (SST) were weaker during the EC condition and were largely absent during the EO condition (Fig. 1B), which is also apparent from the change in cross-correlation functions of BLPs (Fig. 1D). In addition, the high-frequency gamma power changes during the SST showed quantitative differences across the cortex with the sensory regions showing the most prominent changes (Fig. 1C).

The SST phenomenon was also observed in the global mean spectrogram of LFP from the LFP-fMRI study. While the SSTs (red arrows in Fig. 2) induced large, global decreases in concurrently acquired CBV signals, the gamma-power bursts (black arrows) without clear SST pattern did not.

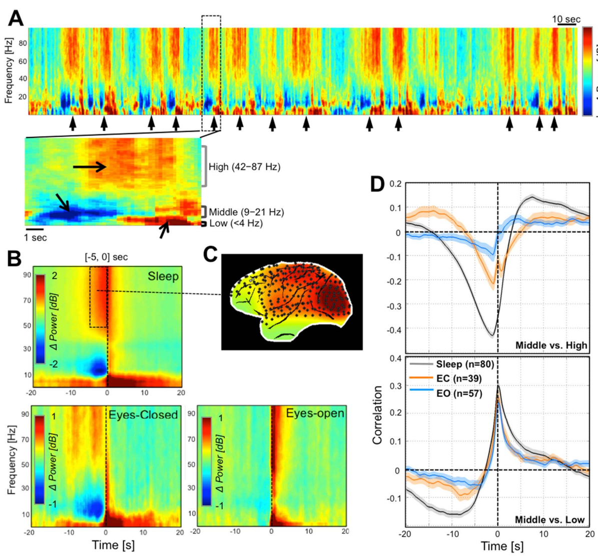

Fig. 1 SST events observed in the global mean spectrogram of ECoG.

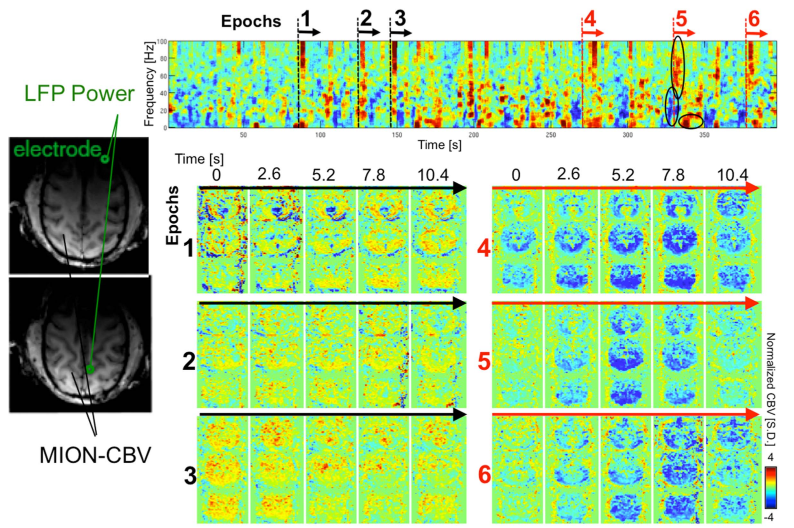

Fig. 2 Similar SST pattern in channel-averaged LFP power signal and associated changes in concurrent CBV signal.

Discussion SST events occur spontaneously in electrophysiological signals and share several characteristics with global rsfMRI signal, including their dependency on brain state, their widespread cortical involvement, and their predominance in sensory areas. Their co-occurrence in the LFP-fMRI data suggest that SST events, rather than gamma-burst alone, may underlie global fMRI signal fluctuations. SSTs may reflect a subcortical rivalry between the waking- and sleep-promoting systems at low vigilance level, since neurons in these two systems have also been found to exhibit sequential modulations during state transitions[8].

Conclusion A brain-state-dependent SST event observed in electrophysiology was identified as a potential contributor to the global rsfMRI signal.

References [1] Fukunaga, M et al. *MRI,* 2006 [2] Wong, CW et al. *NeuroImage*, 2013; [3] Kiviniemi, VJ et al. *MRI*, 2005; [4] Licata, SC et al. *NeuroImage* 2013; [5] Schölvinck, ML et al. *PNAS*, 2010; [6] Liu, X et al. 2013 ISMRM meeting [7] Liu, X et al. *Cere. Cor.*, 2014; [8] Takahashi, K et al. *Neuroscience*, 2010.