Metabolic imprint of EEG slow oscillations as observed by BOLD-fMRI during deep sleep

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Introduction:

During the deeper stages of sleep, many of the neurons in mammalian brain show synchronized fluctuations in neuronal firing rate that are driven by slow (<1Hz) oscillations in membrane potential (Steriade, 1993). These slow oscillations (SO) have been observed extra-cranially by electroencephalography (EEG) and it has been hypothesized that they might facilitate the adjustments in synaptic strength through synchronized modulation of cortical activity (Massimini, 2003, 2004). In this work, we investigated the SO by mapping their associated metabolic activity with BOLD-fMRI.

Methods:

Simultaneous EEG and fMRI data were collected for up to 3 hours, starting after 2am after subjects were sleep deprived for 44 hours. Subjects (n=18) were encouraged to fall asleep. EEG was collected using 16 channels with a BrainAmps system and pre-processed with Analyzer (BrainVision). BOLD-fMRI was collected on a 3T (GE) scanner equipped with a 16-channel coil (NovaMedical) using an EPI sequence (TE: 45ms, TR:3s, 25 slices, gap:0.5mm, 3.45x3.45x4.5mm^3) modified to reduce sound pressure level (96dB compared to 110dB for regular EPI) by decreasing the bandwidth to 62.54kHz and limiting gradient slew-rate to 25 T/m/s. Cardiac (pulse oximeter) and respiratory (bellows) signals were also collected, together with TTL pulses indicating scanner slice timing. fMRI pre-processing included slice timing correction and rigid body motion correction. RETROICOR-derived cardiac and respiratory phase, cardiac rate and the respiration volume per unit time were regressed out (Shmueli, 2007). Data were also high-pass filtered (≥0.005Hz) to remove baseline drifts. Sleep was scored (by DP) for each subject based on the EEG data in intervals of 12 seconds. For each subject, an interval of 10 minutes of deep sleep was selected, satisfying the criteria of having a high delta activity level and a sleep score of 2, 3 or 4. For this interval, the SO activity was defined as the energy of the EEG at the frequency interval 0.66-0.99Hz, and computed based on the FFT for each 3s intervals at electrodes C3-C4-P3-P4. The SO signal was correlated with the BOLD-fMRI on a voxel-by-voxel basis. Correlation maps were then converted to MNI space and r values converted to z-scores prior to group averaging.

Results and Discussion:

Group analysis on eight subjects that experienced at least 10 minutes of deep sleep showed consistent correlations in a number of brain areas at correlation lags between 3 and 12 seconds (BOLD trailing EEG). These areas included Thalamus, Caudate, Putamen and unimodal and heteromodal sensory cortices (see figure 1). Spatial patterns varied with correlation lag, with the earliest (positive) correlation seen in the Thalamus, followed by (negative) activity of the sensory cortices and late negative Thalamic activity (figure 2). The combined involvement of Thalamus and sensory cortices in the phenomenon of slow oscillations is consistent with earlier studies using invasive electrophysiology in animals (Steriade, 1993). We hypothesize that the periodic hyperpolarizations associated with SO activity leads to an overall depression of neuronal activity, leading to BOLD-observable blood flow changes. This activity is not uniformly distributed over the cortex and varies over time.

Conclusion:

This study shows the first evidence of a metabolic effect of the sleep slow oscillation. The results suggest that the effects of the SO on neuronal activity have a consistent spatio-temporal patterns that involves Thalamic and neo-cortical areas.

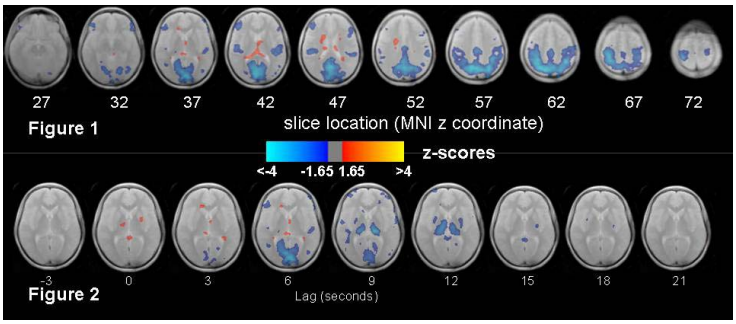

Figure 1: correlations between BOLD-fMRI and SO for whole brain at lag 6s. (z coordinates in MNI space)

Figure 2: time evolution of correlations between BOLD- fMRI and SO for one slice (MNI z=37)

References: Steriade, J Neuroscience 1993 (13-8-3252); Massimini, J Neurophysiology 2003 (89-1205); Massimini, J Neurosciece 2004 (24-31-6862); Shmueli, Neuroimage 2007 (38-306-320).