

Brain Functional Connectivity During Sleep

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Introduction:

Spatio-temporal patterns of correlated activity are being observed in an increasing number of resting-state BOLD fMRI studies and appear to convey information about the functional connectivity of human brain [1, 2]. The origin of this activity during rest is still unknown and could relate to a purely vascular phenomenon, or could have a metabolic component that could signify e.g. active thought processes or a homeostatic role. To investigate the conditions that facilitate the occurrence of resting state BOLD activity, and the role of active thought processes, we designed an experiment during which the subject experienced varying levels of drowsiness, while monitoring the subjects' alertness by concurrently measuring scalp EEG.

Materials and Methods:

Simultaneous EEG and fMRI data were collected on two subjects over the course of a 40-minute day-time experiment. During the initial 5 minutes, a visual task was presented stimulating foveal and peripheral vision alternatingly for 30s each; subsequently, a 4 minute eyes closed-eyes open (EC-EO) (1 min./stage) was performed. During the remaining 31 min., the subjects relaxed with eyes closed, and were instructed to fall asleep. BOLD fMRI signal from 5 slices through the visual cortex was collected on a 3T (GE) scanner equipped with a 16-channel (NOVA Medical) coil (single shot EPI, TE:45 ms, TR:3s, burst mode, 90° flip angle, 1.7x17x3.0mm³, gap 5.0 mm, 5 slices, 800 volumes). EEG was collected from 64 channels (Synamp2 & Maglink, Compumedics) at sample rate 10 kHz, low-pass filtered at 2 kHz. EEG data were pre-processed using Scan4.5beta version (Compumedics) and analyzed in Matlab. Power spectra at delta (0.5-4 Hz) and alpha (8-12Hz) bands were computed for the gradient-free interval 940-2988ms for each TR. Evaluation of alertness during the resting state was performed by calculating the ratio R of delta and alpha power: $R < 1$ indicated the alert awake state (sleep level 0) whereas $R > 1$ indicated sleep (sleep level > 0). To investigate spatial correlation of BOLD fluctuations during sleep spatial ICA was performed (FSL 3.1 University of Oxford, Oxford, UK).

Results and Discussion:

Subject 1 (S1) reported to have been awake during the whole scan and Subject 2 (S2) to have fallen asleep. EEG analysis confirmed this and showed that S1 (Fig 1, left) was attentive in the visual task, relax and awake during most of the experiment, but drowsy around minute 20. S2 (Fig 1, right) was attentive during the visual task, drowsy during the EC-EO segment and few minutes thereafter, and asleep until minute 28, then woke up. Data from only 30 minutes are presented because of strong motion artifacts during remainder experiment.

BOLD signal fluctuation level mimicked sleep level: periods where sleep level exceeded 0 coincided with periods of increased fluctuation. The maximum increase in fluctuation level was about 100% for both subjects, as compared to the alert awake period immediately following the task. A strong correlation between the level of delta activity and the standard deviation of the fMRI (S1 $r=0.8611$; S2 $r=0.6579$) was also observed. ICA showed that the BOLD fluctuations exhibit strong correlations in apparent functionally connected areas (e.g. Fig. 2), similar to those observed in earlier connectivity studies [1, 2] during the resting state. In a parallel study without EEG [3], we found that the patterns observed during sleep are highly reproducible within (n=3) and across subjects (n=7).

These results suggest that during sleep strong and spatially correlated BOLD activity occurs that is not caused by active cognitive processes.

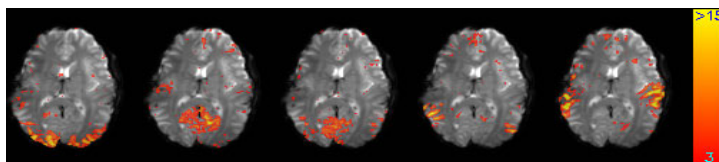


Figure 2: example of different ICs in one slice from S2 during sleep.

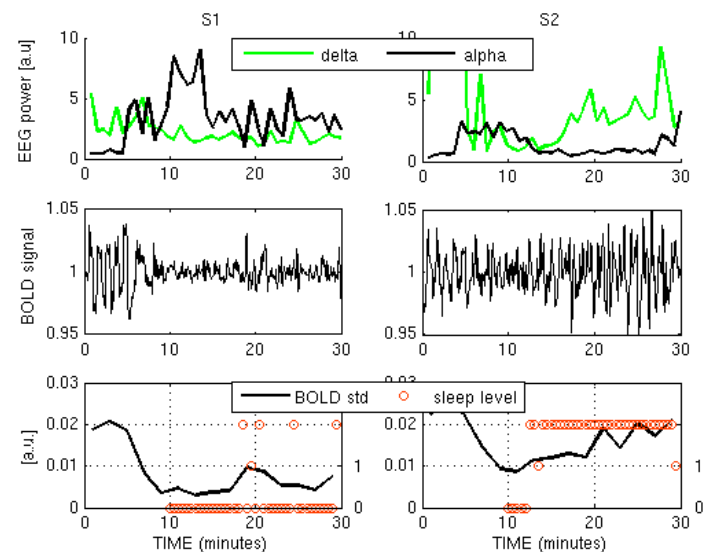


Figure 1: Top: EEG alpha (black) and delta (green) band power over the course of the experiment. Middle: BOLD signal in visual cortex. Bottom: standard deviation of the BOLD signal, computed every 2 min.(black). Red circles indicate sleep level continuous at 0 awake, continuous at > 1 sleep, in between: drowsy. Left: data from subject 1 (awake-drowsy). Right: data from subject 2 (asleep). Notice the coincidence of periods with high BOLD fluctuations with episodes of high delta and low alpha power.

References: [1] Biswal, MRM 1995. [2] Greicius, PNAS 2003. [3] Fukunaga, submitted.