BOLD low frequency fluctuations during slow wave sleep: An EEG/fMRI study

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Introduction: Connectivity among functional areas has been studied with fMRI for several years. Of particular interest has been the "default-mode network", originally hypothesized to subserve functions and processes that occur during awake rest in absence of goal direct action. These functions could include monitoring of the environment, conscious awareness, and self-reflective thought [1]. Because slow wave sleep is a state during which these functions are at low level or absent, we hypothesized that if default-mode activity reflects these active cognitive processes, it should likewise be diminished during slow wave (deep) sleep.

Methods: Volunteers consented to a 3.5-day inpatient study according to IRB requirements. After 44 hours total sleep deprivation and at approximately 2:30 a.m., we performed simultaneous EEG and fMRI with a maximum of 3 h continuous scans allowed per session. Data from four subjects is presented.

EEG was collected simultaneously from 16 scalp locations using a BrainAmps system and pre-processed with Analyzer (BrainVision). Frequency analysis was performed in IDL in order to identify periods with slow wave sleep as determined from relative increases in EEG delta activity and decreases in EEG alpha activity [2]. The first continuous interval with high relative delta activity (≥10 minutes of >39% delta activity and a ratio delta to alpha of at least 1.5) was selected for each volunteer for fMRI connectivity analysis.

BOLD fMRI data were collected using a 3T (GE) scanner equipped with a 16-channel coil (Nova Medical) using an EPI sequence (TE: 45 ms, TR: 3 s, 25 slices, gap 0.5 mm, 3.75x3.75x4.5 mm^3) modified to reduce the sound pressure level (96 dB(A) down from 110 dB(A)) by decreasing the bandwidth to 62.54 kHz and limiting gradient slew rate to 25 T/m/s. Cardiac and respiratory signals were also collected, together with TTL pulses indicating scanner slice timing. Functional MRI pre-processing included slice timing correction and rigid body motion correction. Data were also high-pass filtered (≥0.006Hz) to remove baseline drifts. The global signal change, the cardiac rate and the respiration volume per unit time were regressed out. Data sets were then converted to percentage signal change and a spatial Gaussian filter (FWHM = 4 voxels) was applied to the whole brain data. To detect the default-mode network, a time course seed in precuneus (centered at Talairach coordinate: [-5,-49,40]) [1] was defined for each volunteer. Correlations between the seed and all brain voxels were computed for the deep sleep interval.

Results: Subjects showed varying levels of sleep. Two subjects (S2 and S3) had continuously increased levels of EEG delta for 15 minutes, and the two others (S1 and S4) showed increased levels of EEG delta for at least 40 minutes (see Table 1). Default-mode network activity was evident during these slow wave episodes, as indicated by the pattern of correlations between the precuneus seed and posterior cingulate, inferior parietal and middle frontal areas (see Figure 1).

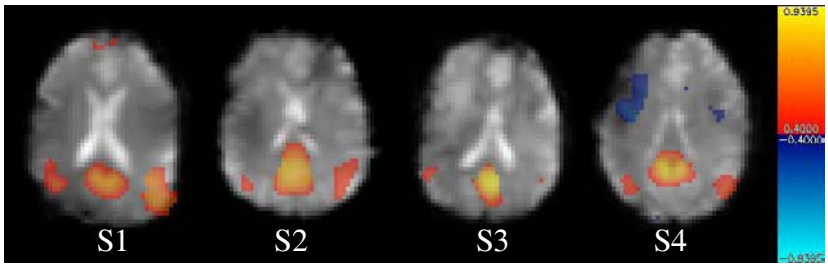

Figure 1: correlation maps for each volunteer (threshold: r=0.40)

	S1	S2	S3	S4
delta (0.5-4 Hz) %	43.46	39.57	42.61	48.57
theta (4-8Hz) %	23.76	26.46	25.12	23.76
alpha (8-12 Hz) %	14.77	16.02	15.72	13.69
beta (12-20 Hz) %	18.01	17.95	16.55	13.98
time (minutes)	45	15	15	40

Table 1: distribution of EEG frequencies during the intervals of interest.

Conclusion: Correlated BOLD fMRI activity in the default mode network is maintained during slow wave sleep. This finding expands our earlier finding in light sleep [3] and suggests that active cognitive processes involving monitoring of the environment and self-reflective thought are not likely to be the origin of this activity. The functional role of the resting state fluctuations remains unclear.

References: [1] Raichle et al., PNAS 98, 2001, p 676; [2] Rechtschaffen & Kales, A manual of standardized terminology, techniques and scoring system for sleep stage of human subjects. 1968; [3] Horovitz et al. ISMRM 2006, p 531.