Sleepiness and Accuracy Correlate Abnormal BOLD-fMRI responses during Sleep Deprivation

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INTRODUCTION: Sleep deprivation (SD) can affect cognition. fMRI studies[1] suggest that SD reduces accuracy, as well as cortical and subcortical activation during working memory (WM) tasks. Here we investigated the effect of SD on accuracy and brain activation using a set of visual attention (VA) and WM tasks with graded levels of difficulty and high-field fMRI. We hypothesized that subjects would have decreased performance accuracy and abnormal activation in the VA and WM networks after 24 hours of SD, which would correlate with self-reports of sleepiness and performance accuracy during the fMRI runs.

METHODS: Sixteen healthy non-smoking and right-handed men (age: 36±5 years, education: 14±2 years) participated in the study. All subjects had two fMRI sessions in two different days (more than one week apart): normal sleep (NS; all subjects overnight on-site for a total of 8 hours), and 24 hours of sleep deprivation (SD; all subjects were supervised 24 hours). Session order was randomized across subjects. During each of the fMRI sessions the subjects performed two sets of fMRI-tasks with different levels of difficulty: (VA) mental tracking of 2, 3, or 4 balls amongst 10 moving balls[2], and (WM) recognition of 0-, 1-, and 2-back targets in a sequential-letter paradigm[2]. After a training session outside of the scanner, subjects underwent functional MRI in a 4-Tesla MRI scanner, using a single-shot gradient-echo EPI sequence [TE/TR = 20/1600 ms, 4 mm slice thickness, 1-mm gap, 35 coronal slices, 64x64 matrix size, 20-cm FOV, 200-kHz bandwidth, 187 (WM) and 231 (VA) time points; sound pressure level of acoustic noise = 92 dBA]. Task performance and subject motion were monitored in real-time during fMRI, to assure accuracy > 80% and motion < 1mm-translations and < 1°-rotations. After motion correction, spatial normalization to the Talairach frame (3x3x3 mm^3 voxel size), and spatial smoothing (8-mm Gaussian), activation maps were calculated for each subject and task using the general lineal model in SPM2. Group analyses of individual BOLD maps were performed using random-effects analyses (one-way within-subjects ANOVA and simple regressions in SPM2). Region of interest (ROI) analyses (cubic, 27 voxels) were conducted at the cluster centers of brain activation to extract the average BOLD signal from these regions. Cross correlations analyses of resting fMRI noise were conducted to study the functional connectivity (fcMRI) among interacting ROIs.

RESULTS: Subjects self-reported higher sleepiness during the SD session than during the NS session ($p<0.0001$, t-test). Figure 1 shows that for the VA and WM tasks, sleep deprivation significantly impaired subject's accuracy, especially during the more demanding conditions (WM: 2-back; VA: 4-balls). The SD-effect on accuracy was stronger for the VA tasks that for the WM tasks (Fig 1). As in previous studies[2], increased difficulty decreased subject's accuracy for both tasks; this load-effect was stronger for the SD session than for the NS session. The WM and VA tasks produced load-dependent bilateral activation in parietal, occipital, and prefrontal cortices, the cerebellum and the thalamus, and deactivation of sensory cortices (A1 and V1) as reported previously[2]. Activation/deactivation patterns were similar for WM and VA (Fig 1). For both tasks, activation was higher in the thalamus and lower in parietal and prefrontal cortices for the SD session than for the NS session (Fig 1), paralleling the behavioral results; deactivation of the precuneus was higher for the NS session than for the SD session. The effect of increased task difficulty (WM-load and VA-load) on cortical activation was higher for SD than for NS. For both tasks, activation of the anterior cingulate gyrus (ACG; BA 24) correlated with sleepiness and accuracy (Fig 2). The connectivity between the thalamus and the precuneus was higher for the NS session than for SD session.

CONCLUSIONS: Increased activation of the thalamus, decreased cortical activation, and lower deactivation of the precuneus suggest that under sleep deprivation, accurate performance during VA and WM tasks requires larger recruitment of resources in brain regions involved with alertness, possibly to compensate for impaired attentional processing. Together, the observed correlations of differential (SD-NS) BOLD responses in the ACG with self-report measures of sleepiness or accuracy during cognitive tasks indicate that the ability to engage the ACG is disrupted in sleep deprivation, which in turn may account for the impaired performance on these tasks as they become more complex. This also suggests that subjective descriptors (self report measures of sleepiness) and cognitive performance (accuracy) can predict abnormal brain activation in the ACG after 24 hours of sleep deprivation. The key role of the thalamus and the precuneus in alertness is highlighted by their lower interconnectivity after SD.

REFERENCES: 1-Chee et. al. Neuroimage **31**: 419-428, 2006; 2-Tomasi et. al. Hum Brain Mapp **27**: 694-705, 2006.

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Fig 1: (Right) Performance accuracy on working memory (WM) and visual attention tasks (VA) for the sleep deprive (SD, red) and normal sleep (NS, green) conditions, and (Left) the corresponding BOLD-fMRI activation/deactivation. Sixteen healthy men.

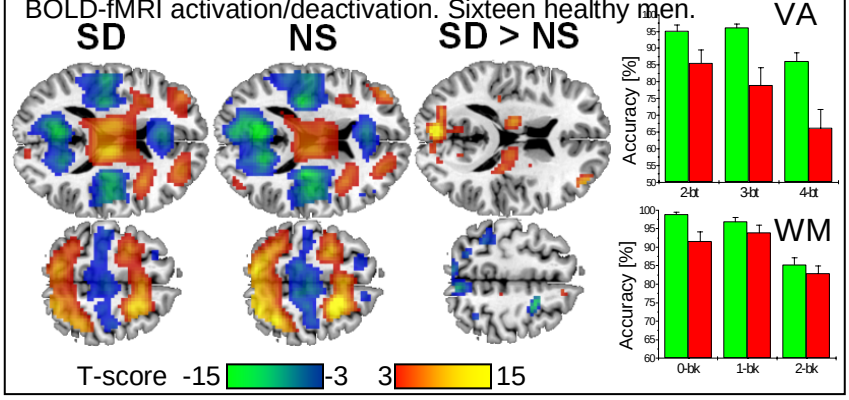

Fig 2: Brain regions showing significant correlations between signal changes and changes in sleepiness (left) during the more demanding tasks (WM: 2-back; VA: 4-balls) or performance accuracy (all tree difficulty levels per task are included, right, WM: blue; VA: red).