Brain Activation Patterns and Individual Differences in Working Memory Impairment During Sleep Deprivation

Comment on Mu Q; Mishory A; Johnson KA et al.   Decreased Brain Activation During a Working Memory Task at Rested Baseline is Associated with Vulnerability to Sleep Deprivation.   SLEEP 2005;28(4):433-46

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STABLE INDIVIDUAL DIFFERENCES IN VULNERABILITY TO COGNITIVE PERFORMANCE IMPAIRMENT DURING SLEEP DEPRIVATION HAVE BEEN DISCUSSED SPORADICALLY since the 1960s,[1–5] and have gained particular attention since the turn of the century.[6–8] Last year, it was demonstrated that such differential vulnerability to sleep deprivation is both systematic and robust[9]—that is, it constitutes a trait. This implied that individual performance responses to sleep deprivation should be predictable, which provided a foundation for a search for baseline predictors (phenotypic markers) of differential vulnerability. Across a number of studies, a large variety of candidate predictors has been considered,[6,9–14] but to date no persuasive evidence for phenotypic markers has been found.[15]

In the present issue, Mu and colleagues continued the search for baseline predictors of vulnerability to cognitive impairment from sleep loss,[16] focusing on brain activation patterns measured with functional magnetic resonance imaging (fMRI) of the blood oxygenation level-dependent (BOLD) signal during cognitive task performance. The BOLD signal is a relative measure believed to reflect changes in synaptic activity.[17,18] It allows the investigation of adjustments in purported functional neural networks in response to experimental manipulations. Mu and colleagues employed BOLD fMRI in a study of the effects of transcranial magnetic stimulation on sleep-deprived cognitive performance.[19] As part of this study, 33 healthy male subjects performed the Sternberg working memory task[20] (SWMT) and a control task in the fMRI scanner at rested baseline and following 30 hours of sleep deprivation. From this sample, 10 "sleep deprivation-resilient" individuals were identified whose SWMT performance was improved after sleep deprivation relative to baseline. Subsequently, 10 age- and education-matched "sleep deprivation-vulnerable" individuals were selected whose SWMT performance was deteriorated after sleep deprivation relative to baseline. Both groups showed decreases in their BOLD activation patterns (for SWMT performance versus control task performance) following sleep deprivation relative to baseline.

However, the sleep deprivation-vulnerable group displayed significantly less global brain activation than the sleep deprivation-resilient group in the sleep-deprived state as well as in the baseline state.[16] It thus appeared that brain activation patterns during the SWMT differed between the sleep deprivation-vulnerable and -resilient individuals, suggesting that baseline brain activation may be a predictor of differential vulnerability to verbal working memory impairment due to sleep loss.

For sleep deprivation studies involving working memory tasks, it is a challenge to dissociate the effects of sleep deprivation from the effects of task learning (i.e., practice effect) and aptitude. Recognizing the potential confound of learning, Mu and colleagues required subjects to practice the SWMT 10 times.[16] Nevertheless, it is likely that residual learning occurred—at least among the 10 "resilient" subjects whose performance improved from baseline to sleep deprivation—and consequently there may have been individual differences in residual learning as well. Table 1 would suggest that there were no significant baseline differences in SWMT performance (reaction times and error rates), although the values in Table 1 do not correspond to those given in the section "Clarification of possible confounds across scan sessions within subjects."[16] However, working memory tasks typically exhibit pronounced individual differences in aptitude,[21,22] which in the present study may have been exposed during sleep deprivation (i.e., as an interaction between aptitude and the influence of sleep loss). Therefore, with regard to the observed differences in brain activation patterns between the vulnerable and resilient groups at baseline and following sleep deprivation, it is not clear what the contributions were of potential individual differences in the learning curve, intrinsic differences in aptitude, and differential vulnerability to sleep deprivation *per se*. This ambiguity may be avoided by studying brain activation responses to performance on the psychomotor vigilance task,[23] because this task[24] exhibits neither a practice effect[25] nor significant aptitude differences.[26]

On the other hand, the effects of individual differences in aptitude and differential vulnerability to sleep deprivation may converge in the concept of "cognitive reserve" ("brain reserve").[27] The cognitive reserve hypothesis posits that the neural effect of an experimental intervention (such as sleep deprivation) is mediated through reserve, such that individuals with more reserve are able to withstand a greater insult before performance is affected. To the extent that aptitude for a working memory task may be a reflection of cognitive reserve,[28] the effect of sleep deprivation could fundamentally interact with aptitude through individual differences in cognitive reserve. This would result in individual

differences in the depletion of cognitive reserve and therefore in the magnitude of working memory performance impairment during sleep deprivation. A study by Drummond and colleagues using fMRI to investigate brain activation during performance on a logical reasoning task after 35 hours of sleep deprivation[29] suggested that the utilization of "cognitive reserve" entails not just consumption of a given subject-specific pool of brain resources, but also subject-specific compensatory recruitment of additional brain regions that may not be engaged during baseline task performance. In that study, though, sleep deprivation resulted in increased brain activation as measured by the BOLD signal,[29] whereas the study of Mu and colleagues documented only decreased brain activation and no evidence of compensatory recruitment.[16] In addition, an event-related fMRI study of individual differences in the effects of 48 hours of sleep deprivation on non-verbal recognition memory performance by Bell-McGinty and colleagues[30] showed activation increases in some brain regions and decreases in other brain regions. These different studies[16,29,30] varied notably as to which specific brain regions showed responsivity to sleep deprivation.

Such divergent findings raise difficult questions about how increases and decreases in BOLD brain activation patterns in response to sleep deprivation should be properly analyzed and interpreted. Experiments have revealed the importance of the properties of the cognitive performance tasks at hand[31] (and perhaps control tasks as well). On a neurobehavioral level, Van Dongen and colleagues found that among 13 different performance tasks, trait individual differences in performance impairment due to sleep loss clustered on three orthogonal dimensions: cognitive processing tasks (all of which involved working memory); the psychomotor vigilance task; and self-evaluation tasks.[9] A dissociation of individual differences in working memory performance versus self-evaluation responses was again seen in the present study of Mu et al.[16] Further neuroimaging studies focusing on multiple categories of cognitive performance could serve to disentangle the task-specific effects and the solely sleep deprivation-specific aspects, if any, of individual differences in performance impairment from sleep loss. While such studies may or may not yield any reliable baseline predictors, investigation of the brain with sophisticated paradigms and state-of-the-art neuroimaging techniques holds promise for elucidating the complex mechanisms underlying differential vulnerability to sleep deprivation.

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