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White Matter Microstructural Properties are Related to Inter-Individual Differences in Cognitive Instability after Sleep Deprivation

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Abstract—Several diseases are characterized by cognitive instability, which is amplified in the conditions of sleep deprivation (SD). Cognitive instability in SD can be examined by the number of lapses on the psychomotor vigilance test (PVT), which is considered to be a gold standard in the field. However, the number of PVT lapses widely range according to inter-individual differences, from apparent cognitive resistance to severe cognitive impairment. In this study, tract-based spatial statistical analyses with multiple diffusion tensor imaging-derived characteristics (i.e., fractional anisotropy (FA), mean diffusivity, radial diffusivity, and axial diffusivity) were employed to investigate the relationships between the number of PVT lapses and the diffusion characteristics. A hierarchical linear regression model was then used to assess the contributions of tract-specific FA values in predicting PVT lapses. Finally, dichotomized analysis was used to investigate white matter (WM) differences between resilient and vulnerable groups. Our results showed significant negative correlations between numbers of PVT lapses and FA in multiple WM tracts, with the FA variations in the superior longitudinal fasciculus and splenium of the corpus callosum accounting for nearly 37.5% of individual variability in PVT lapses. In addition, dichotomized analyses indicated that the resilient participants exhibited significantly higher FA values compared with the vulnerable participants. Together, these findings suggest that cognitive instability after SD was closely associated with individual differences in WM integrity.

Key words: sleep deprivation, cognitive instability, individual difference, diffusion tensor imaging, psychomotor vigilance test.

INTRODUCTION

The ability to maintain a moderate level of performance on tasks over time is important for carrying out daily activities. However, task performance has been found to be characterized by an increased number of lapses (delayed responses) in individuals with cognitive instability. This instability is commonly observed in several groups with conditions including sleep deprivation (SD), aging, attention deficit hyperactivity disorder, schizophrenia and dementia (MacDonald et al., 2009). Understanding the neural mechanisms underlying cognitive instability is important for both healthy and clinical populations because instability can confer unique predictive information about cognitive function that is independent of mean-level performance (Kelly et al., 2008). Cognitive instability has been linked to structural brain characteristics, particularly the white matter (WM) integrity, in a growing number of studies. The integrity of the WM in both adults and children has been found to be related to performance variability by several diffusion tensor imaging (DTI) studies (Fjell et al., 2011; Peters et al., 2014). These studies suggested that lower fiber integrity might decrease the efficiency of neural signal transmission, disrupt the conduction of action potentials, and increase the instability of task performance (Fjell et al., 2011; Tamnes et al., 2012).

The effect of SD on cognition is characterized by destabilized performance rather than eliminated capability to perform (Doran et al., 2001). The magnitude of cognitive instability is amplified in conditions of SD in which numbers and durations of lapses are increased

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Abbreviations: DTI, diffusion tensor imaging; FA, fractional anisotropy; PVT, psychomotor vigilance test; RTs, reaction times; RW, rested wakefulness; SD, sleep deprivation; WM, white matter.

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compared with well-rested conditions (Basner et al., 2013). Cognitive instability in SD can be assayed by one leading paradigm, i.e., the psychomotor vigilance task (PVT), which is a test of reaction times (RTs) to a cue that occurs at random inter-stimulus intervals (Lim and Dinges, 2008). Lapses on the PVT, defined as RTs exceeding 500 ms or slower than twice the mean RT acquired during rested wakefulness (RW), have been considered as the gold standard of cognitive instability (Yeo et al., 2015). During such lapses, some serious catastrophes and accidents have been known to occur (Chee and Tan, 2010). Moreover, PVT lapses induced by SD have been found to exhibit substantial differences between individuals (range from apparent cognitive resistance to severe cognitive impairment) (Kuna et al., 2012; Van Dongen, 2012). Furthermore, some resistant individuals have been found to sustain a superior level of attention with no lapses over 24 h of SD, while some vulnerable individuals exhibited evident PVT lapses in the early stage during deprivation, and escalated to very high rates as deprivation continued (Basner et al., 2013). Importantly, the inter-individual differences in PVT lapses after SD had been shown to be trait-like, which were stable over repeated exposures to SD, regardless of recent sleep history (Van Dongen et al., 2004; Rupp et al., 2012).

In PVT lapses, neural correlates and other potential biomarkers underlying the differential vulnerability to SD are currently being examined, but remains unclear (Van Dongen, 2012). Moreover, PVT lapses, according to current neurobiological evidence, emerged when the efficiency of a neural signal transmission became compromised across multiple brain regions (Lim and Dinges, 2008). Efficient communication in the human brain relies on the integrity of WM tracts (Roberts et al., 2013). Furthermore, WM microstructure has been found to be systematically linked to individual differences in task performance in a rising number of DTI studies, including those involving motor skills (Tomassini et al., 2011), memory (Fuentemilla et al., 2009) and attention (Ge et al., 2013). Specially, individual differences in decline of PVT performance speed during SD were found to be closely associated with the microstructural properties of frontoparietal axonal pathways in a recent study by Cui et al. (2015). This raises the question of whether the inter-individual differences in PVT lapses could be influenced by the differences in WM structures. The present study addressed this question using both DTI and well-established PVT. We hypothesized that: (1) the WM fractional anisotropy (FA) would be negatively correlated with the number of lapses; (2) some most representative WM fiber tracts in predicting the number of lapses could be identified using a hierarchical multiple regression model (Golestani et al., 2014); (3) resistant group would show higher WM FA than the vulnerable group.

EXPERIMENTAL PROCEDURES

Subjects

All research procedures were conducted in accordance with the Declaration of Helsinki and were approved by the People's Hospital of Zhengzhou University Subcommittee on Human Studies. Forty participants were recruited from a group of college students. The recruitment criteria and study procedure were similar to those in our previous study (Xu et al., 2015; Zhu et al., 2016). All participants underwent a psychiatric interview and medical examination and were screened to ensure that they met the inclusion and exclusion criteria. The inclusion criteria were: (1) 18–35 years of age, (2) right-handed and (3) nonsmoker. The exclusion criteria were: (1) a history of alcohol or drug abuse, (2) a present or past history of any psychiatric or neurologic disorders according to the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorder-IV, (3) a history of sleep disorders according to International Classification of Sleep Disorders version 2 (Medicine, 2005), (4) an extreme morning or extreme evening type as assessed according to a questionnaire (Roenneberg et al., 2003), and (5) work that required shift hours. All participants were required to maintain a regular sleep schedule and to refrain from consuming alcohol, caffeine, and chocolate, and from napping for 1 week. Each person was given a wrist Actiwatch (Actiwatch, Philips Respironics, Mini Mitter) to monitor their sleep pattern. The participants slept for 7.3 ± 1.5 h per night (range 6–9 h per night). Participants with poor sleep habits were not invited to participate in subsequent sessions. All participants provided written informed consent after the experimental procedures were fully explained.

Four of the 40 participants ceased study participation after the total SD session. Thus, 36 individuals successfully completed this study. All were healthy graduates (19 males; mean age 21.9 ± 1.6 years old; range, 19–26 years old) and had declared that they had not consumed any medications, alcohol, stimulants or caffeine for at least 24 h prior to scanning.

Study procedure

The order of the RW session and SD session was randomized in a cross-over fashion, with an approximately 1-week interval to minimize possible residual effects of SD on cognition. Participants were tested in pairs (two participants scanned after one another, with the scanning time kept constant) to encourage active participation and engagement. During the RW condition, participants reached the laboratory at 8:00 AM. Compliance to a regular sleep schedule was verified by checking the participant's sleep diary and wrist Actiwatch. After participants completed self-reports for behavioral measurements and 10 min of the PVT, they were scanned. In the SD session, two technicians remained with the sleep-deprived volunteers throughout the night to ensure participants maintained continuous wakefulness. Every hour from 8:00 PM to 6:00 AM, the participants completed 10 min of the PVT. During the remaining time, they were allowed to engage in non-strenuous activities such as reading and watching videos in a standard light environment (340 lux). Environmental temperature was maintained at approximately 23 °C. No food was given after midnight.