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Resting spontaneous activity in the default mode network predicts performance decline during prolonged attention workload

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A B S T R A C T

After continuous and prolonged cognitive workload, people typically show reduced behavioral performance and increased feelings of fatigue, which are known as “time-on-task (TOT) effects”. Although TOT effects are pervasive in modern life, their underlying neural mechanisms remain elusive. In this study, we induced TOT effects by administering a 20-min continuous psychomotor vigilance test (PVT) to a group of 16 healthy adults and used resting-state blood oxygen level-dependent (BOLD) functional magnetic resonance imaging (fMRI) to examine spontaneous brain activity changes associated with fatigue and performance. Behaviorally, subjects displayed robust TOT effects, as reflected by increasingly slower reaction times as the test progressed and higher self-reported mental fatigue ratings after the 20-min PVT. Compared to pre-test measurements, subjects exhibited reduced amplitudes of low-frequency fluctuation (ALFF) in the default mode network (DMN) and increased ALFF in the thalamus after the test. Subjects also exhibited reduced anti-correlations between the posterior cingulate cortex (PCC) and right middle prefrontal cortex after the test. Moreover, pre-test resting ALFF in the PCC and medial prefrontal cortex (MePFC) predicted subjects' subsequent performance decline; individuals with higher ALFF in these regions exhibited more stable reaction times throughout the 20-min PVT. These results support the important role of both task-positive and task-negative networks in mediating TOT effects and suggest that spontaneous activity measured by resting-state BOLD fMRI may be a marker of mental fatigue.

Introduction

Maintaining a steady level of attention and performance is an important and essential requirement for many daily jobs. However, people typically display slower response times, more errors (of omission and commission), and increased feeling of fatigue while engaging in a task over prolonged periods of time, which is known as “vigilance decrement” or “time-on-task (TOT) effects” (Langner and Eickhoff, 2013; Mackworth, 1948, 1968; Pattyn et al., 2008; See et al., 1995).

Fatigue due to prolonged workload and/or sleep loss is pervasive in contemporary society and can lead to serious consequences, such as accidents while driving or administering medical care (Arnedt et al., 2005; Dinges, 1995; Dubal and Jouvent, 2004). However, not all individuals show the same extent of vulnerability to fatigue and there are large inter-individual differences in responses to sleep loss and cognitive workload (Lim et al., 2010; Parasuraman et al., 2009). Individual differences in TOT effects have been associated with dopaminergic polymorphisms, which suggested that increased availability of dopamine may promote activity in striatal and prefrontal regions associated with attention (Lim et al., 2012a).

Previous studies have used multiple neuroimaging techniques to examine the neural correlates of TOT effects, including positron emission tomography (PET), functional magnetic resonance imaging (fMRI), and electroencephalography (EEG). Paus et al. (1997) examined time-related brain function changes during continuous performance on a 60-min auditory vigilance task and found decreased regional cerebral blood flow (CBF, measured using PET) in the thalamus, frontal, parietal, and temporal cortices in the right hemisphere as a function of TOT. Coull et al. (1998) also used PET and measured CBF changes in frontal and parietal cortices during non-selective and selective attention tasks. They observed decreases in performance as TOT increased during the non-

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selective attention task but not during the selective attention task. Furthermore, performance decrement during the non-selective task was accompanied by reduced CBF in the right fronto-parietal network. Lim et al. (2010) used arterial spin labeling (ASL) perfusion fMRI and measured CBF changes during continuous performance of a 20-min psychomotor vigilance test (PVT) and observed reduced CBF in the frontal, cingulate, and parietal regions after the task. CBF changes from pre-test to post-test in the fronto-parietal network correlated with performance decline. Collectively, these studies consistently illustrate the important role of the fronto-parietal attention network in TOT effects.

Recently, fMRI has been increasingly used to assess intrinsic spontaneous brain activity during task-independent resting states and has consistently revealed various resting-state brain networks, including the default mode network (DMN) and the fronto-parietal attention network (FAN) (e.g., Damoiseaux et al., 2006; Zhu et al., 2013). The DMN is a task-negative network consisting of the posterior cingulate cortex/precuneus (PCC/PCu), medial prefrontal cortex (MePFC), and the lateral parietal cortex (Fox et al., 2005; Zhang and Raichle, 2010; Zhu et al., 2013) and is thought to be involved in intrinsic and stimulus-independent thoughts (Mason et al., 2007). Brain activity in the DMN is usually higher at rest and lower during performing goal-directed cognitive tasks. In contrast, the FAN is a task-positive network and activity in this network is usually higher during performing cognitive tasks and lower when in the resting state. Significant anti-correlations between spontaneous activity in the DMN and FAN have been consistently reported in normal healthy subjects (Fox et al., 2005; Gao and Lin, 2012; Kelly et al., 2008).

A few recent studies have used resting-state fMRI and examined changes in spontaneous brain activity patterns associated with TOT effects. Breckel et al. (2013) used resting-state fMRI and compared the topological and spatial properties of brain networks before and after an attentional task and found increased connectivity strength and clustering, decreased connection distance, and less efficiency in brain networks immediately after the task. In addition, individuals who were more resilient to TOT effects showed faster recovery of brain networks after prolonged attentional effort. Giessing et al. (2013) examined the effects of nicotine during a prolonged go/no-go attention task, and found robust TOT effects that were associated with decreased connection distance and increased clustering of brain networks. However, none of these studies have examined the influences of TOT effects on DMN function and it remains unknown whether TOT impairs spontaneous resting activity in the DMN and the balance between the task-positive and task-negative networks.

In this study, we used resting-state blood oxygen level dependent (BOLD) fMRI to examine intrinsic and spontaneous neural activity and connectivity changes in resting brain networks, particularly in the DMN, after prolonged attention workload. Consistent with previous studies (Lim et al., 2010; Sun et al., 2014a, 2014b), we used a continuous 20-min PVT to induce TOT effects. The PVT is a simple, reliable and highly sensitive reaction time task and free of aptitude and leaning effects (Dinges et al., 1997; Lim and Dinges, 2008).

The amplitude of low-frequency fluctuation (ALFF) was used as the metric for assessing spontaneous neural activity changes in this study. The ALFF measures the power or intensity of low frequency (<0.08 Hz) oscillations of the BOLD time courses, which is considered to be physiologically meaningful and reflective of regional spontaneous neural activity (Yang et al., 2007; Zang et al., 2007; Zou et al., 2008; Duff et al., 2008; Jiang et al., 2011; Xu et al., 2014). Previous studies have shown that ALFF has high test-retest reliability and is closed related to CBF (Zuo et al., 2010; Li et al., 2012a, 2012b), suggesting that ALFF may be a useful index to examine state-dependent resting brain function changes associated with TOT effects. We hypothesized that TOT would alter ALFF in the DMN. In addition, we used seed-based functional connectivity (FC) analysis to examine DMN connectivity changes after prolonged attention workload. Functional connectivity reflects the temporal correlation of low-frequency fluctuation between distinct brain regions and provides another index of functional integration of resting brain function. We hypothesized that TOT would impair the balance between the DMN and the FAN. Finally, although the aim of this study is to examine resting brain function changes after TOT effects, we also performed a conventional event-related fMRI analysis to examine task-related activation changes during the 20-min PVT.

Materials and methods

Participants

Sixteen healthy undergraduate and graduate students (11 females, 21.3 ± 1.3 years) participated in this study. Two subjects were excluded due to excessive head motion in the scanner. All participants were righted-handed, normal vision (with or without correction), reported no history of affective disorders, neurological diseases and no regular use of medication. Participants who qualified for enrollment were instructed to obtain 7–9 h sleep per night during the two nights prior to the experiment and not to consume caffeine, alcohol, or any other psychoactive substances during the 24 h before the experiment. In addition, subjects completed the Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989) to assess their recent sleep quality and history. Subjects were compensated for their effort and time after participating in the study. All participants provided written informed consent according to the guidelines of the Department of Psychology at Sun Yat-sen University and the School of Psychology at Southwest University in China.

Psychomotor vigilance test (PVT)

A Matlab and Psychtoolbox-based version of the PVT was used in the study. The PVT is a simple reaction time test with varying and random inter-stimulus intervals ranging from 2 to 10 s (Dinges et al., 1997; Lim and Dinges, 2008). Before entering the scanner, subjects were given a brief 1-min opportunity to practice the PVT. During the PVT, participants were instructed to maintain their attention on a red-outlined rectangle in the center of a black screen. A millisecond counter, which acts as the target, appears within the red-outlined rectangle in yellow font. When subjects respond to the target, the millisecond counter freezes and the rectangle becomes outlined in yellow rather than red; thus, subjects are able to see their reaction time. The rectangle then returns to red and the subject must fixate until the next target (the millisecond counter) appears. Participants were instructed to respond as quickly as possible without making errors of commission ("false alarms"). False alarms occur if subjects hit the button before a target is presented. When this occurs, the words "False Alarm" appear on the screen. If subjects do not respond to the target within 500 msec, it is considered an error of omission ("Lapse"). However, subjects are not given any feedback when their reaction time exceeds 500 msec. The millisecond counter continues counting up to 30,000 msec or the subject's response, whichever comes first. If subjects do not respond within 30,000 msec, the rectangle resets for the next target. The length of PVT was 20 min in order to elicit the TOT effects and to increase between-subject variance in performance. All participants rated their subjective fatigue level on a 9-point scale before and after the PVT.

Similar to previous study (Lim et al., 2010), the following variables were extracted as a measure of overall level of PVT performance: median reaction time (RT), standard deviation of RT, and number of lapses (RT > 500 ms). To assess the TOT effects, the 20-min PVT was divided into 4-min quintiles and the median RT was obtained for each quintile. The percentage changes in median RT from the first to the last quintile (ratio = (Last Quintile − First Quintile)/First Quintile * 100%) were calculated as the index for performance declines.

Data acquisition

Functional imaging was acquired using a Siemens TRIO 3T MRI scanner in the key Laboratory of Cognition and Personality at the Southwest

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