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## Research Report

# Neural effects of prolonged mental fatigue: A magnetoencephalography study

Akira Ishii<sup>a,\*</sup>, Masaaki Tanaka<sup>a</sup>, Yoshihito Shigihara<sup>a</sup>, Etsuko Kanai<sup>b</sup>,  
Masami Funakura<sup>b</sup>, Yasuyoshi Watanabe<sup>a,c</sup>

<sup>a</sup>Department of Physiology, Osaka City University Graduate School of Medicine, 1-4-3 Asahimachi, Abeno-ku, Osaka 545-8585, Japan

<sup>b</sup>Digital & Network Technology Development Center, Panasonic Co., Ltd., 1006 Kadoma, Kadoma City, Osaka 571-8501, Japan

<sup>c</sup>RIKEN Center for Life Science Technologies, 6-7-3 Minatojima-minamimachi, Chuo-ku, Hyogo 650-0047, Japan

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## ABSTRACT

Mental fatigue, manifest as a reduced efficiency for mental work load, is prevalent in modern society. It is important to understand the neural mechanisms of mental fatigue and to develop appropriate methods for evaluating mental fatigue. In this study we quantified the effect of a long-duration mental fatigue-inducing task on neural activity. We used magnetoencephalography (MEG) to examine the time course change of neural activity over the long duration of the task trials. Nine healthy male volunteers participated in this study. They performed two mental fatigue-inducing tasks on separate days. The order of task presentation was randomized in a single-blinded, crossover fashion. Each task consisted of 25-min mental fatigue-inducing 0- or 2-back task session for three times. Subjective rating of mental fatigue sensation and electrocardiogram, and resting state MEG measurements were performed just before and after each task session. MEG data were analyzed using narrow-band adaptive spatial filtering methods. Alpha band (8–13 Hz) power in the visual cortex decreased after performing the mental fatigue-inducing tasks, and the decrease of alpha power was greater when they performed 2-back task trials. The decrease in alpha power was positively associated with the self-reported level of mental fatigue sensation and sympathetic nerve activity level. These results demonstrate that performing the prolonged mental fatigue-inducing task causes overactivation of the visual cortex, manifest as decreased alpha power in this brain region. Our results increase understanding of the neural mechanisms of mental fatigue and can be used to develop new quantitative methods to assess mental fatigue.

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## 1. Introduction

Fatigue is a common symptom in modern society. More than half of the general adult population in Japan complain of fatigue (Watanabe, 2007). Mental fatigue is defined as a

psychobiological state caused by prolonged periods of demanding cognitive activity (Boksem and Tops, 2008). Mental fatigue is manifest as a reduced efficiency of mental work load (Chaudhuri and Behan, 2004) and has become one of the most significant causes of accidents in modern society (Dinges, 1995; Shen et al.,

\*Corresponding author. Fax: +81 6 6645 3712.

E-mail address: [a.ishii@med.osaka-cu.ac.jp](mailto:a.ishii@med.osaka-cu.ac.jp) (A. Ishii).

2008). Understanding the neural mechanisms of mental fatigue is important for the future development of treatment strategies. Currently, the neural mechanisms of mental fatigue are not fully understood.

We have previously reported changes in neural activities that are caused by performing mental fatigue-inducing tasks (Shigihara et al., 2013; Tanaka et al., 2012b). We employed two types of tasks, i.e., 0-back task and 2-back task, as fatigue-inducing mental tasks, since 0- and 2-back task trials has been successfully applied to induce mental fatigue to examine the neural mechanisms of mental fatigue (Mizuno and Watanabe, 2007; Shigihara et al., 2013; Tanaka et al., 2012b). The 0-back task was used to represent a lower mental-load task, which could be performed without the use of working memory, while the 2-back task was used to represent a higher mental-load task, which required working memory (Braver et al., 1997). Mental fatigue-inducing tasks led to the suppression of spontaneous magnetoencephalography (MEG) alpha band (8–13 Hz) power in the frontal gyrus and beta band (13–25 Hz) power in the left precentral gyrus, suggesting simultaneous overactivation of the thalamo-frontal feedback loop and the enhanced inhibitory system to suppress overactivation of this loop (Shigihara et al., 2013). The thalamo-frontal feedback loop is related to complex cognitive functions such as attention, memory, and mental imagery (Burruss et al., 2000; Gevins and Schaffer, 1980; Klimesch, 1999; Tesche et al., 1995), and overactivation of this loop reflects heavy cognitive load; while the enhanced inhibitory system represents excessive self-defense mechanisms to suppress work output in order to avoid homeostatic catastrophe (Shigihara et al., 2013).

The fatigue-inducing mental tasks used in our previous studies were 30 min in duration. The mental work load experienced in daily working situations is of longer duration, and individuals must often maintain their performance in order to accomplish assigned work load. As such, the neural changes caused by fatigue-inducing mental task trials with more prolonged time duration are of great interest and may be more beneficial for the better understanding of the mental fatigue in our daily lives. The aim of our present study was therefore to clarify the neural mechanisms of mental fatigue caused by prolonged work load. Our present study consisted of three repetitions of 2-back and 0-back task sessions, each of which was 25 min in duration. Evaluation sessions were performed at baseline and immediately after each 2-back and 0-back task sessions. In the evaluation sessions, we assessed subjective rating of mental fatigue sensation using visual analogue scale (VAS). In addition, we recorded electrocardiogram (ECG) in the evaluation session and performed frequency domain analysis of the R-R wave intervals to obtain low-frequency (LF) power and high-frequency (HF) power, since it has been shown that increases in the LF/HF ratio and decreases in HF power were associated with mental fatigue (Mizuno et al., 2011; Tanaka et al., 2009).

## 2. Results

### 2.1. VAS scores

There was a main effect of time course [ $F(1.5, 11.8)=10.72$ ,  $P<0.001$ ] but no effect of task [ $F(1.0, 8.0)=0.056$ ,  $P=0.820$ ], and

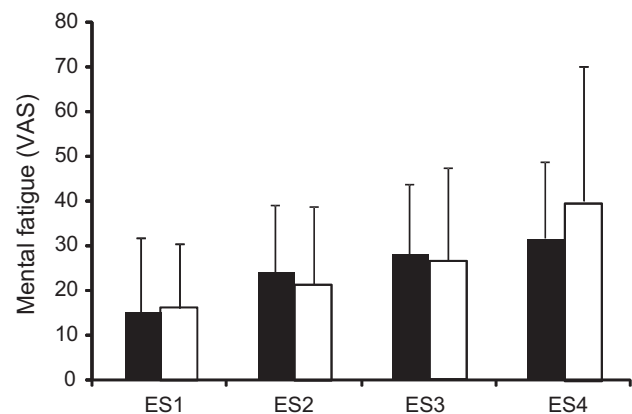
no time course  $\times$  task interaction [ $F(1.3, 10.8)=0.538$ ,  $P=0.661$ ] on self-reported mental fatigue (Fig. 1). Paired t-tests with Bonferroni correction showed an increase of mental fatigue sensation in ES3 and ES4 compared to ES1 across both conditions combined (ES3,  $P=0.013$ ; ES4,  $P=0.019$ ; Fig. 1).

### 2.2. Frequency analyses of ECG

There was a main effect of time course [ $F(3, 24)=5.301$ ,  $P=0.006$ ] but no effect of task [ $F(1, 8)=0.040$ ,  $P=0.846$ ], and no time course  $\times$  task interaction [ $F(3, 24)=0.484$ ,  $P=0.697$ ; Fig. 2A] on %LF. Paired t-tests with Bonferroni correction showed decrease of %LF in ES4 compared to ES3 across both conditions combined ( $P=0.025$ ; Fig. 2A). There was no main effect of time course [ $F(3, 24)=0.616$ ,  $P=0.611$ ] or task [ $F(1, 8)=0.163$ ,  $P=0.697$ ], and no time course  $\times$  task interaction [ $F(3, 24)=1.171$ ,  $P=0.341$ ] on %HF (Fig. 2B). Similarly, there was no main effect of time course [ $F(3, 24)=1.520$ ,  $P=0.235$ ] or task [ $F(1, 8)=2.834$ ,  $P=0.131$ ] and no time course  $\times$  task interaction [ $F(3, 24)=1.096$ ,  $P=0.370$ ] on LF/HF ratio (Fig. 2C).

### 2.3. Changes in oscillatory brain activities

Decrease of alpha band power in the visual cortex was observed in ES4 compared to ES1 in the 0-back task (Fig. 3A) and the 2-back task (Fig. 3B) (one-sample t-test, uncorrected  $P<0.001$ ). The contrast image (E4 compared to E1) of the 2-back task relative to the 0-back task showed decreased alpha band power in the brain area extending from Brodmann's area 18 (BA18) (Fig. 3C; paired t-test, uncorrected  $P<0.001$ ). Oscillatory power ratio at the peak voxel in Fig. 3C gradually decreased during the time course of the 2-back task trials, although there was no decrease in the oscillatory power ratio in the 0-back task (Fig. 3D). There were no significant band power changes in other frequency bands.



**Fig. 1 – Visual analogue scale (VAS) for mental fatigue of each evaluation session (ES) during the 0-back task (white columns) and 2-back task (black columns) experiments. Paired t-tests with Bonferroni corrections showed a higher mental fatigue score in ES3 ( $P=0.013$ ) and ES4 ( $P=0.019$ ) compared to ES1 across both conditions combined. Data are presented as mean and SD.**

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