

Effects of Mental Fatigue on Brain Activity and Cognitive Performance: A Magnetoencephalography Study

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Abstract

Background: Mental fatigue is prevalent in modern society. Since mental fatigue causes cognitive impairment and this has been one of the most significant causes of accidents, it is important to understand the neural mechanisms of mental fatigue related to cognitive performance and to develop appropriate methods for evaluating and overcoming mental fatigue. In this study, we quantified the effect of mental fatigue on neural activity and cognitive performance and evaluated the relationship between the change of brain activity and cognitive impairment induced by mental fatigue using magnetoencephalography.

Methods: Thirteen healthy male volunteers participated in this study. They performed mental fatigue-inducing task trials for 30 min. resting state magnetoencephalography measurements and cognitive tasks were performed before and after the fatigue-inducing task. Magnetoencephalography data were analyzed using narrow-band adaptive spatial filtering methods.

Results: Alpha-frequency band (8-13 Hz) power in the visual cortex decreased after performing the mental fatigue-inducing task. The decreased level in the alpha-frequency band power was positively associated with the impaired cognitive task performance.

Conclusions: These results demonstrate that performing the mental fatigue-inducing task causes over-activation of the visual cortex, manifested as the decreased alpha-frequency band power in this brain region, and the over-activation was associated with the cognitive impairment. Our results increase understanding of the neural mechanisms of mental fatigue and these may be utilized to develop new quantitative methods to assess mental fatigue.

Keywords: Alpha frequency; Cognitive performance; Magnetoencephalography (MEG); Mental fatigue; Visual cortex

Introduction

Fatigue is defined as a condition or phenomenon of declined ability and efficiency of mental and/or physical activities caused by excessive mental and/or physical activities, or illness; fatigue is often accompanied by peculiar sense of discomfort, desire to rest, and reduced motivation, referred to as a fatigue sensation (translated from Japanese into English by M.T.) [1]. Today, more than half of the general adult population in Japan complains of fatigue [2]. Mental fatigue manifests as a reduced efficiency of cognitive workload [3] and has become one of the most significant causes of accidents in modern society [4,5]. Therefore, it is important to clarify the neural mechanisms of mental fatigue, in particular those mechanisms related to the impaired cognitive performance, for the future development of overcoming strategies of mental fatigue.

Changes in the neural activities caused by performing mental fatigue-inducing task trials have been previously investigated [6,7]. Just before and after fatigue-inducing task trials, the neural activities in an eyes-closed resting state were evaluated by using magnetoencephalography (MEG); a mental fatigue-inducing task led

to the suppression of the spontaneous MEG alpha-frequency band (8-13 Hz) power, i.e., event-related desynchronization (ERD), in the cerebral cortex, suggesting an over-activation of the brain [6,7]. Although these studies clarified the neural mechanisms of mental fatigue to some extent, the mechanisms related to the impaired cognitive performance remained to be clarified.

The aims of our present study were to clarify the effect of mental fatigue on brain activity and cognitive performance and to evaluate the relationship between the change of brain activity and cognitive impairment induced by mental fatigue using MEG. The MEG data were analyzed using narrow-band adaptive spatial filtering methods and the alpha-frequency band ERD under the eye-closed condition was evaluated. In order to assess the cognitive performance, cognitive tasks were performed before and after a fatigue-inducing mental task session.

Material and Methods

Participants

Thirteen healthy male volunteers (age, 21.2 ± 0.8 years [mean \pm SD]) were enrolled. According to the Edinburgh handedness inventory

[8], all participants were right-handed. Current smokers, participants with a history of mental or brain disorders, and those taking chronic medications that affect the central nervous system were excluded. All participants provided written informed consent before participation. This study was approved by the Ethics Committee of Osaka City University and was conducted in accordance with the principles of the Declaration of Helsinki. Minors or children were not involved as the participants of our study.

Experimental design

The experiment consisted of one fatigue-inducing mental task session, two MEG sessions, and two cognitive task sessions (Figure 1). During the fatigue-inducing mental task session (3rd session), the participants performed 2-back test trials for 30 min. During the MEG sessions (1st and 4th sessions), MEG recordings were performed with the participant's eyes closed for 3 min. Finally, during the cognitive task sessions (2nd and 5th sessions), they performed traffic light task trials for 6 min. Just before and after the fatigue-inducing mental task session, they were asked to subjectively rate the mental fatigue level using a visual analogue scale (VAS) ranging from 0 (minimum) to 100 (maximum) [9].

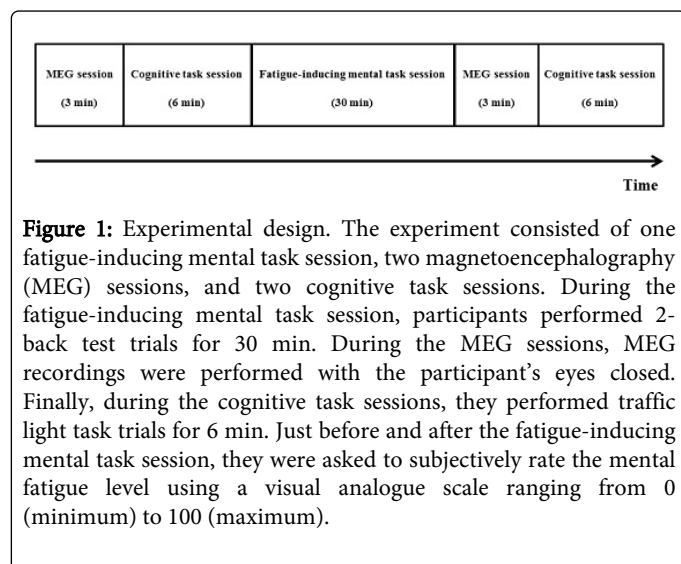


Figure 1: Experimental design. The experiment consisted of one fatigue-inducing mental task session, two magnetoencephalography (MEG) sessions, and two cognitive task sessions. During the fatigue-inducing mental task session, participants performed 2-back test trials for 30 min. During the MEG sessions, MEG recordings were performed with the participant's eyes closed. Finally, during the cognitive task sessions, they performed traffic light task trials for 6 min. Just before and after the fatigue-inducing mental task session, they were asked to subjectively rate the mental fatigue level using a visual analogue scale ranging from 0 (minimum) to 100 (maximum).

During the fatigue-inducing mental task session, the participants performed 2-back test trials for 30 minutes [10]. The reliability and validity of this task for causing mental fatigue have been confirmed [6,11-13]. One of four types of white letters was continually presented on a black background in the display of a laptop computer every 3 seconds. The letter size was 30 mm × 30 mm. During the trials, the participant had to judge whether the target letter presented at the center of the screen was the same as the letter that had appeared two presentations earlier. If it was, they were to press the right button with their right middle finger, and if it was not, they were to press the left button. They were instructed to perform the task trials as quickly and as correctly as possible. The result of each 2-back test trial, that is, a correct response or error, was continually presented on the display of the computer.

During the cognitive task session, the participants performed a traffic light task for 6 minutes [12]. The reliability and validity of this task to evaluate mental fatigue have been confirmed [12]. As described in detail previously [12], this task presentation consisted of traffic

lights (a Japanese letter, which means blue or red, was placed on either a blue or red light), traffic signs for walkers (right or left), and turns (right or left) shown on a black background in the display of a laptop computer. They performed the task trials for 6 min. In this task, they had to judge whether the target letter presented at the center of a traffic light was blue or red. If the letter meant blue in Japanese, regardless of the color of the traffic light or traffic signs for walkers or turns, they were to press the right button with their right middle finger, otherwise, they were to press the left button with their right index finger. Each trial was presented 100 ms after pressing either of the buttons. During the task period, blue or red trial, traffic signs for walkers (right or left), and turns (right or left) were presented randomly, and the occurrence of each color and type of sign was equal. The Stroop trials (mismatching the color of the traffic light with the letter) and the non-Stroop trials (matching the color of the traffic light with the letter) were presented with equal frequency. They were instructed to perform the task trials as quickly and as correctly as possible. The results of each cognitive task trial, that is, a correct response or error, was continuously presented on the display of the computer.

This study was conducted in a quiet, temperature-, and humidity-controlled, magnetically shielded room at Osaka City University Hospital. On the day before the study, all the participants refrained from intense mental and physical activities and caffeinated beverages, consumed a normal diet, and maintained normal sleeping hours.

MEG recordings

MEG recordings were performed using a 160-channel whole-head type MEG system (MEG vision; Yokogawa Electric Corporation, Tokyo, Japan) with a magnetic field resolution of 4 fT/Hz^{1/2} in the white-noise region. The sensor and reference coils were gradiometers 15.5 mm in diameter and 50 mm at baseline, and each pair of sensor coils was separated at a distance of 23 mm. The sampling rate was 1000 Hz with a 1 Hz high-pass filter and a 500 Hz low-pass filter.

MEG data analyses

As described in detail previously [14-18], MEG signal data were analyzed offline after analogue-to-digital conversion. Magnetic noise originating from outside the shield room was eliminated by subtracting the data obtained from reference coils using a software program (MEG 160; Yokogawa Electric Corporation), followed by artifact rejection using careful visual inspection. The MEG data were split into segments of 1000 ms in length using a software-trigger. The data were band-pass filtered at 8-13 Hz by a fast Fourier transform using Frequency Trend (Yokogawa Electric Corporation) to obtain alpha-frequency band signals, using the software Brain Rhythmic Analysis for MEG (BRAM; Yokogawa Electric Corporation) [16]. Localization and intensity of the time-frequency power of cortical activities were estimated using BRAM software, which used narrow-band adaptive spatial filtering methods as an algorithm [19]. The oscillatory power in each voxel was assessed, and the ERD level was calculated as $10 \times \log_{10} [(oscillatory\ power\ before\ the\ fatigue-inducing\ mental\ task) / (oscillatory\ power\ after\ the\ fatigue-inducing\ mental\ task)]$. Data were then analyzed using Statistical Parametric Mapping (SPM8, Wellcome Department of Cognitive Neurology, London, UK), implemented in Matlab (Mathworks, Sherbon, MA). The MEG anatomical/spatial parameters used to warp the volumetric data were transformed into the Montreal Neurological Institute (MNI) template of T1-weighted images [20] and applied to the MEG data. The

anatomically normalized MEG data were filtered with a Gaussian kernel of 20 mm (full-width at half-maximum) in the x, y, and z-axes (voxel dimension was $5.0 \times 5.0 \times 5.0$ mm). The decreased oscillatory power, ERD, for the alpha-frequency band within the time window of 0 to 1000 ms after the fatigue-inducing mental task session was measured on a region-of-interest basis to obtain the neural activation pattern caused by mental fatigue. The resulting set of voxel values for each comparison constituted a SPM of the t statistics (SPM{t}). The SPM{t} was transformed to the units of a normal distribution (SPM{Z}). The threshold for the SPM{Z} of individual analyses was set at $P < 0.05$ (corrected for multiple comparisons). The weighted sum of the parameters estimated in the individual analyses consisted of "contrast" images, which were used for the group analyses [21]. Individual data were summarized and incorporated into a random-effects model so that inferences could be made at a population level [21]. SPM{t} and SPM{Z} for the contrast images were created as described above. Significant signal changes for each contrast were assessed by means of t statistics on a voxel-by-voxel basis [21]. The threshold for the SPM{Z} for group analyses was set at $P < 0.05$ (corrected for multiple comparisons). The extent threshold in terms of the number of voxels was more than 10 voxels. Anatomical localization of significant voxels within each cluster was done using Talairach Demon software [22].

Magnetic resonance imaging overlay

Anatomic MRI was performed using a Philips Achieva 3.0TX (Royal Philips Electronics, Eindhoven, The Netherlands) for all the participants to permit registration of magnetic source locations with their respective anatomic locations. Before MRI scanning, five adhesive markers (Medtronic Surgical Navigation Technologies Inc., Broomfield, CO) were attached to the skin of each participant's head (the first and second markers were located 10 mm anterior to the left tragus and right tragus, the third at 35 mm superior to the nasion, and the fourth and fifth at 40 mm to the right and left of the third marker). MEG data were superimposed on MRI scans using information obtained from these markers and MEG localization coils.

Statistical analyses

Values are presented as mean \pm SD, unless otherwise stated. The paired t-test was used to evaluate significant differences between two conditions. Pearson's correlation analyses were conducted to evaluate the relationships between the cognitive performances and the MEG responses. All P values were two-tailed, and values less than 0.05 were considered statistically significant (Table 1). Statistical analyses were performed using IBM SPSS 20.0 (IBM, Armonk, NY).

Results

To assess alterations in cognitive performance and the subjective level of mental fatigue after the fatigue-inducing mental task session, the changes of the error rates of traffic light task trials and a VAS score of mental fatigue after the mental fatigue session were evaluated.

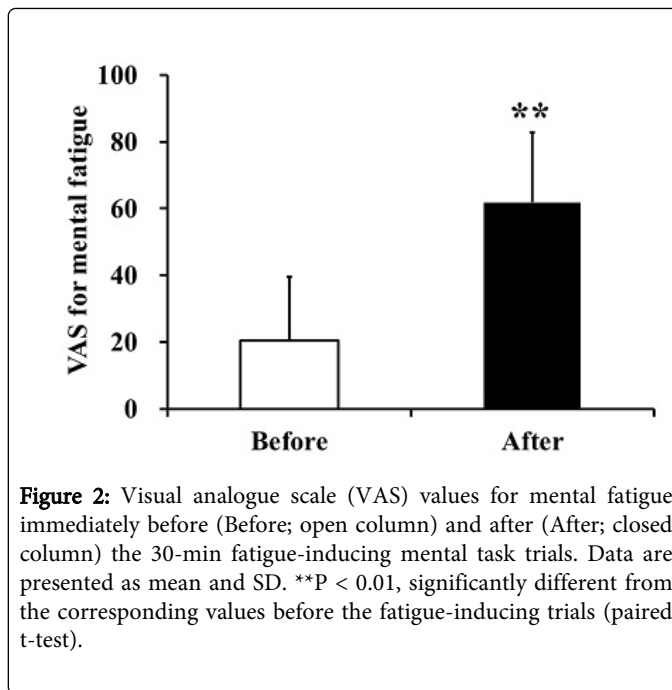


Figure 2: Visual analogue scale (VAS) values for mental fatigue immediately before (Before; open column) and after (After; closed column) the 30-min fatigue-inducing mental task trials. Data are presented as mean and SD. ** $P < 0.01$, significantly different from the corresponding values before the fatigue-inducing trials (paired t-test).

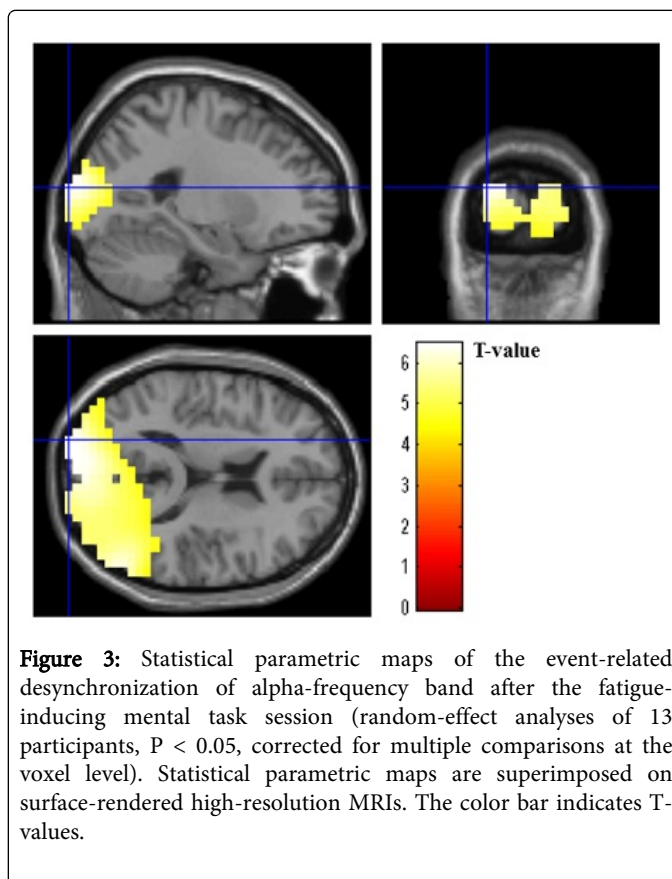


Figure 3: Statistical parametric maps of the event-related desynchronization of alpha-frequency band after the fatigue-inducing mental task session (random-effect analyses of 13 participants, $P < 0.05$, corrected for multiple comparisons at the voxel level). Statistical parametric maps are superimposed on surface-rendered high-resolution MRIs. The color bar indicates T-values.

Although the error rate of Stroop trials was not increased after the mental task trials (before $7.1 \pm 3.0\%$, after $7.8 \pm 3.8\%$, $P = 0.503$, paired t-test), the error rate of non-Stroop trials was significantly increased (before $2.6 \pm 2.4\%$, after $3.5 \pm 2.9\%$, $P = 0.005$, paired t-test). The VAS

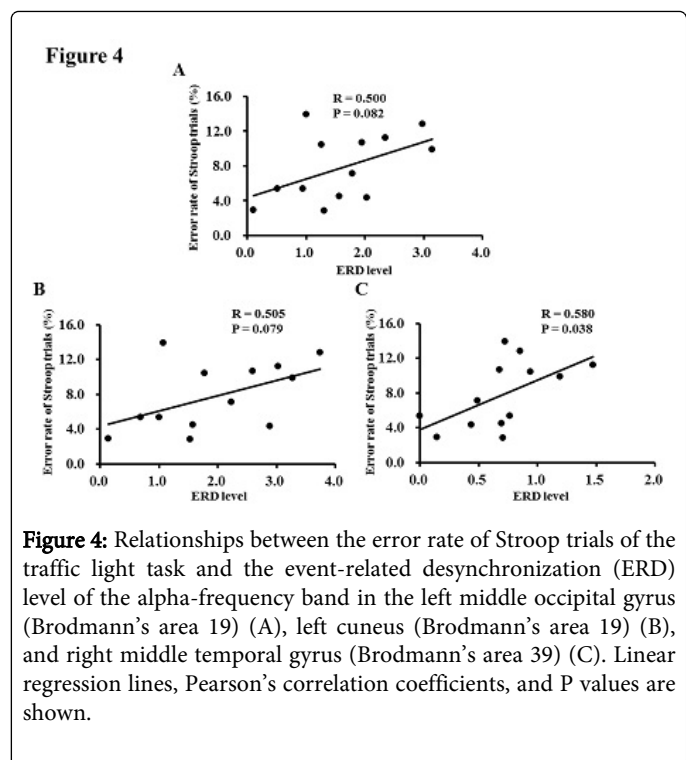
score of mental fatigue was significantly increased after the mental task trials (Figure 2).

To identify the brain regions affected by the mental fatigue, the decreased oscillatory power, as defined by the ERD for the alpha-frequency band, was evaluated after the fatigue-inducing mental task session within the time window of 0 to 1000 ms. Results are shown in (Figure 3). Among all brain regions, the bilateral visual cortices showed significant ERDs (random-effect analyses of 13 participants, $P < 0.05$, corrected for multiple comparisons at the voxel level).

Location	Brodmann's area	Coordinate (mm)			Z-value
		x	y	z	
Middle Occipital Gyrus	19	-23	-102	15	4.17
Cuneus	19	-13	-97	20	4.17
Middle Temporal Gyrus	39	57	-67	20	4.14

x, y, z: Stereotaxic coordinates of peak of activated clusters. Random-effect analyses of 13 participants ($P < 0.05$, corrected for multiple comparisons at the voxel level).

Table 1: Brain regions that showed event-related desynchronization of alpha-frequency band after the fatigue-inducing mental task session.



Finally, to evaluate the relationships between the ERD levels of alpha-frequency band in the visual cortices and the performance of cognitive task trials, correlation analyses were performed. The error rate of Stroop trials in the traffic light task tended to be positively associated with the ERD levels in the left middle occipital gyrus (Brodmann's area [BA] 19) (Figure 4A; $R = 0.500$, $P = 0.082$) and the left cuneus (BA19) (Figure 4B; $R = 0.505$, $P = 0.079$). In addition, the

error rate of Stroop trials in the traffic light task trials was positively associated with the ERD level in the right middle temporal gyrus (BA39) (Figure 4C; $R = 0.580$, $P = 0.038$). The error rate of non-Stroop trials of traffic light task was not associated with the ERD levels in these brain regions.

Discussion

In this study, we assessed the changes of the neural activity and cognitive performance caused by performing a mental fatigue-inducing task. We showed that a decrease in the alpha-frequency band powers in the visual cortices was induced by mental fatigue. This finding is consistent with the results of our previous studies reporting that a decrease in the alpha-frequency band power in the brain assessed using MEG [6,7] or electroencephalography (EEG) [18] under the eye-closed condition is related to mental fatigue. In addition, the decreased levels in the alpha-frequency band power in the visual cortices were positively associated with the impaired cognitive performance. These results demonstrate that mental fatigue causes brain over-activation that is related to reduce cognitive performance.

The relationship between mental fatigue and cognitive performance is not well understood. However, mental fatigue induces decline in executive functions such as executive attention [23], sustained attention [24-27], goal-directed attention [28], alternating attention [24], divided attention [29], response inhibition [30], planning [31,32], and novelty processing [33]. In particular, conflict-controlling selective attention (response inhibition) was highly vulnerable to mental fatigue [12]. Conflict-controlling selective attention is evaluated using the error rate of the traffic light task, and was impaired after performing fatigue-inducing mental task trials, even though the cognitive performances related to executive functions such as alternating attention, divided attention, sustained attention, and working memory were not altered [12].

Oscillatory brain rhythms originate from synchronous synaptic activities of a large number of neurons [34]. Multiple, broadly distributed, and continuously interacting dynamic neural networks are achievable through the synchronization of oscillations at a particular time-frequency band [35]. Combined fMRI and EEG studies showed a negative correlation between alpha-frequency power and BOLD signal in the cortex [36,37]. Alpha-frequency band power is associated with the information processing by deactivation of the brain regions [38]. It has been thus considered that increase in the alpha-frequency band power reflects the inhibition of cortical information processing, whereas the decreased spontaneous alpha-frequency band power, i.e., the ERD reflects the release from inhibition associated with spreading of activation processes [39]. Therefore, the suppression of alpha-frequency band power during the eye-closed resting condition shown in our study can be interpreted as the over-activation of the visual cortex in order to cope with the heavy demands of information processing in this brain region against the fatigue-inducing mental task, although this over-activation of the visual cortex caused cognitive impairment.

The present study has two limitations. First, the number of the participants was relatively small. To generalize the results of our studies, studies involving a large number of participants are essential. Second, we did not examine the neural activities during performing the 2-back test, because the muscle activity required to press the button can cause electromagnetic noise. Therefore, we focused on the neural activities during an eyes-closed resting state.

In conclusion, we identified the changes in resting-state oscillatory brain activity by performing the mental fatigue-inducing task. Mental fatigue may induce over-activation of the visual cortex, which is related to impaired cognitive performance. We believe that our findings are of great value for the better understanding the neural mechanisms of mental fatigue as well as the establishing the evaluation method to measure mental fatigue quantitatively, which would contribute to the future overcoming mental fatigue.

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