



## Research article

# Inter-hemispheric frontal alpha synchronization of event-related potentials reflects memory-induced mental fatigue



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## HIGHLIGHTS

- We assessed bilateral ERP alpha synchronization changes in memory-induced fatigue.
- Frontal ERP alpha coherences were higher than other brain regions in memorization.
- Frontal ERP alpha coherences decreased from the non-fatigued to fatigued state.
- Bilateral frontal ERP alpha coherence can be used to assess memory-induced fatigue.

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## ABSTRACT

Mental fatigue is often associated with continuous brain activities in our daily life. It can diminish efficiency and increase errors. However, the related physiological features are still not clear and under exploration. The present study investigated changes of inter-hemispheric synchronization in event-related potentials (ERPs) due to mental fatigue during sustained memory processing. Twenty-six participants performed a continuous two-back memory task for around 2.5 h. Prefrontal and frontal synchronies in the alpha frequency band (8–13 Hz) were analyzed because of their close relationships with memory functions. Coherence was used to examine bilateral synchronization changes of ERP power and phase. We compared ERP coherences in both non-fatigued and fatigued states. We also observed the variation of ERP coherences during the continuous task. High overlaps of inter-hemispheric ERP waveforms were observed at prefrontal and frontal cortex in both non-fatigued and fatigued conditions. During the whole experimental procedure, ERP alpha coherences at frontal regions (FP1–FP2 and F3–F4) were significantly higher than at central (C3–C4), parietal (P3–P4) and occipital (O1–O2) regions. Alpha synchronization in anterior electrode pairs showed significant declines with increasing mental fatigue during the memory task. Our findings about changes in frontal ERP alpha synchronization might be used as biomarkers to assess mental fatigue induced by prolonged memory demands.

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## 1. Introduction

Mental fatigue is a subjective feeling of being tired usually related with continuous demanding cognitive activities, which can be reflected in increasing unwillingness to work and deteriorated concentration on the tasks at hand [1,2]. When people continue

working in a fatigued condition, they are prone to show lower efficiency, longer reaction times and more errors [3,4]. Unlike physical or muscle fatigue, mental fatigue was reported to be associated with psychological factors and measurable physiological parameters such as neural activities and eye movements [4,5]. However, despite long-standing discussions about neural mechanisms and psychophysiological factors, the crucial underpinnings related with mental fatigue are still not clear. Therefore, we may gain a better understanding by looking for more perspectives. In the present study, we were interested in electrophysiological features of mental fatigue, experimentally induced by sustained memory tasks.

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In particular we investigated influences on inter-hemispheric ERP synchronization.

The hemispheres of the human brain are anatomically symmetric to a large extent. This important property can be reflected by high hemispheric similarities of the EEG, which is the electrical activity produced by the brain and measurable from the cortex and scalp [6]. Symmetry can also be seen in ERPs which are the average of EEG segments evoked by a series of similar stimuli [7]. Generally speaking, a cognitive task can evoke almost the same amount of brain activity in both hemispheres. However, asymmetrical involvement in different hemispheres can be observed in some cognitive tasks, which is called lateralization [8]. For example, the left hemisphere is more involved in verbal memory, and the right hemisphere plays a more important role in spatial memory [9].

An oscillatory model of Gruber et al. illustrates that ERPs are composed of various evoked waves at different frequency bands [10]. When a stimulus is presented, a significant phase resetting of oscillations is generated in all frequencies. Brain waveforms also become synchronized in absolute phase within short time periods. One way to quantitatively measure EEG synchronization is coherence, which is computed with the spectra of two EEG signals recorded simultaneously from different cortical sites. Coherence is sensitive to changes of both power and phase correlations, and is interpreted as a measure of functional relationships between brain areas [11]. Previously, EEG synchronization has already been applied to study brain connectivity during mental fatigue [12–14]. For example, Kong et al. performed a driving fatigue test and measured EEG phase synchronization through Hilbert transform [12] and found significant increases in the theta and alpha bands at frontal and parietal regions.

The frontal lobe has a close relationship with memory function, as shown in many reports, reviewed by Fletcher and Henson [15]. In previous studies, mental fatigue was demonstrated to affect the memory process in the frontal lobe. For example, Shigihara et al. [16] induced mental fatigue with sustained 0-back and 2-back memory tasks. Changes of brain activities were observed via magnetoencephalography (MEG). Results showed decreased alpha power in bilateral frontal gyrus. In a series of functional imaging experiments, fatigue effects on working memory performance were studied before and after sleep deprivation for more than 24 h. Significant decreases of brain metabolic rate and activations were observed in cortical regions such as the prefrontal and posterior parietal cortex [17–19].

As an important component of EEG waves, alpha synchronization was reported to not only support attentional, executive and contextual functions, but also be closely related with memory [20–22]. Klimesch and his colleagues conducted a series of experiments to investigate the relationship between alpha EEG synchronization and memory processing. In one of their early studies, participants performed a memory search paradigm during which EEG signals were measured. Bad performers showed more alpha desynchronization than good performers [23]. In one of their later experiments [21] about retrieval of previously learned words, good performers showed stronger desynchronization in the lower alpha band (7–10 Hz), whereas participants with relatively bad performance showed more desynchronization in the upper alpha band (8–12 Hz).

The present study specifically explored the influence of memory-induced mental fatigue on frontal alpha synchronization of inter-hemispheric ERPs. We expected that the bilateral frontal regions would have stronger connection strength as compared to symmetrical sites in other cortical regions during the memory task. Changes in frontal alpha synchronization were also expected from the non-fatigued to fatigued state.

## 2. Material and methods

### 2.1. Participants

Twenty-six participants (fifteen females) were randomly recruited from a large group of people who worked or studied in our institute; their mean age was 25.7 years ( $SD=3.1$ ), ranging between 23–34 years. All volunteers were right-handed, with normal or corrected-to-normal eyesight. They also reported to have no mental disorders or illnesses, and not consume tea or coffee on a daily basis. Participants signed informed consent before the experiment; they received compensation after the session. The present study was in compliance with relevant rules and was approved by the ethical committee of the Beijing Navy General Hospital.

### 2.2. Materials and apparatus

We sampled the EEG with a set of recording apparatus, including a 40-channel electrode cap in the 10–20 system (Quik-cap, Neuroscan Inc., USA), an EEG amplifier (Nuamps, Neuroscan Inc., USA), and Curry7 software (Neuroscan Inc., USA). Our recording electrodes included five symmetrical pairs across bilateral hemispheres, namely, FP1, FP2, F3, F4, C3, C4, P3, P4, O1 and O2. EEG was recorded at a sampling rate of 1 kHz, while impedance was below 5 k $\Omega$ . We used bilateral mastoids as reference.

The fatigue-inducing procedure generally followed one of our previous studies [24]. Participants stayed in a dimly lit and noise-attenuated room and performed a sustained 2-back memory task implemented by E-prime software (Psychology Software Tools Inc., Pittsburgh USA). They responded with a mouse in the right hand, facing a 14-inch laptop at a distance of 70 cm.

### 2.3. Experimental procedure

Participants had slept well and avoided drinking coffee or alcohol 24 h prior to the experiment. After some practice trials, the Chalder Fatigue Scale was used before (and again after) the whole procedure. This scale includes 6 dichotomous items for mental fatigue and 8 items for physical fatigue [2,25]. For the 2-back task white capital English letters from A to K in the alphabet were individually and randomly presented in the center of the black monitor. Each stimulus was shown for 250 ms, followed by a blank screen for 2500 or 2800 ms. There were five blocks in total, each including 600 trials and lasting for 25 min. The target and non-target ratio was 1–2. Participants made decisions as quickly as possible whether the present stimulus was the same as the second-to-last stimulus. The left mouse button was pressed for target stimuli and the right button for non-target stimuli. There was a 3 min interval followed by each block for a short break.

### 2.4. Data analysis

EEG was preprocessed by Curry7 software. Baseline correction and ocular artifact reduction were performed with software default settings. EEG segments with amplitudes higher than  $\pm 100 \mu\text{V}$  were excluded. After filtering EEG waves at a band-pass of 0.5 Hz to 30 Hz, we averaged EEG epochs ranging from 1 s prior to and 2 s after each stimulus (3000 points in total) in target trials for every individual. ERPs in the first experimental block were considered measured in a non-fatigued condition, and the data in the last (fifth) block were recorded in a fatigued condition. Coherence and statistical analysis were carried out with MATLAB (Mathwork Inc., USA), and SPSS 22.0 software (SPSS Inc., Chicago, IL).

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