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Modulating emotion processing using transcranial alternating current stimulation (tACS) - A sham-controlled study in healthy human participants

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Abstract— **As an emerging non-invasive neuromodulation technique, transcranial alternating current stimulation(tACS) has been reported to be used in mood regulation, cognitive modulation and brain trauma recovery by applying specific frequency currents. However, the neuromodulatory mechanisms and effects of tACS on emotion processing are unclear. In this study, a single-blind experiment with 44 healthy subjects in 1:1 randomized groups (experimental group given 10 Hz-tACS and control group given sham-stimulation) was conducted. The effects of tACS applied to the prefrontal lobe on the brain's emotional state and emotional cognitive processing in response to emotional stimulation patterns were explored by designing two experimental paradigms of an 8-minute open and closed eye resting task and an emotional face oddball task. Power spectrum and event-related potentials were extracted to explore the effect of tACS on brain rhythm modulation and attention modulation. It was found that the experimental group showed significantly enhanced alpha rhythm in the whole brain range after tACS, especially in the parieto-occipital lobe. The rate of misclassification of neutral emotions into negative emotions was significantly lower and the amplitude of P2 and P3 of event-related potentials were significantly higher when performing the emotional face task after tACS, while the control group did not have this phenomenon. These results suggest that tACS can modulate and enhance alpha rhythm activity by synchronizing alpha oscillations in the frontoparietal attention network, thereby improving subjects' negative emotion cognitive bias and enhancing their emotion processing by increasing early and late levels of emotional attention.**

I. Introduction

Emotion processing refers to the process by which an organism endures and relieves emotional distress in order to experience other emotions and allow behavior to continue [1]. One of the clinical manifestations of depression, a common mental illness, is a problem with emotion processing. Beck, an American psychologist, proposed the cognitive model that the development of depression is related to negative cognition. Numerous studies have since confirmed that the brains of depressed patients are more prone to a negative cognitive processing bias when processing information [2, 3]. He then proposed a neural model of negative emotion processing bias associated with structural and functional brain abnormalities [4]. Carlisi also argued that the negativity bias is mediated by cortico-subcortical [5]. Research in neuroscience has shown that emotion processing has important research implications in the exploration of mechanisms and clinical treatment of various mood disorders such as depression, anxiety, and narrative disorders.

Specific brain regions are closely linked to emotion processing [6]. The frontal lobe is involved in cognitive processing and plays an important role in top-down cognitive processes and emotion processing, and is an important neural basis for emotion processing. Recent developments in neuroimaging techniques have shown that there is an interconnection between emotions and brain structure and function, allowing for more objective assessment of emotions. Electroencephalography(EEG) technology has become a hot topic of current research due to its advantages of high temporal resolution, portability, safety and reliability. EEG contains a wealth of electrophysiological information, and alpha rhythm (8-13 Hz) oscillations are thought to facilitate the integration of brain networks and top-down communication with the cortex, thus facilitating the processing of emotion processing [7, 8]. In addition, event-related potentials(ERPs) of the EEG are a specific type of brain-evoked potentials that reflect neurophysiological alterations in the brain's processing of stimuli and are associated with a variety of mental activities of emotion processing and cognition. Research has shown that the P2 is associated with more complex emotion assessment and cognition, and P3 is the one endogenous component that is currently receiving the most attention [9, 10].

As an emerging neuromodulation technology, tACS regulates cortical oscillatory rhythms by stimulating the brain with low-intensity alternating currents [11, 12]. Studies have shown that tACS of the prefrontal lobe can improve insomnia, depression, and anxiety and enhance cognitive brain function in subjects [13]. tACS produces effects on cognitive functions in a frequency-specific form, e. g., Kanai's study found that alpha rhythmic electrical stimulation increased perceptual levels [14]. Bilateral alpha-tACS on the prefrontal lobes promoted decision-making ability at the lexical level [15]. Vossen's study showed alpha enhancement after alpha-tACS, reflecting neuroplasticity and the potential of tACS as a therapeutic tool [16]. Moreover, because brain oscillatory rhythms and phase synchronization are closely related to cognitive levels, tACS has emerged as a promising technical tool for modulating emotion processing.

This paper investigated the effect of tACS on emotion processing, and then explored the underlying neural mechanisms further. This paper is organized as follows: Section II addresses the methodology, including the experimental setup and data processing. Section III details the results analysis. The conclusion is stated in section IV.

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II. METHODS

A. Participants

Forty-four right-handed healthy volunteers (21 males and 23 females, mean age 22.53 ± 1.38, range 20 to 26 years old) were recruited to participate in this study. Before the experiment, subjects were randomly and equally divided into an experimental group given tACS and a control group given sham-stimulation. All participants have no history of neurological or psychiatric disorders and signed an informed consent before experiment. The study was approved by the ethical committee of Tianjin University.

B. Design of the Experimental Paradigm

8min open-closed eye rest task: The procedure of 8min open-closed eye rest task was depicted in Fig. 1(a). The OCCOCOOC mode was used, with O for open eyes and C for closed eyes. Subjects wore headphones (SONY MDR-EX155AP) during the experiment, remained awake and reduced physical movements. When the task started, subjects would hear the voice prompts "Please open your eyes" and "Please close your eyes" in that order. Subjects kept their eyes open and looked at the red circle in the center of the computer screen in front of them when they heard the "open eyes" prompt, and closed their eyes when they heard the "close eyes" prompt. When the task was over, the subject would hear a 2-second "beep" sound and the red circle would turn into a blue circle, indicating the end of the experiment.

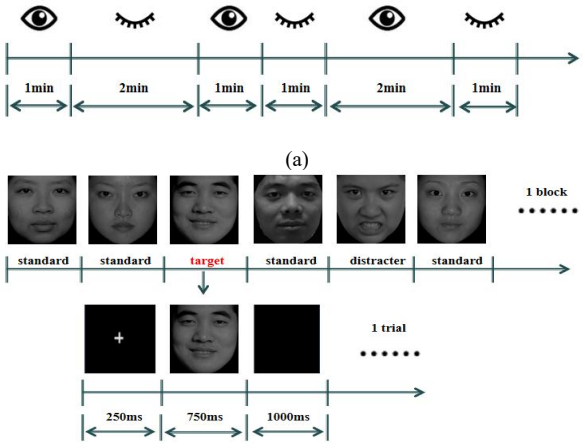

Figure 1. (a) 8min open-closed eye rest task flow chart; (b) Emotional face oddball task flow chart.

Emotional face oddball task: The procedure of emotional face oddball task was depicted in Fig. 1(b). This task consisted of 6 blocks in which positive, negative and neutral emotional face pictures with a ratio of 1.5:1.5:7 were randomly presented alternately in each block and used as stimulus targets. Three of the blocks were positive emotional face tasks, which required subjects to respond to a keystroke when positive emotional pictures appearing on the computer screen, i. e., to press the space bar when a positive emotional picture was presented, and not to respond when a neutral emotional face and a negative emotional face (distractor stimuli) were presented. The other 3 blocks were the negative emotional face task, i. e., pressing the space bar when presented with a negative emotional picture and not responding when presented with a neutral emotional face and a positive emotional face (distractor stimuli). The duration of each block was 6 minutes, and before the experiment started there was a voice prompt for the next experimental task (identifying positive emotional faces or negative emotional faces). Each block contained 180 trials, and each trial would begin with a white cross in the middle of the computer screen for 250 ms, indicating that the task was about to begin, followed by a picture of an emotional face for 750 ms, and finally a time interval lasting 1000 ms, during which the participant was asked to make an emotional recognition and perform the corresponding keystroke response as soon as possible. The behavioral results were recorded.

This study optimized 162 positive, negative and neutral emotional faces based on the Chinese Facial Affective Picture System (CFAPS) and used different emotional face pictures as stimulus targets. Research showed that faces with emotions (happy or angry, etc.) attract more attention [17]. The Oddball paradigm is one of the classical EEG paradigms for studying ERP, and this study was designed to explore the effect of tACS on attentional bias in emotion processing by the emotional face oddball paradigm.

Transcranial alternating current stimulation(tACS): The tACS modulation was divided into an experimental group and a control group. In the experimental group, tACS was applied to subjects via a transcranial electrical stimulator system (Neuroconn, Germany) with initial phase set to 0, stimulation frequency of 10 Hz, stimulation intensity of 1.5 mA, and stimulation duration of 20 minutes. Two sponge electrodes (5 × 7 cm^2) were placed in bilateral forehead positions (F3 and F4), and impedance was kept below 10 KΩ. In the control group, subjects received sham-stimulation and no stimulation was applied except for a brief tACS with 10 sinusoidal cycles of rising current and 10 sinusoidal cycles of falling current at the beginning (same frequency and intensity as in the experimental group), thus avoiding the placebo effect on the results.

C. Experiment Procedure Design

The whole experiment lasted for 7 days, and the resting and task EEG signals were collected on the first day, followed by tACS/sham-stimulation once a day for 5 days, and the resting and task EEG signals were collected again on the last day. The flow chart of experiment is shown in Fig. 2.

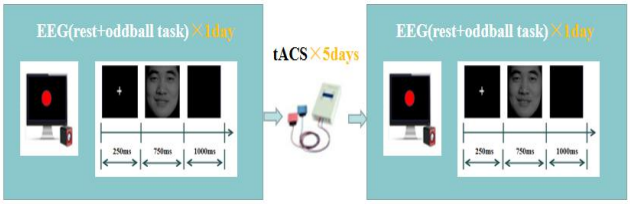

Figure 2. The flow chart of experiment.

D. Data collection

The SynAmps2 EEG signal acquisition device, developed and manufactured by Neuroscan, USA, was used in this study. The Ag/AgCl electrodes were placed in accordance with the 10-20 electrode system and the right mastoid (M2) was used as the reference electrode. The signals were digitized at 1000 Hz and stored in a PC for offline analysis. Throughout the EEG

recording, the impedances of the electrodes were maintained below 10 KΩ.

E. Behavioral and EEG processing

Behavioral and statistical analyses： Correctness, wrong score rate, and reaction time was analyzed in this study. Wrong score rate referred to subjects' classification of neutral stimulus errors as positive (neutral score positive) and negative (neutral score negative), and indicated the rate at which subjects identified neutral emotions as positive and negative, representing the cognitive bias of emotion processing. Before statistical analysis, trials with response times less than 200 ms and greater than 1500 ms were excluded, while trials with behavioral data greater than or less than the within-group mean plus/minus three times the variance were excluded for all subjects. Behavioral data before and after stimulation were analyzed within groups using paired-samples t-test.

Offline preprocessing: Basic processing such as variable reference, downsampling and filtering was performed. All channels were re-referenced to bilateral mastoid, the resting EEG data sampling rate was downsampled from 1000 Hz to 500 Hz, and the task state data was downsampled to 200 Hz. A band-pass filter of 0.5 to 45 Hz in the EEG data to reduce power-line interference and high-frequency noise. Independent component analysis (ICA) was used to manually remove noise from eye movements, EMG signals and other interfering signals.

Power spectrum and event-related potentials (ERPs): The power spectrum was used to transform the time-domain signal into a frequency-domain power spectrum for a more intuitive analysis of the tACS modulation effect. The welch power spectrum method was used to divide the EEG signal into 5-second data segments, calculate the power spectrum of different frequency bands for each lead, and finally obtain the power of each lead and frequency band and normalize it. The formula to normalize was defined as

$$\sigma' = (\sigma - mean(\sigma))/(\max(\sigma) - \min(\sigma)), \quad (1)$$

where σ' was the normalized energy value, and σ was the energy value before normalization.

ERP components during the emotion processing task phase were analyzed using ERP mean values. The EEG data after preprocessing were segmented by trial, with each segment retaining data from 250 ms before and 1750 ms after stimulation. The first 200 ms signal of each data segment was used as the standard for baseline correction, and those trials with amplitude differences greater than 100 μV were excluded. Finally, the positive task that averaged all subjects' correct keystroke responses was superimposed as the ERP for the positive emotional face recognition task, and the negative task that averaged all subjects' correct keystroke responses was superimposed as the ERP for the negative emotional face recognition task.

III. RESULTS

A. Results of resting EEG

The energy difference of power spectrum and topography of the resting-state in the alpha band before and after tACS were shown in Fig. 3. Values greater than 0 represented a boost in EEG energy after tACS, and values less than 0 represented a decrease in energy. It was found that there was a significant increase in energy near 10 Hz frequency in the experimental group after tACS (t=-2. 63, p<0. 05, see Fig. 3(a)), and this phenomenon was more significant in the parieto-occipital region in the posterior part of the brain. However, no significant changes were found in the control group (see Fig. 3(b)).

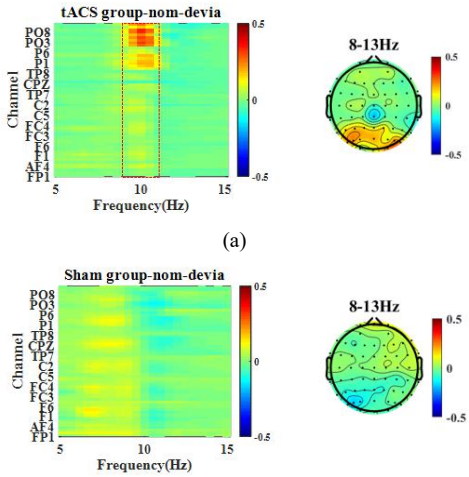

Figure 3. The energy difference of power spectrum and topography of resting-state for (a) experimental group and (b) control group in the alpha band before and after tACS,respectively (posttest-pretest).

B. Results of emotional face tasking state

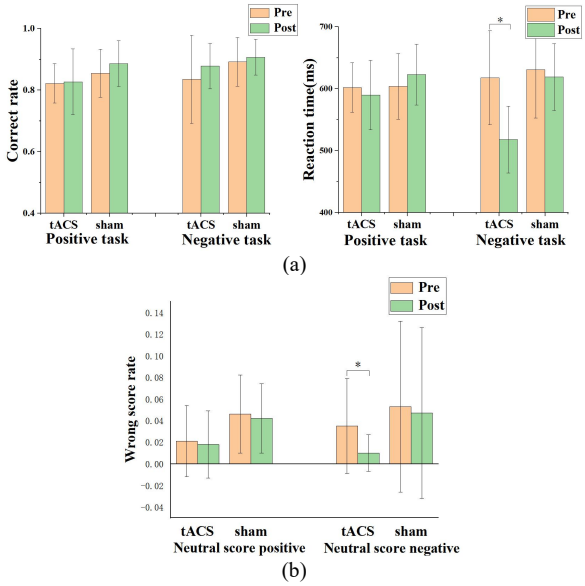

Figure 4. Behavioral results: (a) Correct rate and response time; (b) Wrong score rate.

The behavioral effects of tACS on the emotional face task were shown in Fig. 4. By analyzing the correct rate and reaction time (see Fig. 4(a)), there were no significant differences before and after stimulation in the control group, but the reaction time decreased significantly in the experimental group when the negative task was performed (t=4. 626, p<0. 05). To assess the effect of tACS on emotion

processing bias, this study analyzed the wrong score rate of neutral score positive and neutral score negative (see Fig. 4(b)), and a within-group paired t-test revealed a significant decrease in the proportion of neutral score negative in the experimental group (t=2. 713, p=0. 034), while there were no significant difference in the control group before and after stimulation, indicating that tACS improved the subjects' negative emotional cognitive bias.

To investigate the effects of tACS on the attentional processing of positive and negative emotional faces, this paper compared the changes in P2 and P3 amplitudes of positive target stimuli and negative target stimuli before and after tACS in the experimental and control groups. The results of the changes in P2 and P3 wave amplitudes were shown in Fig. 5. The paired t-test revealed that the amplitudes of positive target stimuli (t=-2. 231, p<0. 05) and negative target stimuli (t=-4. 701, p<0. 05) were significantly larger for the P2, and positive target stimuli (t=-2. 026, p<0. 05) and negative target stimuli (t=-4. 935, p<0. 05) were significantly larger for the P3 after tACS (see Fig. 5(a)), indicating that tACS increased the level of attention to positive and negative emotions in healthy subjects at both early and late stages of emotion processing. In contrast, there were no significant change in P2 and P3 for control subjects (see Fig. 5(b)), indicating that the sham-stimulation did not affect attention allocation during emotion processing.

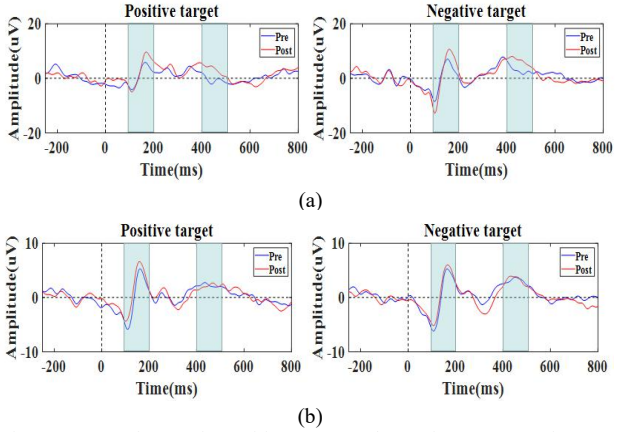

Figure 5. ERP changes in positive target and negative target sessions before and after tACS in (a) Experimental group and (b) Control group.

IV. Conclusion

Resting-state results showed that the experimental group produced a significant energy boost in the alpha band compared to the control group, revealing that tACS targeted the regulation of brain oscillatory rhythms, which in turn affected the brain emotional state of emotion processing. The task state results showed that the proportion of neutral emotions divided into negative emotions was significantly reduced, and the P2 and P3 component amplitudes of ERP were increased in both positive and negative emotion tasks, revealing that tACS can effectively modulate the allocation of attention during emotion processing in healthy subjects, improve the effect of negative emotion cognition, and affect the brain cognitive level of emotion processing.

tACS is an effective means to modulate the brain emotion processing ability, and is expected to be one of the techniques for treating mood disorders and improving the level of emotion processing in patients in clinical settings.

Acknowledgment

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