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Effects of Theta Transcranial Alternating Current Stimulation Over the Frontal Cortex on Reversal Learning

Miles Wischnewski *, Paul Zerr, Dennis J.L.G. Schutter

Donders Institute for Brain, Cognition and Behaviour, Radboud University Nijmegen, The Netherlands

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ABSTRACT

Background: Theta oscillations in the electroencephalogram (EEG) are associated with learning and behavioral adaptation.
Objective: To investigate the effects of theta transcranial alternating current stimulation (tACS) applied to the frontal cortex on reversal learning.
Methods: Healthy volunteers participated in a sham-controlled between subjects design. TACS at 1 mA peak-to-peak was administered during a reward–punishment reversal learning task. Resting state EEG was measured before and after tACS and the task.
Results: Active tACS improved learning ability, but at the same time interfered with applying the rule to optimize behavior. Furthermore, a significant decrease in frontal theta–beta EEG ratios was observed following active tACS.
Conclusions: Results provide behavioral and electrophysiological evidence for influencing reversal learning with exogenous oscillatory electric field potentials applied to the frontal cortex.

Introduction

Adapting one's behavior to changing environments is a key feature that determines the evolutionary success of species [1]. Especially learning from feedback-related reward and punishment signals facilitates the process of adapting to various situations and contributes to mental flexibility [2]. This way, individuals learn to select the proper action under varying conditions based on the consequences of the action. For such reinforcement learning feedback, the processing of reward and punishment signals is crucial to create internal prediction models [3,4].

Neuroscientific research has demonstrated the significance of neural oscillations in the electroencephalogram (EEG) of the frontal cortex during learning and updating of internal prediction models [5,6]. Especially oscillatory frontal cortical activity in the theta (4–7 Hz) and beta (13–30 Hz) range has been proposed to underlie neural processes associated with reinforcement learning and decision making [5–10]. Van de Vijver and colleagues [11] showed that both theta and beta predict next trial success rate, indicating that both frequency ranges are involved during learning in response to an incorrect trial. The findings illustrate the importance of these frequencies in updating information and response inhibition of actions that are no longer beneficial [12,13]. In further support, the available evidence for the involvement of theta and beta oscillations in reinforcement learning stems from studies using reversal learning paradigms that involve rule learning under varying conditions [14,15].

Additionally, it has been shown that local beta range activity of distant cortical networks is temporally correlated during resting-state EEG [16]. Theta activity has been proposed to act as a rhythm associated with interregional activity and relative to higher (beta) oscillatory activity reflects the motivational state of the system [17–20]. The importance of theta–beta EEG ratios during decision making has been demonstrated in healthy volunteers in which higher resting state theta–beta EEG ratios are associated with increased disadvantageous risky choices [17,21]. Exploratory analyses have shown that this relationship is driven by the association between theta oscillation and reward-dependent learning [21]. The results of these studies concur with patient studies in which elevated theta–beta EEG ratios have been linked to risky decision making, impulsivity, lack of attentional focus and poor reversal learning [22–26].

Even though EEG studies illustrate the relevance of theta oscillations in reward–punishment learning, it remains unclear whether theta oscillations directly contribute to reversal learning. By applying weak oscillatory currents to the brain, transcranial alternating current stimulation (tACS) offers a non-invasive way to emulate natural occurring rhythms in the cortex [27,28]. Prior research has

* Corresponding author. Tel.: +31 24 361 2604.
E-mail address: m.wischnewski@donders.ru.nl (M. Wischnewski).

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provided evidence that tACS can entrain endogenous brain rhythms and increase neural synchronization in the corresponding frequency to influence cognitive performance [20,29]. Indeed, several studies using theta tACS have shown changes in performance of working memory [20,30,31], problem solving [32] and decision making [33].

In the present study we investigated the role of theta oscillations between left and right frontal cortices during reversal learning. Therefore, tACS was applied at 6 Hz over bilateral frontal cortex and compared to a placebo stimulation condition. It was hypothesized that theta tACS would improve reversal learning performance. Furthermore, we tested the hypothesis regarding if theta tACS would be effective in improving reversal learning and whether this would go accompanied by a decrease in theta-beta EEG ratio.

Materials and methods

Participants

Fifty adult healthy volunteers (31 females), mean age ± SD, 24.1 ± 7.80 years, participated in the present study. All participants were right-handed as measured by the Edinburgh inventory of handedness, mean ± SD, 43.8 ± 4.37 [34], had normal or corrected-to-normal vision, and no history of neurological or psychiatric conditions. Participants were excluded if they had metallic objects in their head, had any type of stimulator in their body, used medication (except oral contraceptives) or recreational drugs less than 48 hours before the experiment, or suffered from a skin disease or skin allergy. Participants were naïve to the aim of the study and paid for participation. Written informed consent was obtained from all participants. The study protocol was approved by the medical ethical committee of the Radboud University Medical Centre in Nijmegen and carried out in accordance with the standards set by the Declaration of Helsinki (Fortaleza Amendments).

Transcranial alternating current stimulation

Alternating currents were applied by a battery-driven stimulator via two electrodes in saline-soaked sponges (35 cm^2; NeuroConn GmbH, Ilmenau, Germany) which were placed under an EEG cap. Electrodes were positioned over left (between F3 and Fc5) and right (between F4 and Fc6) frontal cortex (Fig. 1B). A sinusoidal stimulation waveform was applied with a peak-to-peak intensity of 1.0 mA and no DC offset at a frequency of 6 Hz. During active tACS, the current was ramped up for 20 seconds, reached its maximum 1 minute before the start of the reversal learning task and lasted until the task was completed (approximately 11 minutes). During sham tACS, the current was ramped up over 20 seconds but discontinued immediately after. The impedance of the tACS electrodes was kept below 10 kΩ during stimulation. Stimulation was applied in a randomized double-blind fashion.

Reversal learning

The task used in the present experiment is a modified version of the reinforcement learning task by Gehring and Willoughby [35]. Participants performed a reversal learning task in which two fictional monetary reward choices were presented vertically. Eight possible stimulus combination were presented in random order (5–25; 25-5; 10–30; 30-10; 15–35; 35-15; 20–40; 40-20) with a jittered inter-trial interval of 800–1200 ms. Participants had to chose the high or the low number. Selection of the large value corresponded to a high-risk decision that would lead to either a relative large reward in case of positive response feedback or relative large punishment in case of negative response feedback. Selection of the small value corresponded to a low-risk decision that would lead to either a relative small reward in case of positive response feedback or a relative small punishment in case of negative response feedback. Participants were instructed to select one of these options by a click on the computer mouse with either left or right thumb (Fig. 1A). Although there was no time constraint for each trial, participants were encouraged to respond as quickly as possible. Feedback was presented 500 ms after the subject's decision by a colored square which indicated whether the response was correct (green square) or incorrect (red square). In the case of a correct response, the points of the participant's choice were added to the summed total score and if the response was incorrect the points of the participant's choice were subtracted from the summed total score. The total score was shown after each trial for 2000 ms. An overview of a single trial is shown in Fig. 1A. In total, the task consisted of 120 trials, consisting of 6 blocks of 20 trials and two strategy reversals (after block 2 and block 4). First, participants learned that high-risk options were

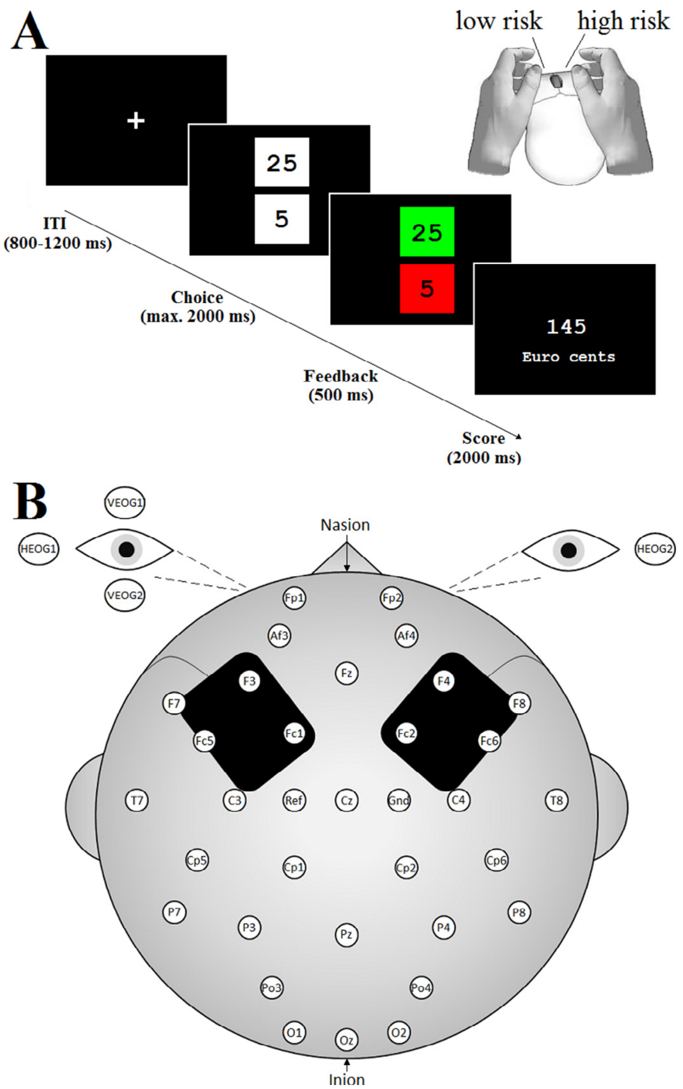

Figure 1. (A) Overview of one trial in the reversal learning task. Participants were presented with two options (here 25 and 5) which they could choose using a computer mouse. Points were added to the total score if the answer was correct and subtracted from the total score if the answer was incorrect. After participants made their choice, color feedback indicated which option was correct and the total score was presented. (B) EEG and tACS set-up of the current experiment. The tACS electrodes were removed during resting-state EEG recordings.