Clinical Neurophysiology 128 (2017) 2227–2232

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

After-effects of transcranial alternating current stimulation on evoked delta and theta power

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ARTICLE INFO

Article history:
Accepted 24 August 2017
Available online 21 September 2017

Keywords:
Electroencephalogram
Event-related activity
Oscillations
Transcranial alternating current stimulation

HIGHLIGHTS

- This study investigated tACS after-effects in evoked frontal oscillatory delta-theta activity.
- Results showed a significant decrease after delta-tACS slightly below stimulation frequency.
- The tACS induced effects may be explained by spike-timing dependent plasticity.

ABSTRACT

Objective: Phase synchronization is suggested to be among the mechanisms that can explain the effects of transcranial alternating current stimulation (tACS). However, little is known about the effects of tACS on event-related oscillatory activity. Therefore the objective was to investigate frequency-related effects of frontal tACS on event-related oscillatory power.
Methods: In a double blind randomized controlled cross-over design, twenty-four participants received 12 min of delta (2.5 Hz), theta tACS (5 Hz) and sham tACS at an intensity of 1 mA peak-to-peak. Event-related delta- and theta-related oscillatory activity was recorded to reward- and punishment-related feedback signals.
Results: Delta tACS decreased feedback-related oscillatory power in the 1.5 and 3.5 Hz frequency range. This effect was driven by power changes below the tACS frequency stimulation.
Conclusion: Exogenous field potentials can attenuate event-related oscillatory activity in a rhythm slightly below the stimulation frequency. Our findings suggest an interaction between tACS and event-related rhythmic activity that extends beyond phase synchronization.
Significance: These findings add novel insights into the mechanisms of tACS after-effects.

1. Introduction

Phase synchronization of rhythmic activity is proposed to be an important mechanism by which exogenous oscillatory electric fields modulate underlying cortical processes (Helfrich et al., 2014; Schutter, 2014; Thut et al., 2011; Zaehle et al., 2010). It has been shown that transcranial alternating current stimulation (tACS) affect endogenous oscillatory activity in a narrow range around the stimulated frequency (Helfrich et al., 2014; Neuling et al., 2015). Additionally, it has been demonstrated that tACS effects can endure beyond the duration of stimulation (Neuling et al., 2013; Vossen et al., 2015).

In spite of the available evidence in support of the neural entrainment hypothesis during tACS, there is evidence that induced changes in oscillatory activity after tACS are more complex (Neuling et al., 2013; Veniero et al., 2015; Vossen et al., 2015). Several lines of research indicate that the after-effects are, at least in part, different from online tACS (Kasten et al., 2016; Veniero et al., 2015; Vossen et al., 2015). For example, Zaehle et al. (2010) proposed that spike-timing dependent plasticity (STDP) may play a role in sustaining effects of tACS after the end of stimulation. According to the STDP model, it is suggested that synaptic strength can be decreased when post-synaptic precede pre-synaptic potentials (Hutcheon and Yarom, 2000; Markram et al., 1997). Consequently, STDP models predict suppressive

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https://doi.org/10.1016/j.clinph.2017.08.029

effects of tACS slightly below the stimulation frequency (Vossen et al., 2015; Zaehle et al., 2010). Indeed, Vossen et al. (2015) showed that increases of endogenous oscillatory activity are independent from tACS phase continuity, indicating that other mechanisms besides entrainment may be involved. Consistent with the STDP model, Vossen et al. (2015) showed that maximal effects of tACS were found on oscillations above the stimulation frequency (+0.5 Hz).

Another relevant factor affecting tACS-induced effects on oscillatory responsiveness is the basal level of neural activity in the cerebral cortex (Neuling et al., 2013). Furthermore, observations that after-effects of tACS depend on the state of the cerebral cortex further illustrates the importance of state factors contributing to the neural signature of tACS (Schutter and Hortensius, 2011; Veniero et al., 2015).

Several studies have shown that tACS-induced effects are linked to changes in performance on behavioral tasks (Helfrich et al., 2014; Kasten and Herrmann, 2017; Schutter and Wischnewski, 2016; Wischnewski et al., 2016). For example, learning from rewards and punishments has been associated with increased evoked oscillatory activity in the delta (1–4 Hz) and theta (4–8 Hz) range between 100 and 600 ms after the onset of the feedback (Cavanagh, 2015; Cohen et al., 2007). Indeed, Wischnewski et al. (2016) showed that reinforcement learning was faster when frontal 6 Hz tACS is applied compared to sham stimulation. Typically tACS-induced behavioral changes are correlated with changes in resting state EEG (Helfrich et al., 2014; Wischnewski et al., 2016). However, effects of tACS on endogenous oscillatory activity during task execution have not yet been explored. In the current study participants performed a simple decision making task with reward and punishment feedback after tACS was applied. The effects of 2.5 Hz and 5 Hz tACS over frontal cortex on feedback evoked oscillatory activity in the delta/theta range were investigated. We hypothesized that tACS would target event-related oscillatory activity at the stimulated frequency. Specifically, in accordance with the STDP model (Vossen et al., 2015; Zaehle et al., 2010), we hypothesized that an increase in oscillatory activity would more likely be found slightly above the stimulation frequency, whereas a decrease in oscillatory activity would more likely be found slightly below stimulation frequency.

2. Methods

2.1. Participants

Twenty-four healthy right-handed volunteers participated (17 females, 21.42 ± 0.52 years) in a double-blind randomized controlled cross-over design. Informed consent was obtained and the study was approved by the Committee on Research Involving Human Subjects of the Radboud University Medical Centre.

2.2. Reward-punishment task

Feedback-related activity was measured in response to punishment (i.e., losing points) and reward-related (i.e., winning points) signals during a decision making task. During this task pairs of three types of neutral objects (i.e., commodes, lamps, and vases) were displayed on a computer monitor and participants were instructed to indicate which of the objects was the most expensive. Object-pairs were presented on the left and right side of the screen (visual angle ~3.5°) for a duration of maximally 2000 ms. During this period participants pressed the left and right button presses to indicate their choice (mean ± SEM response time: 1127.46 ± 53.45 ms). Feedback was delivered immediately after the button press for 1500 ms. Punishment and reward values were provided between −40 and +50 points in steps of 10. Participants were informed that the points of their choice were relative to the points that they would have scored for choosing the alternative object and that the correct answer would always give them the most points. Unknown to the participants points were given at random. The goal of the task was to score as many points as possible. In total the task consisted of 120 trials in which object-pairs were presented in a counterbalanced order, with a jittered inter-trial interval of 100–1000 ms. An example of a single trial is presented in Fig. 1A. In the first session participants performed 10 practice trials to familiarize themselves with the task. In the subsequent sessions participants performed 3 practice trials.

2.3. Transcranial alternating current stimulation

Previous research has shown that feedback signals of punishment and reward evoke activity in the delta (1–4 Hz) and theta (4–8 Hz) frequency range over the anterior regions of the scalp (Cavanagh, 2015; Cohen et al., 2007; Leicht et al., 2013; Marco-Pallares et al., 2008). In three sessions separated by at least 48 h, twelve minutes of 2.5 Hz (delta tACS), 5 Hz (theta tACS) or sham tACS (NeuroConn, Ilmenau, Germany) was administered using a frontopolar (5 × 7 cm)-vertex (10 × 10 cm) montage at an intensity of 1 mA peak-to-peak amplitude prior to the task (Manuel et al., 2014; Fig. 1B). A ramp-up and ramp-down phase of 30 s was applied. Sessions were randomized in a counterbalanced order.

2.4. EEG recording and preprocessing

EEG (Brain Products, Gilching, Germany) was recorded from the scalp at a 1000 Hz sampling rate. EEG activity was recorded from 13 electrodes (F3, F1, Fz, F2, F4, T7, T8, P3, Pz, P4, O1, Oz, O2, Fig. 1B) with an additional four electrodes to measure horizontal and vertical eye movements and a reference electrode on the left mastoid. Raw EEG recordings were filtered between 1 and 30 Hz. The amount of eye blinks (delta tACS = 120.21 ± 12.77, theta tACS = 121.96 ± 12.86, and sham = 121.17 ± 16.10) did not differ between conditions ($F(2,46) = 0.03$, $p = 0.975$) and were corrected using the Gratton and Coles method (Gratton et al., 1983). Additional artifacts were manually removed and removal was similar across conditions (sham: 91.75% remained, delta-tACS: 91.83% remained, theta-tACS: 90.63% remained). Time-frequency analyses were performed using complex Morlet wavelets on a window of −1000 to 1500 ms post feedback onset (50 logarithmic steps) to measure frontal delta and theta evoked power in response to punishment- and reward-related feedback signals. The window between −1000 and 0 ms was used for baseline correction. An identical time-frequency analysis without baseline-correction was performed to investigate differences in spontaneous oscillatory activity. For all analyses the Fz electrode was used as it has been shown to reliably reflect fronto-midline delta-theta activity (Cavanagh et al., 2012; Cavanagh, 2015; Cohen et al., 2007; Leicht et al., 2013; Marco-Pallares et al., 2008).

2.5. Procedure

A campus participant database was used to recruit healthy volunteers. At the start of the first experimental session, volunteers filled out a safety screening and handedness form. After being informed about the procedure of each session, signed informed consent was obtained. Next, EEG and tACS was placed after which participants read the task instructions and performed the practice trials. Next, tACS was applied offline for 12 min in a double blind fashion while participants were seated comfortably in a chair. Immediately after tACS participants performed the task, which