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Phasic Modulation of Human Somatosensory Perception by Transcranially Applied Oscillating Currents

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ABSTRACT

Background: Why are weak sensory stimuli sometimes perceived and other times not? Experimental paradigms using near-threshold stimuli suggest that spontaneous brain network dynamics are involved in separating relevant from irrelevant information. Recent findings in human visual perception provide evidence that the immediate spontaneous brain state, i.e. the phase of alpha oscillations, predicts whether a coinciding stimulus is further processed or not.
Objectives: Here, we investigated whether this concept of a "pulsed inhibition" involved in sensory gating represents a general mechanism of conscious human perception and can be modulated with non-invasive brain stimulation.
Methods: Hence, we used transcranial alternating current stimulation (tACS) at the individualized mu-alpha frequency to entrain somatosensory mu-alpha oscillations, and investigated the effect on somatosensory detection in healthy humans. tACS (or sham, respectively) was applied over primary somatosensory cortices (mu-tACS) while participants performed a detection task of somatosensory near-threshold stimuli.
Results: We found that mean perception thresholds during mu-tACS did not change as compared to sham stimulation. However, during mu-tACS, somatosensory detection thresholds varied as a function of the applied tACS phase. This effect was not found when tACS was applied over occipital areas at participant's individual visual alpha frequency.
Conclusion: Our data indicate that tACS applied at an endogenous frequency is capable of modulating human somatosensory perception by inducing phase-dependent periods of excitation and inhibition, i.e. entraining ongoing mu-alpha oscillations. These findings support the idea that the "pulsed inhibition" framework for sensory gating applies to somatosensory mu-alpha oscillations and might therefore represent a general, but sensory-specific mechanism of conscious human perception.

Introduction

The presentation of near-threshold stimuli may or may not result in a sensory percept. It has been suggested that such variability in perceptual performance is linked to oscillatory neuronal background activity. There is converging evidence that the alpha rhythm, long reflected as an index of cortical idling [1], has functional implications for various cognitive processes. Specifically, alpha oscillations seem to affect information processing of sensory cortices [2–4]. Alpha power modulations have been linked to attentional shifts and the anticipation of upcoming stimuli [5–13], working memory functions [14–17] and the conscious perception [i.e. defined as reporting the detection of stimuli] [18–25]. Common to these studies is the fact that low alpha activity seems to index enhanced neural processing while increased alpha activity seems to index reduced processing. Analogously BOLD activity in sensory regions was shown to be negatively correlated with alpha power [26–28]. Besides the effect of amplitude of the alpha rhythm, the phase of ongoing oscillations was also shown to impact perception [19–21]. In line with these experimental findings, it was

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suggested that alpha has a gating role in information processing and that it specifically exerts influence by an oscillatory mechanism of pulsed inhibition [2,3,29,30].

However, many of these findings are based on experiments conducted in the visual domain and its prominent visual alpha rhythm. However, several alpha rhythms pertaining to different generators have been described previously [31–34]. It therefore remains an open question whether the proposed mechanism of pulsed inhibition is domain-specific or applies to alpha rhythms in general. In the somatosensory domain, the predominant neural background oscillation is mu-alpha (or rolandic alpha) [35]. For this alpha rhythm, the exact relationship between oscillatory features, such as amplitude or phase, and somatosensory perception still remains elusive [10,22,24,25,36–41].

Transcranial alternating current (tACS) stimulation is a new tool to investigate relationships between oscillatory neuronal activity and behavior. This technique allows to non-invasively apply oscillatory currents to the human brain thereby modulating ongoing neuronal oscillatory activity in a frequency-dependent way [42,43]. Interactions between externally applied and ongoing neural oscillations are most pronounced when endogenous stimulation frequencies are being used, presumably via an entrainment of the neuronal rhythm [43–46].

Here we aimed at investigating whether tACS applied at the individual mu-alpha frequency (mu-tACS) during a somatosensory detection task can modulate behavioral variance in somatosensory perception by entraining ongoing mu-alpha oscillations. We hypothesized that mu-tACS induces (i) a tonic increase of the somatosensory detection threshold by an overall increase in mu-alpha amplitude and (ii) a periodicity in perceptual performance locked to the applied tACS phase.

Methods and materials

Participants

Eighteen healthy participants (10 female, mean age 27.2, SD = 3.12) participated in a single-blinded tACS-experiment. According to the Oldfield questionnaire for the assessment of handedness [47], all participants were right-handed. Prior to the study, participants gave written informed consent to participate in the experiment and underwent a neurological examination. Participants were not taking any medication. The study was designed and conducted according to the Declaration of Helsinki and was approved by the ethics committee of the University of Leipzig. Five participants had to be discarded from the later analysis. Three participants did not show any distinct event-related desynchronization during the pre-experiment in order to identify their individual mu-frequency as the target frequency for tACS. Two additional participants were discarded as they reported to have fallen asleep during the experiment. Thirteen subjects were thus considered for consecutive analysis steps.

Transcranial alternating current stimulation (tACS)

Electric stimulation was delivered with a battery-operated stimulator system (ELDITH, Neuroconn, Ilmenau, Germany) via two rubber electrodes (40 × 40 mm) placed over CP3 and CP4. The impedance was kept below 10 kΩ by applying electrode gel (Ten20, D.O. Weaver, Aurora, CO, USA) between skin and electrode. The stimulation intensity was kept at 1 mA peak to peak resulting in a maximum current density of 62.5 $\mu A/cm^2$. The study consisted of two sessions with either sham or verum stimulation. The verum stimulation consisted of 5 min of tACS at participant's individual mu-alpha frequency (mu-tACS). For sham stimulation, 10 s of noise stimulation was applied. For both tACS and sham, the intensity was ramped up for 10 s and down for 1 s (see Fig. 1C). By using a short-duration sham protocol, we aimed at making sham and verum stimulation indistinguishable in terms of their perception. Additionally, the broadband frequency distribution of the brief noise stimulation protocol was used to minimize any potential effects on somatosensory mu-alpha oscillations and behavior.

EEG

The EEG was recorded at a sampling rate of 2500 Hz using a BrainAmp amplifier (Brain Products, Munich, Germany) with electrodes placed at positions C3, C4, and POz of the international 10–10 system [48]. The online reference was placed above position FCz and for potential offline rereferencing signals from electrodes above both mastoids were recorded as well. For offline analysis EEGLAB [49] and custom MATLAB scripts (The MathWorks, Natick, MA, USA) were used.

Experimental design

The experiment consisted of two sessions separated by at least one week. Both sessions contained the pre-experiment to determine each participant's individual mu-alpha peak frequency and the main experiment consisting of a somatosensory detection task. In one session mu-tACS and in the other sham stimulation were applied during the detection task of the main experiment. The order was counterbalanced across subjects.

Participants were seated in a comfortable chair inside a shielded EEG chamber while engaged in both parts of the experiment.

Pre-experiment

The pre-experiment was conducted to determine each participant's individual mu-alpha frequency. For this purpose, each participant completed a passive somatosensory experiment with simultaneous EEG recordings. One hundred and fifty electric suprathreshold stimuli were applied to the right index finger via two VELCRO ring-electrodes using a DS7 isolated bipolar constant current stimulator (Digitimer Ltd., Welwyn Garden City, Hertfordshire, UK) while participants were fixating a centrally presented cross on a screen. The electric stimuli were delivered with a mean interstimulus interval of 2050 ms and a maximum jitter of 900 ms. The intensity was manually set to a level at which stimuli were easily detectible but not painful. Immediately after the pre-experiment, the EEG data were analyzed with respect to the event-related desynchronization (ERD) of the mu-rhythm (see Ref. 35) (see Fig. 1A). The frequency with the maximum ERD was identified to serve as the target stimulation frequency for the subsequent experiment. Only subjects that showed a clear mu rhythm as indexed by the ERD took part in the main experiment.

Main experiment

For the main experiment participants were engaged in a 16 min 24 s long somatosensory detection task. For this purpose, 480 electric stimuli with an inter-stimulus interval of 1050–3050 ms (mean of 2050 ms) varying in intensity were presented to the right index finger via two VELCRO ring-electrodes using a customized DS7 isolated bipolar constant current stimulator (Digitimer Ltd., Welwyn Garden City, Hertfordshire, UK) while participants were fixating a centrally presented cross on a screen. Participants were instructed to report each stimulus they felt by pressing a button with the left hand. The intensity of each stimulus was constantly adjusted to each participant's current somatosensory perception threshold by using