Brain Stimulation (2008) 1, 97–105

BRAIN STIMULATION

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Comparatively weak after-effects of transcranial alternating current stimulation (tACS) on cortical excitability in humans

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Objective
Interference with brain rhythms by noninvasive transcranial stimulation that uses weak transcranial alternating current may reveal itself to be a new tool for investigating cortical mechanisms currently unresolved. Here, we aim to extend transcranial direct current stimulation (tDCS) techniques to transcranial alternating current stimulation (tACS).

Background
Parameters such as electrode size and position were taken from those used in previous tDCS studies.

Methods
Motor evoked potentials (MEPs) revealed by transcranial magnetic stimulation (TMS), electroencephalogram (EEG)-power, and reaction times measured in a motor implicit learning task, were analyzed to detect changes in cortical excitability after 2-10 minutes of AC stimulation and sinusoidal DC stimulation (tSDCS) by using 1, 10, 15, 30, and 45 Hz and sham stimulation over the primary motor cortex in 50 healthy subjects (eight-16 subjects in each study).

Results
A significantly improved implicit motor learning was observed after 10 Hz AC stimulation only. No significant changes were observed in any of the analyzed frequency bands of EEG and with regard to the MEP amplitudes after AC or tSDCS stimulation. Similarly, if the anodal or cathodal DC stimulation was superimposed on 5, 10, and 15 Hz AC stimulation, the MEP amplitudes did not change significantly.

Conclusions
Transcranial application of weak AC current may appear to be a tool for basic and clinical research in diseases with altered EEG activity. However, its effect seems to be weaker than tDCS stimulation, at

This study was funded by the Bernstein Center for Computational Neuroscience (01GQ0432) (A.A.) and the Rose Foundation (C.P.).

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Submitted August 9, 2007; revised October 12, 2007. Accepted for publication October 14, 2007.

doi:10.1016/j.brs.2007.10.001

least in the present context of stimulus intensity and duration. Further studies are required to extend cautiously the safety range and uncover its influence on neuronal circuitries.

Keywords transcranial alternating current stimulation; transcranial magnetic stimulation; electroencephalogram; motor cortex; serial reaction time task

Neuroplasticity is an ongoing, self-organizing, adapting process that is widespread in cortical areas; it allows the brain to learn and adapt to new environmental situations. External influences on neuroplastic processes may be used for functional improvement of diseases, in particular for improving cortical functions such as learning or for studying brain function per se. Several methods exist to influence excitability of the brain by external means. The most well-known is transcranial magnetic stimulation (TMS) introduced about 20 years ago.[1] It followed transcranial electrical pulsed stimulation, which because of its painful stimulation characteristic never proceeded to a routine application method.[2] Another electrical approach, weak direct current stimulation of the brain (transcranial direct current stimulation [tDCS]), was investigated intermittently within the last four decades, but entered into neurobiologic and clinical plasticity research[3,4] only after its efficacy was unambiguously demonstrated by quantifying its effects during and after stimulation by single-pulse TMS over the motor cortex.[5] TDCS is able to induce long-lasting changes in cortical excitability in different brain regions in a reversible, relatively selective, painless, and safe manner. Generally, motor cortex excitability is enhanced by anodal and decreased by cathodal stimulation, as seen in studies that used single-pulse TMS. Even though in humans the effects of tDCS were first demonstrated on the motor system, it also influences visual, somatosensory, and cognitive functions.[6,7]

Transcranial alternating current stimulation (tACS) of the brain is a new technique. It aims to interfere with ongoing oscillations in the brain. This technique may have important implications for neuropsychiatric disorders, for example, it has been concluded that measures of gamma synchrony offer a valuable window into the core integrative disturbance in schizophrenia.[8] Recently, it was shown that inducing slow oscillation-like potential fields by transcranial application of oscillating potentials (0.75 Hz) during early nocturnal nonrapid eye–movement sleep, (a period of emerging slow wave sleep) enhances the retention of hippocampus-dependent declarative memory in healthy humans.[9] The slowly oscillating potential stimulation induced an immediate increase in slow wave sleep, endogenous cortical slow oscillations, and slow spindle activity in the frontal cortex. Brain stimulation with oscillations at 5 Hz—another frequency band that normally predominates during rapid eye–movement sleep—decreased slow oscillations and left declarative memory unchanged.

The aim of the current study is to further expand the stimulation spectrum between DC and AC stimulation. For this, we defined a frequency spectrum between 1 and 45 Hz transcranial electrical stimulation and analyzed motor-evoked potentials (MEPs) and electroencephalogram (EEG) spectrum before and after AC stimulation, both with and without an anodal and cathodal DC shift. Intracellular and EEG recordings in animals[10] have shown that modulating the excitability of cortical pyramidal cells generates a powerful and coherent feedback to the thalamus, resulting in highly coherent oscillations similar to those measured during natural sleep. These experiments are compatible with a role of the cortex in triggering and synchronizing oscillations generated in the thalamus, through cortico-thalamico-cortico loops, thus providing a possible cellular mechanism to explain the origin of large-scale coherent oscillations in the thalamocortical system. By stimulating the sensorimotor cortex with the use of tACS, oscillations can be triggered and may also reset ongoing rhythmic activity of local pacemaker networks consequently synchronizing brain oscillations.

Furthermore, behavioral tasks were used to study AC-driven changes in performance during a variant of the serial reaction time task (SRTT),[11-13] which is a standard paradigm to test implicit motor learning. In this task, subjects perform finger movements repetitively without being aware of a sequential order. We applied tACS or sham stimulation to the primary motor cortex during performance of the task.

Methods and materials

Subjects

Fifty subjects (24 men and 26 women) participated in the studies. None of the subjects took regular or acute medication. Participants gave informed written consent. The experiments were approved by the Ethics Committee of the University of Göttingen, and conformed to the Declaration of Helsinki. All subjects were right handed, according to the Edinburgh handedness inventory.[14]

Transcranial alternating current stimulation (tACS)

Ten healthy subjects (22-43 years old, mean age = 26.4 ± 8.0, 3 men) participated in the TMS study. Eight healthy subjects (22-32 years old, mean age = 25.75 ± 3.28, 3