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Electroencephalographic Effects of Transcranial Random Noise Stimulation in the Auditory Cortex

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ABSTRACT

Background: Transcranial random noise stimulation (tRNS) is an innovative technique of non-invasive electrical stimulation. tRNS over the parietal cortex has improved cognitive function in healthy controls and, applied to the auditory cortex, tRNS has shown beneficial effects on tinnitus.
Objective/hypothesis: Here we aimed to investigate the effects of tRNS over the auditory cortex on resting state and evoked activity in healthy subjects.
Methods: We used EEG to measure tRNS induced changes in resting state activity and in auditory steady state responses (ASSRs). Stimuli were 1000 Hz carrier frequency tones, amplitude modulated at 20 Hz and 40 Hz and applied in randomized order. Fourteen subjects participated in a placebo-controlled randomized design study; each received 20 min of tRNS applied over auditory cortices with 2 mA, with a one week interval between real and sham stimulation.
Results: We found a significant increase in the ASSR in response to 40 Hz frequency modulated tone and a non-significant trend toward an increase in mean theta band power and variability of the theta band power for the resting state data.
Conclusions: Our finding of tRNS induced increased excitability in the auditory cortex parallels previous findings of tRNS effects on motor cortex excitability and is in line with current concepts of tRNS mechanisms such as increase of stochastic resonance.

Introduction

Transcranial random noise stimulation (tRNS), transient direct current stimulation (tDCS) and transcranial alternating current stimulation (tACS) are non-invasive techniques of transcranial electrical stimulation (tES). These tES techniques are used in the attempt to modulate cortical activity and plasticity in both the healthy and diseased brain.

The tDCS technique uses direct current to stimulate the area of interest. The membrane potential of neuronal cells changes in response to tDCS based on electrode position; cathodal stimulation decreases membrane potential while anodal stimulation increases it [1]. It has also been demonstrated to alter spontaneous cortical activity [2]. In contrast, tACS uses alternating current at a fixed frequency to entrain cortical oscillations [3]. Both electrical stimulation techniques have been found to be effective for therapy. tDCS has been used for treatment of depression [4] and schizophrenia [5]; tACS has been found to be an effective treatment for Parkinson's disease [6]; both therapies have been used to treat tinnitus [7]. In the search for the optimal tACS frequency it has to be considered that different types of neurons respond to different frequencies of stimulation [8], that the cortical rhythms of healthy and pathological patients differ [3], and that the effect of stimulation between individuals can greatly vary [9]. Since the exact neuronal changes that occur within pathologies vary greatly between diseases and between patients, transcranial random noise stimulation (tRNS) has been developed as a therapeutic option that would potentially stimulate many different types of neurons and desynchronize different cortical rhythms.

Methodologically, tRNS is a form of tACS where the current alternates at random normally distributed frequencies instead of at a fixed frequency. However in contrast to tACS which modulates cortical oscillations, the proposed mechanism of tRNS is signal amplification through stochastic resonance [10]. An advantage of tRNS is that due to its variability in its time course neurons are stimulated largely independent of their spatial orientation. Thus as compared to tDCS, tRNS can circumvent problems of directionality of the induced electrical field. Accordingly tRNS has demonstrated

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more pronounced effects on motor cortex excitability than other excitatory transcranial stimulation methods like anodal tDCS or intermittent theta burst TMS [11]. Moreover with its balanced current stimulation tRNS is considered safer than tDCS, which induces a polarizing stimulation which in turn can induce skin lesions under certain conditions [10].

To date, few papers have been published about the effects of tRNS, those that do exist encompass a range of cognitive domains. Motor cortex excitability changes have been investigated and it has been found that there is increased motor cortex excitability for the hand region following tRNS stimulation as measured by motor evoked potentials (MEPs) [10,12]. A study looking at the influence of tDCS and tRNS on the primary motor cortex for the leg found that high spectrum tRNS significantly increased the excitatory activity of the leg muscle for up to 40 min post stimulation, with a peak at 30 min post stimulation [13]. The effects of tRNS are also dependent on the stimulation intensity, stimulation spectrum, and task demands. For stimulation frequency, it was found that at 1 mA the effects of tRNS on the motor cortex are excitatory, but at 0.04 mA the effects are inhibitory in terms of the hand MEP [11].

In regard to stimulation spectrum options for tRNS, there are three different ranges currently in use: full-spectrum (0.1–640 Hz), low spectrum (0.1–100 Hz) and high spectrum (101–640 Hz). It was found that for the motor cortex, high spectrum stimulation seems to be more effective than low spectrum stimulation [10]. High spectrum tRNS has also been found to be most effective for enhancement of mathematical ability speed [14] and perceptual learning [15]. Alternatively, a tRNS and fMRI study found that high spectrum stimulation had an excitatory effect on a resting brain, but decreased excitability when participants completed a motor task during the stimulation [16].

A few studies have directly contrasted the effects of tDCS with high spectrum tRNS and all have found differential effects. Concerning MEPs elicited from the leg area of the primary motor cortex, it was found that both tDCS and tRNS have excitatory effects, but that the time courses of these effects were different. tDCS took longer to show significant excitatory effects (20–60 min post stimulation), while tRNS was found to have an immediate effect on the amplitude of the elicited MEPs with a peak amplitude at 30 min and a total duration of increased excitation limited to 40 min [13]. A recent study suggests that tRNS has similar effects on motor cortex excitability like tDCS when it is used with an offset, which means that there is a mean electrode drift over the stimulation period in one direction. No effects were seen in this study for tRNS without offset [17].Two studies have compared tDCS, high spectrum tRNS and low spectrum tRNS over visual cortex. One found that tRNS had a larger effect on visual discrimination accuracy, an effect that was seen immediately after stimulation, when compared with the other types of stimulation [15]. The second found a trend toward significance for learning after tDCS and tRNS, but not for tACS [16]. Clinically, tDCS, tACS and tRNS over the auditory cortex were compared in regard to tinnitus loudness and the related distress. It was found that tRNS was more effective in reducing these symptoms than the other two electrical stimulation methods [7]. Additionally, a case report for the treatment of major depression found that tRNS was more effective in reducing symptoms than tDCS [18]. tRNS has also been proposed as a therapy for schizophrenia [19], and neuropathic pain [20]. While the literature on tRNS effects is growing both in healthy subjects and in patients, the information about the neuronal mechanisms is mainly restricted to studies investigating tRNS effects on motor cortex excitability.

Due to the paucity of available research on tRNS effects on non-motor cortical areas, the purpose of this paper is to examine the effects of tRNS over the auditory cortex on resting state and stimulus-evoked neuronal activity in the healthy brain. We used 20 min of high spectrum tRNS over the auditory cortex and compared the effects, measured by EEG, on resting state and auditory evoked activity by means of auditory steady state response (ASSR) after a real and sham stimulation. Changes in ASSR will provide direct evidence that tRNS is interfering with auditory evoked activity of the auditory cortex. Changes in resting state oscillations will provide evidence that tRNS is capable to modulate oscillatory resting-state brain activity.

Methods

Sample and procedures

Fourteen healthy students with normal hearing from the University of Regensburg participated in this study (7 female; 24.6 ± 1.9 years). All participants were right handed as tested by the Edinburgh Handedness inventory [21] and had no previous or present severe somatic, neurologic, or psychiatric problems. None of the participants was taking psychopharmacologic drugs. The study was approved by the local ethics committee of the University of Regensburg.

Each participant was tested in two sessions in a randomized order. Sessions lasted approximately 2 h and were spaced exactly one week apart to avoid carry over effects from the real stimulation. Prior to the first testing session each participant signed the informed consent and completed an audiometry measurement, a general questionnaire, and a vocabulary test providing IQ equivalents based score which are correlated with measures of general intelligence (Mehrfachwahl-Wortschatz-Intelligenztest B) [22]. Participants all had adequate hearing, defined by having no hearing loss above 35 dB for any frequency, and normal to high intelligence (mean IQ = 121.25, SD = 15.98).

During each testing session the participants were comfortably seated in a clinical arm chair for the duration of the experiment. At the first session, the auditory threshold was obtained for each ear for the two stimuli tones. The tones were created using a 1000 Hz carrier frequency which was frequency modulated at 20 Hz and 40 Hz. Auditory stimuli were set for presentation at 50 dB sensation level. Stimuli were administered via noise canceling insert headphones and triggered using Presentation® software (Version 0.71, www.neurobs.com). After the threshold was found in the first session and at the beginning of the second session, the EEG cap was applied and the electrode impedances were lowered to below 10 kΩ. Prior to the start of the EEG recording, subjects were instructed to sit as still as possible with their eyes closed without falling asleep.

The first part of the measurement consisted of 5 min of resting EEG followed by 7 min of EEG with auditory stimulation. The auditory stimulation consisted of 140 repetitions (70 for each tone) with a length of 800 ms, presented in a random order with a variable interval of 1800–2200 ms, for a total of 7 min. Next, the EEG recording was turned off and the participant received either real or sham tRNS for 20 min. Immediately following the stimulation, the EEG was started again and recorded during another 7 min of the same auditory stimulation followed by 5 min of rest (Fig. 1).

Electroencephalography (EEG) measurement

For EEG measurement we used a BrainAmp DC amplifier (Brain Products GmbH, Germany) with Ag/AgCl sintered pin electrodes (EASYCAP GmbH, Germany). A total of 50 head electrodes with the reference over FCz and the ground over AFz were recorded according to the international 10-10 EEG system, with six electrodes (those that lay over the tRNS electrodes) deactivated on each side of the head (because of tRNS in these ares; left: FT7, FC5, T7, C5, TP7, CP5; right: FT8, FC6, C6, T8, CP6, TP8). Signals were recorded with