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No modulatory effects by transcranial static magnetic field stimulation of human motor and somatosensory cortex

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ABSTRACT

Background: Recently, it was reported that the application of a static magnetic field by placing a strong permanent magnet over the scalp for 10 min led to an inhibition of motor cortex excitability for at least 6 min after removing the magnet. When placing the magnet over the somatosensory cortex, a similar inhibitory after effect could be observed as well.
Objective: Our aim was to replicate the inhibitory effects of transcranial static magnetic field stimulation in the motor and somatosensory system.
Methods: The modulatory effect of static magnetic field stimulation was investigated in three experiments. In two experiments motor cortex excitability was measured before and after 10 or 15 min of magnet application, respectively. The second experiment included a sham condition and was designed in a double-blinded manner. In a third experiment, paired-pulse SSEPs were measured pre and four times post positioning the magnet over the somatosensory cortex for 10 min on both hemispheres, respectively. The SSEPs of the non stimulated hemisphere served as control condition.
Results: We did not observe any systematic effect of the static magnetic field neither on motor cortex excitability nor on SSEPs. Moreover, no SSEP paired-pulse suppression was found.
Conclusion: We provide a detailed analysis of possible confounding factors and differences to previous studies on tSMS. After all, our results could not confirm the static magnetic field effect.

Introduction

Recently, transcranial static magnetic field stimulation (tSMS) was introduced as a novel brain stimulation technique [1]. According to the authors, it offers an easy applicable possibility to modulate the cortical excitability in the motor system by holding a strong permanent magnet over the scalp. They observed an inhibitory effect on the excitability of the human motor cortex following 10 min of tSMS, independent of magnet polarity. The inhibitory effect of tSMS was confirmed in a replication study [2] applying 15 min of tSMS. In both studies, the modulatory effect was quantified using motor evoked potentials (MEP) with transcranial magnetic stimulation (TMS). Within 6 min, the inhibitory effect on MEP amplitude vanished and amplitudes returned to baseline levels. Whereas in the first study no modulation of resting motor threshold (RMT) was found [1], in the replication study an inverse correlation between RMT and MEP amplitudes was observed [2]. Another study addressed the effects of 20 min of tSMS on short-latency intracortical inhibition (SICI) in the motor system [3]. SICI was found to reversibly increase after tSMS. In addition, MEP amplitudes were found to be decreased and RMT increased after tSMS and also after exposure to the SMF of an MRI scanner.

The inhibitory effect of tSMS found in the motor system has been shown to be measurable in other cortical regions. For instance, somatosensory evoked potentials (SSEPs) were used to investigate the effect of tSMS on the somatosensory cortex [4]. Applications of a magnet over S1 for 10 and 15 min were investigated. An attenuation of the P14N20 amplitude with the effect turning back to

Abbreviations: MEP, motor evoked potential; MRI, magnetic resonance imaging; RMT, resting motor threshold; SMF, static magnetic field; SSEP, somatosensory evoked potential; TMS, transcranial magnetic stimulation; tSMS, transcranial static magnetic field stimulation.

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baseline levels within 10 min was reported. During tSMS no change in the P14N20 amplitude was observed. A recent study of the same authors shows an inhibitory effect of tSMS over M1 on the N33 (P25N30) SSEP amplitude at C3' [5] but no effect on the P14N20 amplitude.

Moreover, findings in the visual cortex were reported. One study demonstrated a significant increase of alpha-wave activity recorded by electroencephalography (EEG) during occipital tSMS application [6]. It was suggested that an increase in alpha-wave activity indicates an inhibition of cortical excitability of the visual cortex. Furthermore, they showed that this effect was accompanied by a slowed performance in a visual search task during and after application of the magnet isolated on the most difficult task conditions.

In another study, it was demonstrated that tSMS of the visual cortex of two monkeys lead to reversible deficits in a visual detection task [7]. Moreover, tSMS led to a reduction of neural activity in two anesthetized cats [7].

Additionally, it was demonstrated that tSMS can be considered safe, as 2 h of tSMS do not increase marker levels of neural and glial lesion markers (Neuron specific enolase and S100) [8].

However, an actual working mechanism of tSMS has not been shown, and the cortical networks being involved in the inhibitory effects upon different cortices are still unknown. In the first study, it was argued that tSMS is unlikely to act on the level of corticospinal axons of pyramidal cells because MEPs evoked by transcranial electrical stimulation remain uninfluenced by tSMS [1]. Thus, it was suggested that the inhibitory effect of tSMS is very likely to act on a cortical level.

Our aim was to evaluate the tSMS induced inhibition by replicating the modulation in the motor and somatosensory system. Therefore, we performed two MEP-experiments in the motor system, with the second experiment being designed as a double-blinded study. Furthermore, we explored the effects of tSMS on the somatosensory cortex to replicate the findings in the somatosensory system.

Material and methods

Subjects

All subjects were screened for any neurological, psychiatric or endocrinologic disorders and regular drug intake. Additionally, all subjects were asked for cranial surgeries in their past and any metal objects implanted in the head region. All subjects of experiment 1 and 2 were right handed according to a modified version of the Edinburgh Inventory Scale [9]. Seventeen subjects participated in experiment 1, of which only 15 (7 male, mean age: 22.7 ± 3.3years) entered statistical analysis due to exclusion for reasons described below. Twenty subjects (10 male, mean age: 22.4 ± 2.2 years) participated in experiment 2, with two subjects already having participated in experiment 1. In the third experiment, 23 subjects were included. After measurement, three subjects were excluded because of an inconvenient signal-to-noise ratio, providing 20 subjects (10 male, Mean age: 24.1 ± 2.4) for statistical analysis. All subjects gave their written informed consent and were paid for their participation. The study followed the declaration of Helsinki and all experiments were approved by the Ethics Committee of the University of Ulm.

Measurement of excitability

MEPs in the resting muscle were evoked by single pulses of TMS and delivered using a Magpro X100 stimulator (Mag Venture A/S, Farum, Denmark), connected to a figure-of-eight coil (MC-B70).

First of all, the motor "hotspot" generating the highest amplitudes in the right first dorsal interosseous muscle (FDI) with suprathreshold TMS pulses, was identified and marked on the subject's scalp. The coil position was kept tangentially to the scalp with the handle pointing backwards in an angle of 45° to the sagittal plain [10]. Coil position at the hotspot was maintained using a neuronavigation system (BrainView 2, Fraunhofer IPA, Stuttgart). TMS intensity for monitoring excitability was calibrated individually to elicit a mean MEP amplitude of about 1 mV. Single TMS pulses for MEP monitoring were applied continuously with a frequency randomly jittering within 0.125 Hz and 0.2 Hz (interstimulus interval: 5–8sec) with the intention to decrease anticipation and habituation.

MEPs of the right FDI were recorded using surface electrodes in a belly-tendon montage. Signals were bandpassed (10–2000 Hz) and amplified using a Toennies universal amplifier (Erich Jaeger GmbH, Hochberg, Germany), sampled with 5000 Hz and online presented, analyzed, and stored on a PC for offline-analysis using DasyLab 13.0 (measX GmbH und Co. KG, Mönchengladbach, Germany).

Relaxation of the FDI was controlled online by an acoustic feedback signal and recordings with muscle activity were excluded offline. Two subjects in experiment 1 had to be excluded due to continuous pre-innervation of their FDI.

SSEPs in experiment 3 were recorded from C3' (left S1) and C4' (right S1) with a reference at FZ (according to the EEG 10–20 system). C3′ was defined as 4.5 cm occipital to the motor hotspot found over the left motor cortex by TMS. C4′ was marked after performing the same procedure on the right side. The median nerves were stimulated on both sides at the wrist with paired-pulses. The interstimulus interval was set to 30 ms to produce reliable paired-pulse suppression [11]. Stimulation intensity was set to 2.5 times sensory-threshold, thus subjects reported a noticeable prickling in the thumb, index- or middle finger.

On each side, 240 paired-pulses were administered, with a stimulation frequency of 2 Hz, first on the right wrist and after 30 s pause on the left one. Thus one block of both sided measurements lasted 4 min and 30 s.

As in the former experiments, bandpassing (10–2000 Hz) and amplification were realized using a Toennies universal amplifier. Signals were sampled with 5000 Hz and presented online using DasyLab 13.0. A time frame of 45 ms before the first stimulation pulse and 105 ms after the second pulse was recorded and stored for offline analysis of latency and peak to peak amplitudes.

Static magnetic field stimulation

For tSMS, a cylindrical neodymium magnet (NdFeB) of 30 mm height and 45 mm diameter (model S-45-30-N, Supermagnete, Gottmandingen, Germany) was used. The maximum energy density of the magnet was 358kJ/m3 (45MGOe) with a nominal strength of 628 N (64 kg) and a weight of 360 g. The surrounding magnetic field density perpendicular to the magnets pole surface was measured with a digital Teslameter (FM 210, „MagMess", Bochum, effective sensor area = 2.065 mm^2), yielding values in concordance with recently reported measurements on the same magnet class from the same manufacturer [12]. It was shown that field density remains comparable to studies using a slightly different magnet class with a diameter of 50 mm [5]. Assuming a scalp thickness of 2 cm, a maximum magnetic field density of about 160 mT is present at the cortical level perpendicular beneath the magnets south pole surface.

The magnet was held manually over the predetermined motor hotspot (experiments 1 and 2). In experiment 1, tSMS was applied for 15 min with the north pole pointing to the scalp, in experiment