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Static magnetic field can transiently alter the human intracortical inhibitory system

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HIGHLIGHTS

- Homogeneous and inhomogeneous static magnetic fields suppress the human motor cortex.
- Short-latency intracortical inhibition was increased after magnetic exposure.
- The enhancement of the GABAergic system can be used for clinical purposes.

ABSTRACT

Objective: Although recent studies have shown the suppressive effects of static magnetic fields (SMFs) on the human primary motor cortex (M1) possibly due to the deformed neural membrane channels, the effect of the clinical MRI scanner bore has not been studied in the same way.
Methods: We tested whether the MRI scanner itself and compact magnet can alter the M1 function using single- and paired-pulse transcranial magnetic stimulation (TMS).
Results: We found the transient suppression of the corticospinal pathway in both interventions. In addition, the transient enhancement of the short-latency intracortical inhibition (SICI) was observed immediately after compact magnet stimulation.
Conclusions: The present results suggest that not only the inhomogeneous SMFs induced by a compact magnet but also the homogeneous SMF produced by the MRI scanner bore itself can produce the transient cortical functional change.
Significance: Static magnetic stimulation can modulate the intracortical inhibitory circuit of M1, which might be useful for clinical purposes.

1. Introduction

Magnetic resonance imaging (MRI), which utilizes static and time-varying magnetic fields, is widely used in neuroscience research, as well as in daily clinical practice. Recent developments of various neuroimaging techniques using MRI enabled us to clarify functional brain activation depicted by BOLD signal change (Ogawa et al., 1990) and microstructural difference via water diffusion (Le Bihan et al., 1986).

The biological effects of electromagnetic fields have been extensively assessed for the time-varying magnetic fields (Kangarlu et al., 1999; de Vocht et al., 2006), where eddy currents might cause heating or nerve stimulation. In the case of clinical MRI, biological effects are generally considered harmless for the human body. In addition, static magnetic fields (SMFs) can produce biological effects in several ways (Aldinucci et al., 2003; Chakeres and de Vocht, 2005). The most common mechanism is eddy currents induced by displacements of the head in SMFs, which might cause vertigo or other transient sensations in MRI patients and volunteers (Glover et al., 2007; Mian et al., 2013). Other possible sources are Lorentz's force, magnetic force, and magnetic torque. However, little is known about the specific biological effects of SMFs on the human cortical neural circuit.

Recent studies suggested that local SMFs over the human primary motor cortex (M1) produced by a small high-powered neodymium magnet can modulate the cortical excitability, which can last a few minutes after the removal of the magnet (Oliviero et al.,

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2011; Silbert et al., 2013). Although the physiologic mechanism of this plastic change is not known, animal experiments indicated the alteration of the ion channel function embedded in the membrane (Rosen, 2003b). It is possible that high-powered SMFs can transiently affect the orientation of the membrane phospholipids due to their diamagnetic anisotropy.

However, it has been rarely studied whether homogeneous SMF including the whole head, such as an MRI scanner bore, can modulate the cortical excitability (Schlamann et al., 2010), similar to the compact magnet. This question is particularly important, because functional MRI is widely used in neuroscience research.

In addition, to selectively test the human M1 function and to clarify the physiologic effects of SMFs, the paired-pulse transcranial magnetic stimulation (TMS) technique is suitable, which can assess the human intracortical inhibitory circuits mediated by gamma-aminobutyric acid (GABA)-A receptors (Kujirai et al., 1993; Chen, 2004; Ziemann, 2004). Here, we tested the biological effects of SMFs on human M1 and, specifically, the effects of SMFs on the intracortical circuit function.

2. Methods

2.1. Subjects

Thirty neurologically healthy subjects (25 males and five females; age, 23.0 ± 2.5 years, mean ± SD) participated in this study. None of the participants had a history of neurological illness by self-report. All volunteers were right handed as determined by Oldfield's handedness inventory (Oldfield, 1971). The protocol was approved by the Ethics Committee of Kyoto University Graduate School of Medicine (Kyoto, Japan). Written informed consent was obtained from all subjects prior to this study.

2.2. SMF exposure for the motor cortex

We used two different methods to stimulate the left M1 by SMFs: the MRI scanner bore and the cylindrical neodymium magnet.

For inhomogeneous SMFs, we used a cylindrical nickel-plated (Ni–Cu–Ni) NdFeB magnet of 50-mm diameter and 30-mm thickness, with a weight of 442 g (Model N-50; NeoMag, Chiba, Japan). The maximum energy density was 406 kJ/m^3 (48–51 MGOe), with a nominal strength of 863 N (88 kg). The surface magnetic flux density was about 5340 G. The distance between the scalp and the M1 was about 20 mm. A nonmagnetic stainless-steel cylinder of the same size was used for sham stimulation as the control group. The magnet and nonmagnet were positioned by using an arm-type light stand (C-stand, Avenger, Cassola, Italy) over the representational area for the right abductor pollicis brevis (APB) muscle identified by TMS and held tangentially against the subject's head with the north pole oriented toward the subject. It has been reported that the magnetic polarity is irrelevant for neuromodulation (Oliviero et al., 2011).

For homogeneous SMFs, we used a 3.0-T MRI scanner bore (Siemens Trio; Siemens Medical Systems, Erlangen, Germany). No imaging was performed, so only SMFs were present. The head was guided to the desired orientation. Padding and wedges were used for comfort and stability. The participants remained stationary on the bed until the end of the intervention, and then slowly withdrawn after MRI exposure.

2.3. TMS measurement

TMS was performed with one Magstim 200 magnetic stimulator or two stimulators connected by a Bistim module that allows delivery of two magnetic stimulations through the coil. A single pulse of TMS was delivered using a flat figure-of-eight magnetic coil at the optimal scalp position to induce a motor response for the right APB. The optimal position was marked on the scalp by a soft-tip pen. The direction of the induced current was from posterior to anterior. The electromyogram (EMG) was recorded from the right APB. The EMG signals were amplified, band-pass-filtered (5–2000 Hz), and digitized at a rate of 10 kHz using the Map1496 system (Nihon-Santeku Co., Osaka, Japan). During TMS measurement, each subject was seated comfortably in a reclining armchair.

The resting motor threshold (rMT) for the right APB muscle was defined as the minimal stimulator output eliciting a motor evoked potential (MEP) of >50 μV in at least five out of 10 consecutive pulses. For the evaluation of the corticospinal excitability, we measured the peak-to-peak MEP amplitudes of the right APB muscle for 10 trials and the averages were taken. The intensity of the test stimulus was adjusted to produce an MEP of ~1 mV from the target APB muscle before the intervention (SI 1 mV).

We measured short-latency intracortical inhibition and facilitation (SICI and ICF) to evaluate the cortical inhibitory and excitatory neural circuits. Paired-pulse magnetic stimuli were applied over the left M1, with a subthreshold conditioning stimulus (CS) at 80% of the rMT followed by a suprathreshold test stimulus (TS) at SI 1 mV with interstimulus intervals (ISIs) of 3 and 12 ms, respectively (Groppa et al., 2012). The test MEP amplitudes were adjusted to be constant at ~1 mV throughout the experiment. The size of the mean conditioned response for SICI and ICF (10 trials each) was expressed as a percentage of the size of the mean test response alone. These techniques allowed us to investigate the different pools of cortical interneurons that modulate the inhibitory and facilitatory neural circuits (Paulus et al., 2008; Badawy et al., 2012).

The silent period (SP) was assessed during the isometric contraction of the right APB at ~20% of the maximum contraction. For SP recording, the stimulation intensity was adjusted to be 140% of the rMT of the right APB before the intervention. Its duration was taken from the onset of TMS to the return of voluntary EMG activity.

2.4. Experimental procedures

Twenty healthy subjects (18 males and two females) participated in the inhomogeneous SMFs intervention using a compact neodymium magnet and nonmagnet as sham stimulation. Subjects were asked to lie on a reclining chair to apply SMFs using the magnet over the left M1. The intervention duration was 20 min. In addition to amplitudes of MEP and rMT, we measured the SICI/ICF and SP for the right APB before, 0, 10, and 30 min after the intervention.

Ten other healthy subjects (seven males and three females) participated in the homogeneous SMF intervention using MRI. After measuring the basic TMS parameters (amplitudes of MEP and rMT) before the intervention, subjects were placed at the center of the MRI scanner bore where the most homogeneous magnetic field is achieved for 20 min without performing any task. TMS measurement was performed 0, 10, and 30 min after the MRI exposure (pre, post-0, post-10, and post-30). The TMS measurements took place in a separate room next to the scanner room.

2.5. Statistical analysis

Although the present experiment is not designed as a double-blind study, for MEP measurement, all the data were stored in a computer, and a blinded researcher checked the data without knowing the experimental information.

The normal distribution was tested using the Kolmogorov–Smirnov test.