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Modulation of somatosensory evoked potentials using transcranial magnetic intermittent theta burst stimulation ☆,☆☆

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Abstract

Objective: To study the modulation of somatosensory evoked potentials (SEP) using transcranial magnetic intermittent theta burst stimulation (iTBS) over human primary motor (M1) and sensory (S1) cortices.
Methods: Eleven healthy subjects participated in the study. Median nerve SEP were elicited by electrical stimulation at the right wrist before and after 600-pulse iTBS over M1 or S1 of the left hemispheres at the intensity of 80% active motor threshold.
Results: iTBS over S1 facilitated the N20o–N20p, N20p–P25 and P25–N33 amplitudes significantly and the maximal effect appeared 15 min after the stimulation. The facilitating effect was observed when the initial phase of the current in the brain was directed antero-medially, whereas the facilitation did not appear when the inverted coil direction was applied. On the other hand, no changes were observed after iTBS over M1. The latencies of the measured onsets and peaks were not affected through the experiments.
Conclusions: iTBS over S1 has the facilitating effect on the central somatosensory pathway, and the position and direction of the coil are the determinant factors of the effects.
Significance: iTBS can be useful technique to induce synaptic plasticity in human central somatosensory pathway.

Keywords: Transcranial magnetic stimulation; Theta burst stimulation; Somatosensory evoked potential; Somatosensory cortex; Neuroplasticity; Human

1. Introduction

Single pulse and repetitive transcranial magnetic stimulation (rTMS) have achieved wide acceptance as non-invasive methods to evaluate human cortical function. The effects of a single pulse of TMS last for less than 1 s, whereas rTMS has prolonged effects on cortical excitability that may outlast the stimulation by 30–60 min or more. Long lasting effects on cortical excitability have also been described after repeated pairings of a TMS pulse with somatosensory input, a procedure termed paired associative stimulation (PAS) (Wolters et al., 2005).

The majority of neurophysiological studies have involved the motor cortex and its connections. In contrast there is relatively little information on the effect of TMS over sensory cortex. Surprisingly, some previous studies have found that somatosensory evoked potentials (SEPs) are unaffected by TMS over the sensory cortex even though stimulation with the same parameters over M1 has powerful effects. Enomoto et al. (2001) used low frequency rTMS (1 Hz) at intensities known to produce suppression of corticospinal excitability when given over motor cortex. When applied over the sensory cortex, there was no effect on the SEP, whereas the SEP was suppressed after stimulation

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over motor cortex. In contrast, Wolters et al. (2005) used a paired associative method of conditioning the cortex. Repeated pairings of median nerve stimulation with a TMS pulse over sensory cortex increased the SEP if the interstimulus interval was N20 latency; there was no effect if the TMS stimulus was given over M1. Nevertheless, previous work of Tsuji and Rothwell (2002), who paired TMS over M1 with repetitive motor point stimulation of the FDI muscle and found enhanced SEPs, suggests that a weak effect of M1 stimulation in a PAS protocol can be boosted under certain conditions. Despite the varying results on SEPs, most studies agree that TMS of sensory cortex has repeatable effects on sensory thresholds in tactile (Knecht et al., 2003; Satow et al., 2003; Tegenthoff et al., 2005) and temperature modalities (Oliviero et al., 2005).

Theta burst stimulation (TBS) is a new technique of rTMS (Huang et al., 2005) designed on the basis of animal studies for the long-term potentiation and suppression (LTP/LTD) of synaptic connections. TBS has some advantages compared with regular rTMS: TBS can modulate the excitability of human cortex more effectively and rapidly with relatively weak stimulus intensity (i.e. 80% of active motor threshold) in a short time, and it can evoke either facilitating or inhibiting effects according to the stimulation mode (intermittent [iTBS] or continuous [cTBS], respectively). In a recent paper, Ishikawa et al. (2007) found that cTBS over sensory cortex reduced the amplitude of median nerve SEPs, particularly the P25 and later components, whereas cTBS over M1 had the opposite effect. The present short report complements that previous work by examining the effect of iTBS on SEPs to median nerve stimulation.

2. Subjects and methods

2.1. Subjects

Eleven healthy subjects (9 men and 2 women, aged 24–33 [mean ± SD; 28.5 ± 2.7 years]) participated the study and seven out of the eleven subjects completed all conditions of the experiments. The three experiments for a subject were carried out on separate 3 days at intervals of more than several days. The informed consent was obtained from each subject. The study was approved by the Joint Ethics Committee of the National Hospital for Neurology and Neurosurgery.

2.2. SEP

The subject was seated on a reclining chair during the experiment. SEPs were elicited by electrical stimulation of the right median nerve at the wrist at 3 Hz with a pulse width of 0.2 ms using a bipolar stimulator. At first, we obtained the conventional SEPs with the electrical stimulus intensity enough to evoke brisk muscle twitches at the thenar muscle. Second, less intense stimuli were given to evoke 'unsaturated' SEP, which had approximately 70–80% amplitude of the conventional one. The unsaturated SEPs were needed to assure the predicted facilitating effects of TBS. The stimulus intensities were usually about the mean value between the sensory and the motor threshold.

The active and reference Ag–AgCl surface electrodes were placed on the C3′ (2 cm posterior to C3 of International 10–20 system) and Fz, respectively. This montage was adopted according to the previous report (Enomoto et al., 2001). The impedance between the electrodes was kept below 5 kΩ. The peripheral sensory nerve action potentials (SNAP) were also recorded simultaneously with a pair of surface electrodes placed along the right median nerve at the cubital fossa to verify the stimulus intensity. The cathode electrode was placed 3 cm distal to the anode.

SEP and SNAP were recorded in epochs from −10 to 90 ms triggered by the electrical stimuli. The sampling rate was set at 5 kHz, and the potentials were amplified and filtered between 1.6 and 3000 Hz (−3 dB).

We collected and averaged 250 responses in each trial, and more than two trials were examined in each session to ascertain the reproducibility. SEPs were recorded in four sessions (before TBS, 0, 15 and 30 min after TBS).

2.3. Single-pulse TMS

The detail of the technique of TMS and TBS is described in the previous report (Huang et al., 2005).

We used a standard double (figure-of-eight) 70 mm coil (P/N 3191-00) connected to Magstim 200 rapid^2 stimulator (Magstim Co., Whitland, Dyfed, UK) which generates biphasic outputs.

We placed the surface recording electrodes on the right abductor pollicis brevis (APB) muscle with the belly-tendon method. The subject made the steady contraction of the muscle at approximately 10–20% of the maximal force during the measurement of the active motor threshold (AMT).

The coil was placed tangentially to the scalp over the hand motor cortex (M1) of the left hemisphere and the handle of the coil was directed posterolaterally, when the initial phase of the electrical current in the centre of the coil was directed towards the handle.

The series of single pulse TMS were delivered over M1 to obtain the maximal response from the APB muscle. The optimal position ('hot spot') and direction of the coil were confirmed. The stimulus intensity was controlled 1% stepwise with the stimulator's output indicator panel.

AMT was defined as the minimal single pulse intensity required producing motor evoked potentials (MEP) of greater than 200 μV on more than 5 out of 10 trials.

2.4. TBS

TBS is magnetic stimulation with triplets of 50 Hz in a 5 Hz rhythm. In iTBS, a 2-s train of TBS was repeated every 10 s for a total of 190 s (600 pulses). The intensity of iTBS was set at 80%AMT. For the stimulation of M1, the coil was placed over the hot spot with the handle directed posterolaterally. In case of the stimulation of the