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Comparison between short train, monophasic and biphasic repetitive transcranial magnetic stimulation (rTMS) of the human motor cortex

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Abstract

Objective: To compare motor evoked potentials (MEPs) elicited by short train, monophasic, repetitive transcranial magnetic stimulations (rTMS) with those by short train, biphasic rTMS.

Methods: Subjects were 13 healthy volunteers. Surface electromyographic (EMG) responses were recorded from the right first dorsal interosseous muscle (FDI) in several different stimulation conditions. We gave both monophasic and biphasic rTMS over the motor cortex at a frequency of 0.5, 1, 2 or 3 Hz. To study excitability changes of the spinal cord, we also performed 3 Hz rTMS at the foramen magnum level [Ugawa Y, Uesaka Y, Terao Y, Hanajima R, Kanazawa I. Magnetic stimulation of corticospinal pathways at the foramen magnum level in humans. Ann Neurol 1994;36:618–24]. We measured the size and latency of each of 20 MEPs recorded in the different stimulation conditions.

Results: 2 or 3 Hz stimulation with either monophasic or biphasic pulses evoked MEPs that gradually increased in amplitude with the later MEPs being significantly larger than the earlier ones. Monophasic rTMS showed much more facilitation than biphasic stimulation, particularly at 3 Hz. Stimulation at the foramen magnum level at 3 Hz elicited fairly constant MEPs.

Conclusions: The enhancement of cortical MEPs with no changes of responses to foramen magnum level stimulation suggests that the facilitation occurred at the motor cortex. We hypothesize that monophasic TMS has a stronger short-term effect during repetitive stimulation than biphasic TMS because monophasic pulses preferentially activate one population of neurons oriented in the same direction so that their effects readily summate. Biphasic pulses in contrast may activate several different populations of neurons (both facilitatory and inhibitory) so that summation of the effects is not so clear as with monophasic pulses. When single stimuli are applied, however, biphasic TMS is thought to be more powerful than monophasic TMS because the peak-to-peak amplitude of stimulus pulse is higher and its duration is longer when the same intensity of stimulation (the same amount of current is stored by the stimulator) is used.

Significance: This means that when using rTMS as a therapeutic tool or in research fields, the difference in waveforms of magnetic pulses (monophasic or biphasic) may affect the results.

Keywords: Repetitive transcranial magnetic stimulation (rTMS); Monophasic and biphasic pulses; Motor cortex

1. Introduction

Transcranial magnetic stimulation (TMS) is widely used in research and clinical practice. Present stimulators produce two different stimulus waveforms: in one, the induced currents are monophasic whilst in the other the induced current is biphasic. Single pulse studies have shown that there is a difference in the effectiveness of these two waveforms (Corthout et al., 2001; Di Lazzaro et al., 2001; Kammer et al., 2001) that are consistent with the results of the mammalian phrenic nerve stimulation (Maccabee et al., 1998). Thus for a given initial amplitude

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of stimulation pulse, biphasic stimulation is more powerful than monophasic stimulation. In addition, the most effective direction of the initial current for inducing MEPs from the hand area of the motor cortex is opposite between monophasic and biphasic TMS (Kammer et al., 2001).

Less is known about the differences between monophasic and biphasic repetitive TMS (rTMS). Most of studies have used biphasic rTMS (Berardelli et al., 1998, 1999; Chen et al., 1997; Di Lazzaro et al., 2002; Jennum et al., 1995; Maeda et al., 2000a,b; Modungno et al., 2001; Pascual-Leone et al., 1994; Romeo et al., 2000) and indicate that high frequency stimulation tends to induce facilitatory after-effects and low frequency rTMS inhibitory after-effects (Chen et al., 1997; Maeda et al., 2000a,b; Sommer et al., 2002a) while there is a moderate interindividual variability (Maeda et al., 2000a). There is only one report of a comparison of the effects during and after long train rTMS between monophasic and biphasic pluses (Sommer et al., 2002b). Subthreshold 1 Hz monophasic rTMS induced stronger suppressive after-effects on the motor cortex than biphasic rTMS. They compared bins of 18 MEPs during long lasting rTMS (total 900 pulses). No studies have been done to compare effects during short train rTMS between two waveforms of rTMS, The aim of the present study is to extend these observations to a range of different rTMS frequencies with shorter trains (total 20 pulses that is about the same as one bin of Sommer's report) of stimulation at suprathreshold intensity. We will show that 2 or 3 Hz monophasic rTMS had marked facilitatory influence on the motor cortex, whereas biphasic rTMS evoked relatively stable responses.

2. Subjects and methods

2.1. Measurements of induced currents by monophasic and biphasic TMS and estimates of evoked magnetic field

Electric fields elicited by different types of stimulation were monitored using a search coil. The current was transformed into voltage with the resistance within the oscilloscope. The search coil was held parallel to the surface of the stimulating coil. Evoked magnetic field can be estimated by integrating the output from the search coil with an active electronic integrator. The oscilloscope could monitor the changes of both magnetic fields around the stimulating coil and induced currents below the coil.

2.2. Subjects

Thirteen healthy volunteers (11 men and two women, 25–48 years old) took part in the experiments after giving their written informed consent. The experimental procedures used here were approved by the Ethics Committee of the University of Tokyo according to the Declaration of Helsinki. No side effects were noted in any of the individuals tested.

2.3. Electromyographic (EMG) recordings

Surface electromyograms (EMG) were recorded from the first dorsal interosseous muscle (FDI) in all the subjects with Ag-AgCl surface cup electrodes (9 mm in diameter). The active electrode was placed over the muscle belly and the reference over the metacarpophalangeal joint of the index finger. Responses were amplified through filters set at 100 and 3 kHz and recorded by a MEB 2000 (Nihon Kohden, Tokyo, Japan) for the off-line analysis after the experiments. During the experiments subjects maintained the target muscle at rest using an audiovisual feedback of EMG discharges. A session in which any EMGs due to unintentional contraction were recorded was discarded in the analysis.

2.4. Single-pulse transcranial magnetic stimulation (TMS) of the motor cortex

Transcranial magnetic stimulation (TMS) was performed with a figure-of-eight-shaped coil connected to a Magnetic Stimulator (Nihon Kohden, Tokyo, Japan). We gave both monophasic and biphasic repetitive magnetic stimuli with this stimulator. Before the main experiments, we determined the position of the hand motor area in every subject by using monophasic TMS. We held the coil tangentially to the skull with the handle pointing backwards at about 45° laterally, that is perpendicular to the central sulcus and known to elicit most effective induced currents for motor cortical activation (antero-medially directed currents in the brain) (Sakai et al., 1997). To determine the hand motor area, we stimulated several positions separated by 1 cm each other with the same intensity and defined the motor cortex as the site where the largest responses were elicited by the same intensity stimulation. We also confirmed that this position was near to the hot spot for FDI in other stimulation conditions (monophasic, posteriorly directed TMS and biphasic TMSs) by comparing the size of MEPs elicited by those TMSs over several positions separated from the nearest position by 1 cm. The hot spot was the same position in all stimulation conditions used here at least in 1 cm spatial resolution. This is consistent with our previous comparisons of hot spots among eight different coil orientations (Sakai et al., 1997). However, to detect smaller differences in the hot spot positions, in three of the subjects, we explored them in four different stimulation conditions more precisely and compared them among stimulation conditions. The differences in distance between the antero-medially directed monophasic TMS and other stimulation conditions were within 5 mm. In those three subjects, responses elicited by rTMS at such hot spots had the same tendency of the size of responses as those elicited by rTMS at the hot spot for antero-medially directed monophasic stimulation. In the later analyses, therefore, we compared responses evoked by four kinds of rTMS over the hot spot for antero-medially directed current. That position was