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Impact of pulse duration in single pulse TMS

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ABSTRACT

Objective: The intensity of transcranial magnetic stimulation (TMS) is typically adjusted by changing the amplitude of the induced electrical field, while its duration is fixed. Here we examined the influence of two different pulse durations on several physiological parameters of primary motor cortex excitability obtained using single pulse TMS.

Methods: A Magstim Bistim^2 stimulator was used to produce TMS pulses of two distinct durations. For either pulse duration we measured, in healthy volunteers, resting and active motor thresholds, recruitment curves of motor evoked potentials in relaxed and contracting hand muscles as well as contralateral (cSP) and ipsilateral (iSP) cortical silent periods.

Results: Motor thresholds decreased by 20% using a 1.4 times longer TMS pulse compared to the standard pulse, while there was no significant effect on threshold adjusted measurements of cortical excitability. The longer pulse duration reduced pulse-to-pulse variability in cSP.

Conclusions: The strength of a TMS pulse can be adjusted both by amplitude or pulse duration. TMS pulse duration does not affect threshold-adjusted single pulse measures of motor cortex excitability.

Significance: Using longer TMS pulses might be an alternative in subjects with very high motor threshold. Pulse duration might not be relevant as long as TMS intensity is threshold-adapted. This is important when comparing studies performed with different stimulator types.

1. Introduction

Transcranial magnetic stimulation (TMS) is a non-invasive technique which allows stimulation of cortical neuronal networks in the awake behaving human subject. It has become a well established diagnostic tool for conduction studies of central motor pathways in neurology and neurosurgery. It is also a valuable research tool for the assessment of cortical excitability in the motor and visual systems as well as for the modulation of cortical excitability in different cortical regions. Repetitive TMS is capable of inducing changes of cortical excitability outlasting the duration of stimulation, thus making it a potential therapeutic option in a variety of neuropsychiatric disorders (Fregni and Pascual-Leone, 2007; Kobayashi and Pascual-Leone, 2003; Rossini and Rossi, 2007).

The technique of TMS is based on the principle of electromagnetic induction and uses a local rapidly changing magnetic field to induce an electrical field, which in turn leads to an electrical current in conductive tissue without attenuation by structures with high electrical impedance (e.g. the skull) or the necessity of direct contact with electrodes. The basic stimulator design which is still used in all commercially available stimulators was first introduced in 1982 (Polson et al., 1982) for peripheral nerve stimulation and later applied to transcranial cortical stimulation in 1985 (Barker et al., 1985). In order to achieve a sufficiently high rate of change in the magnetic field, a high voltage from a capacitor bank is discharged via a magnetic coil. These components form an oscillator (RLC-circuit) with a resonant frequency f_0 mainly determined by the capacitance C of the stimulator and the inductance L of the coil according to the following equation (simplified for an undamped resonant circuit):

$$f_0 = \frac{1}{2\pi\sqrt{LC}} \tag{1}$$

In conventional magnetic stimulators it is only possible to interrupt the effective stimulus duration at quarters of the full oscillation period leading to the so called 'monophasic' pulse after the first quarter cycle, a 'halfsine' pulse after the first two quarter cycles and the 'biphasic' pulse after a full period (Sommer et al., 2006). In contrast to electrical stimulation, the pulse duration in magnetic stimulation (regarding a single phase) cannot easily be adjusted as this requires changing the resonant frequency and thus

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the stimulator hardware. The intensity of the TMS pulse is controlled by the capacitor voltage, which determines the initial steepness of the induced time-varying magnetic field and thereby the amplitude of the induced electrical field.

Using six different capacitor configurations in order to achieve monophasic TMS pulses of six distinct pulse durations, Barker and colleagues demonstrated that a longer pulse requires more stored energy and leads to stronger coil heating compared to shorter pulses (Barker et al., 1991). However, the stimulation threshold in terms of capacitor voltage (which is proportional to the commonly used percentage of maximum stimulator output) is lower with a higher pulse duration. Comparing the stored energy required to evoke threshold motor responses at different stimulus intensities to analogue measurements with electronically defined time constants, Barker and colleagues were able to estimate cortical membrane time constant in man to be in the order of 150 μs.

Controlling the pulse duration of TMS might open the possibility to preferentially stimulate a specific neuronal population in a spatially overlapping cortical network. It has previously been hypothesized that selection of a shorter pulse duration reduces stimulation of peripheral sensory nerves at skin level for a given intensity of motor cortex stimulation (Geddes, 1987), which has been confirmed by a more detailed simulation (Suihko, 2002).

So far the effect of pulse duration has only been investigated for motor threshold (Barker et al., 1991). The objective of the present study was to systematically investigate the effect of two distinct pulse durations offered by a commercially available TMS system on a set of single pulse parameters of corticospinal excitability.

2. Material and methods

2.1. Subjects

Twelve healthy right-handed human subjects (6 women and 6 men, age range 19–43 years) participated in the experiment after giving informed consent. All subjects were non-smokers. Experimental procedures had the approval of the Ethics Committee of the University of Göttingen and were performed according to the ethical standards laid down in the Declaration of Helsinki.

2.2. Stimulator setup

A commercially available Magstim Bistim^2 stimulator setup (The Magstim Company Limited, UK) was used to produce monophasic TMS-pulses of two distinct durations. This setup allows discharging two identical capacitor banks of the connected Magstim 200^2 stimulators simultaneously through the same coil. In this configuration the two capacitor banks are connected in parallel thus doubling the capacitance of the system. For a monophasic pulse the first phase of the induced electrical field is approximately a quarter cycle of a cosine wave followed by a relatively low electrical field in opposite direction induced by a slow decay of the magnetic field. Thus the first phase of the monophasic pulse can be considered as the "active" part so that calculations regarding pulse duration can be derived from the cosine shape. According to Eq. (1) doubling the capacitance of the system leads to a decrease of the resonance frequency of the system and thus an increase of the pulse duration by a factor of $\sqrt{2}$ ($\approx$1.4) compared to a single stimulator. All parameters of corticospinal excitability were measured both in the simultaneous configuration and with a single stimulator discharging through the Bistim module in order to keep all other components of the system comparable. Fig. 1 illustrates the time course of the magnetic field and the induced electrical field. The magnetic field rise time was 82 μs for the single stimulator and 114 μs for the simultaneous mode.

Transcranial magnetic stimulation (TMS) was applied over the left primary motor cortex. The position of a figure-of-8 coil (70 mm standard double coil 9925-00, coil inductance approximately 16.35 μH, The Magstim Company Limited, UK) connected to the Bistim^2 setup via a coil adapter (3110-00, The Magstim Company Limited, UK) was adjusted to yield maximum MEP amplitudes from the right first dorsal interosseus muscle (FDI, target muscle). MEPs from the right abductor digiti mini muscle (ADM, non-target muscle) were registered to test the focality of stimulation. The coil was held tangentially to the skull with the coil handle pointing posterolaterally at an angle of 45° to the sagittal plane inducing a posterior-anterior directed current in the brain.

Surface EMG was recorded with Ag/AgCl cup electrodes in a belly-tendon montage from the FDI bilaterally and the ADM of the right hand. Analogue signals were band-pass filtered (2–3000 Hz) and amplified (Digitimer D360, Welwyn Garden City, Hertfordshire, UK), sampled at a rate of 5 kHz using a CED Micro 1401 mk II (Cambridge Electronic Design, Cambridge, England) and stored on a lab computer for offline analysis using customized Signal 2.16 software (Cambridge Electronic Design, Cambridge, England).

2.3. Parameters of corticospinal excitability

All of the following parameters were first measured with one of the pulse configuration and after a break of at least 10 min with the other one. The order of pulse configurations was pseudorandom and counterbalanced.

Resting motor threshold (RMT) was determined as the lowest stimulator output at which at least 5 out of 10 consecutive TMS pulses induced MEPs of >50 μV in amplitude in the target muscle (right FDI) with all recorded muscles at rest. Values are given as a percentage of maximum stimulator output (MSO). For active motor threshold (AMT) subjects were asked to keep a tonic contraction of the right FDI of approximately 20–30% of maximum EMG activity. The minimum stimulator output at which at least 5 out of 10 TMS pulses induced MEPs of >200 μV in amplitude was considered the AMT.

MEP-amplitudes were measured peak to peak as recruitment curves in the relaxed muscle both for FDI and ADM of the right hand using intensities of 100–160% RMT. Stimulus intensities were adjusted to RMT to account for interindividual differences. The range of intensities was chosen because 160% RMT was the highest intensity that could be reached in all subjects tested. The intensity was increased in steps of 10% RMT with 10 MEPs recorded at each level. In addition to MEP amplitudes we measured MEP latency, duration of the first phase of the MEP and the area under the first phase of the MEP in the 160% condition only.

MEP amplitudes were also measured in the tonically contracting muscle at stimulus intensities of 120%, 140% and 160% AMT. Subjects were instructed to keep 20–30% of maximum voluntary force in the target and non-target muscles. A sufficient level of activation was visually controlled by the investigator in terms of mean rectified EMG activity. Again 10 MEPs were recorded at each intensity level. In these recordings also the contralateral (cSP) and ipsilateral (iSP) silent period (Ferbert et al., 1992) were assessed. The duration of the cSP was measured for each individual TMS pulse from the time of the stimulus to the point where the rectified EMG activity first reached the level of baseline activity determined in the 100 ms preceding the TMS stimulus. The iSP was assessed in the tonically contracting left FDI muscle in the 160% AMT condition only. Data of all 10 recordings were rectified and averaged. Onset of the iSP was defined as the first point where the EMG activity fell below prestimulus EMG activity determined in the 100 ms preceding the TMS stimulus. The duration of the iSP was measured from the onset of the iSP to the point where the EMG-activity again