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Pulse Width Affects Scalp Sensation of Transcranial Magnetic Stimulation

Angel V. Peterchev [a,b,c,*], Bruce Luber [a,1], Gregory G. Westin [d], Sarah H. Lisanby [a,e,1]

[a] Department of Psychiatry and Behavioral Sciences, Duke University, Durham, NC, USA
[b] Department of Biomedical Engineering, Duke University, Durham, NC, USA
[c] Department of Electrical and Computer Engineering, Duke University, Durham, NC, USA
[d] Division of Vascular and Endovascular Surgery, New York University Langone Medical Center, New York, NY, USA
[e] Department of Psychology and Neuroscience, Duke University, Durham, NC, USA

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ABSTRACT

Background: Scalp sensation and pain comprise the most common side effect of transcranial magnetic stimulation (TMS), which can reduce tolerability and complicate experimental blinding.
Objective: We explored whether changing the width of single TMS pulses affects the quality and tolerability of the resultant somatic sensation.
Methods: Using a controllable pulse parameter TMS device with a figure-8 coil, single monophasic magnetic pulses inducing electric field with initial phase width of 30, 60, and 120 µs were delivered in 23 healthy volunteers. Resting motor threshold of the right first dorsal interosseus was determined for each pulse width, as reported previously. Subsequently, pulses were delivered over the left dorsolateral prefrontal cortex at each of the three pulse widths at two amplitudes (100% and 120% of the pulse-width-specific motor threshold), with 20 repetitions per condition delivered in random order. After each pulse, subjects rated 0-to-10 visual analog scales for Discomfort, Sharpness, and Strength of the sensation.
Results: Briefer TMS pulses with amplitude normalized to the motor threshold were perceived as slightly more uncomfortable than longer pulses (with an average 0.89 point increase on the Discomfort scale for pulse width of 30 µs compared to 120 µs). The sensation of the briefer pulses was felt to be substantially sharper (2.95 points increase for 30 µs compared to 120 µs pulse width), but not stronger than longer pulses. As expected, higher amplitude pulses increased the perceived discomfort and strength, and, to a lesser degree the perceived sharpness.
Conclusions: Our findings contradict a previously published hypothesis that briefer TMS pulses are more tolerable. We discovered that the opposite is true, which merits further study as a means of enhancing tolerability in the context of repetitive TMS.

Introduction

Transcranial magnetic stimulation (TMS) and repetitive TMS are increasingly used as a safe and noninvasive tool to modulate brain function for research and therapeutic purposes. A significant drawback of TMS is, however, the unpleasant and potentially painful sensation experienced during pulse delivery [1–4]. Since the induced electric field drops off with distance from the TMS coil, the field in the tissue underlying the coil is stronger than at the cortical target. We have estimated that the electric field in the scalp is approximately twice as strong as in the underlying cortex for a conventional 70 mm figure-8 coil [5]. There are a number of possible causes of the somatic sensation from TMS at any specific scalp location. The trigeminal nerve is likely stimulated for anterior targets [2,6]. The electric field may activate nociceptors in the scalp, periosteum, and perhaps meninges directly underneath the coil [1]. Nociceptor Aδ fibers, which typically produce pain that is sharp, pricking, and temporally linked with the stimulus, are more likely to be recruited due to their shorter time constant and lower rheobase compared to C fibers, which tend to produce slow, dull, burning pain [6–8]. Similarly, sensory A-fibers related to mechanoreception, thermal reception, and muscle proprioception may be directly activated

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[*] Corresponding author. Fax: +1 919 681 9962.
E-mail address: angel.peterchev@duke.edu (A.V. Peterchev).

[1] Now at the National Institute of Mental Health. Dr. Bruce Luber and Dr. Sarah H. Lisanby contributed to this article while at Columbia University and Duke University, prior to joining NIMH. The views expressed are their own (the authors) and do not necessarily represent the views of the National Institutes of Health or the United States Government.

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[1,6–8]. Further, sensation caused by directly induced muscle contraction can be relevant, particularly away from the vertex [2,8]. Another possible source of sensation is the mechanical vibration (tapping) generated by the electromagnetic forces within the coil, which can activate mechanoreceptors in the scalp [1,9]. Finally, the synchronous auditory stimulation via both bone and air conduction (partially attenuated by earplugs) may modulate the sensation [10]. Any combination of these factors can affect tolerability, and in addition, the sensation of TMS complicates the blinding of subjects to experimental conditions and requires sophisticated sham procedures to replicate the sensation [11,12].

Various approaches to reducing the scalp pain from TMS have been investigated or proposed. Topical anesthetics may reduce rTMS related scalp pain in some subjects, but the robustness of the effect and optimal application need further study [1,3]. In a small sample of healthy subjects, scalp injection of lidocaine or lidocaine and epinephrine reduced scalp pain and was more tolerable than the rTMS pain, although the lidocaine and epinephrine injection may result in subsequent hypersensitivity [1]. As well, introducing a thin foam pad between the coil and the scalp may slightly reduce scalp pain [1], but it is not clear whether this effect is significant and whether it is due to dampening of the mechanical vibration produced by the coil or merely to reduction of the electric field strength in the scalp due to the extra spacing between the coil and the scalp introduced by the pad. At present, none of these methods have found widespread use.

Device design approaches to mitigate TMS induced scalp pain include injecting current through superficial electrodes to counter the TMS induced currents in the scalp, a small secondary surface coil suppressing the surface field, or increasing the size of the TMS coil [13]. Injecting current through scalp electrodes is impractical and may only shift spatially, but not reduce, the field maximum [13]. A secondary surface coil suppressing the surface field is available commercially [14] but it only reduces the peak electric field in the scalp by less than 13% [13]. Finally, increasing the coil size can substantially reduce the scalp field strength, but reduces the focality of the coil resulting in potentially wider spread suprathreshold stimulation both in the scalp and in the brain [13,15].

The device-based approaches described above aim to reshape the electric field spatial distribution to reduce the scalp sensation. Another potential device-based venue is to alter the pulse waveform characteristics so that sensation is modified while cortical effects are preserved. Specifically, the pulse width may affect the relative degree to which various neuronal types are recruited. For example, in peripheral nerves, the motor threshold is lower than the sensory threshold for brief pulses, whereas it is higher than the sensory threshold for longer stimuli [16]. It has been hypothesized that the ratio of cortical motor threshold to scalp sensory threshold may also be lower for brief pulses than for long stimuli, potentially leading to better tolerability of the former [17]. This hypothesis was supported by a simulation study of transcranial electrical stimulation that modeled the activation thresholds for motor cortex pyramidal axons and scalp Aδ nociceptor fibers [18]. Furthermore, briefer pulses decrease the coil energy [19,20] and the coil acoustic output, reducing the loudness [21] and possibly the mechanical tapping as well.

This question of whether pulse width affects discomfort from stimulation is relevant because there are differences in the pulse width across commercial TMS devices and there are now devices that allow adjustment of the pulse width. For example, among the FDA-approved TMS devices for the treatment of depression, there is a twofold range of pulse widths (185–370 µs biphasic pulse period) [22–25]. As well, some commercial TMS devices allow adjustment, albeit limited, of the pulse width [26,27]. Finally, we have developed a family of TMS devices with controllable pulse parameters (cTMS) that allow adjustment of the pulse width over a substantial range, potentially allowing optimization of this parameter [28–30].

In this study we used a cTMS device to explore the effect of pulse width and pulse amplitude on the sensation reported by subjects receiving single TMS pulses over the dorsolateral prefrontal cortex.

Material and methods

This study was part of a larger study that also characterized the corticospinal tract response to TMS with various pulse widths [20]. The general subject and methods information is provided in Reference [20] and summarized below in addition to specific information about the TMS sensation investigation.

Subjects

This study was conducted at New York State Psychiatric Institute/Columbia University where it was approved by the Institutional Review Board. After consenting and screening [20], 23 healthy subjects took part in the TMS sensation study (age range = 19–49 years, mean ± SD = 28 ± 6.6 years; 16 female).

Experimental session

The study comprised a single TMS session. The subjects were seated in a chair, and their heads were supported by a head rest and stabilized between the TMS coil and a padded bracket countering the coil pressure. The subjects wore earplugs for hearing protection. The TMS session consisted of motor threshold determination and IO curve measurement reported previously [20], followed by single-pulse stimulation of the dorsolateral prefrontal cortex reported here, always administered in that order. To evaluate potential side effects, before and after the TMS session subjects were given a side effects checklist and a computerized five-item visual analog scale characterizing mood.

Transcranial magnetic stimulation

This study used a custom built cTMS device that generates monophasic magnetic pulses with independent control of the amplitude and width of the initial phase of the induced electric field (see Fig. 1) [20,28]. The cTMS device was connected to a commercial 70 mm

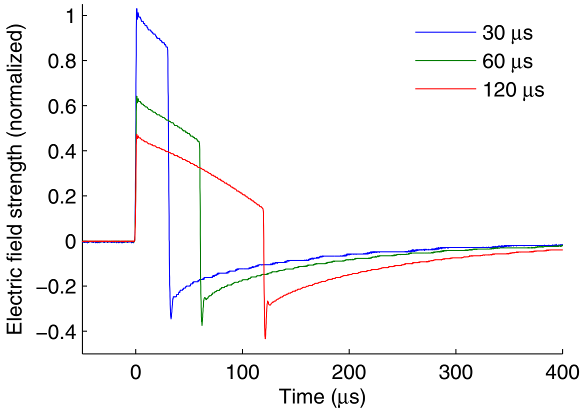

Figure 1. TMS electric field waveforms for pulse widths of 30, 60, and 120 µs. The waveforms were measured with a search coil placed under the TMS coil [20,28]. The pulse amplitude was scaled by the average motor threshold for the respective pulse width in order to illustrate the relative pulse amplitude delivered in the three pulse width conditions.