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Theta burst stimulation: Technical aspects about TMS devices

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Introduction

Theta burst stimulation (TBS), delivers bursts of TMS pulses at gamma frequency (e.g. 50 Hz) which are repeated at theta frequency intervals (e.g. 5 Hz). In animals, TBS can induce long-lasting neural changes in neuronal behaviour [1–3]. Similar observations have been reported when applying TBS in humans [4,5] using TMS. Continuous TBS (cTBS) applies three pulses at 50 Hz frequency (the burst) every 200 ms (5 Hz) [4,5]. There is considerable inter- and intra-individual variability in response to TBS, despite comparable stimulation parameters and methodologies across studies [6–10].

Here we measured the consistency of magnetic fields produced by commercial stimulators when delivering a cTBS protocol, to assess whether variation in magnetic fields within and across bursts, and across a range of intensities, may provide a source of variability.

We measured the intensity of magnetic pulses delivered by MagVenture MagPro×100 (MagVenture, Lucernemarken, Denmark) and by Magstim Rapid2 (Magstim Co., Whitland Dyfed, UK) when a cTBS protocol is applied during 40 sec (600 pulses) [4]. The intensity of the stimulation was set at 40, 50, 60, 70, 80, 90 and 100% of the maximum stimulator output (MSO) for MagProX100 and 50% MSO for Magstim-Rapid2 (maximal intensity allowed at 50 Hz). We used a figure-of-eight coil for both stimulators, MagVenture MCF-B65 coil and Magstim D70-Alpha-Flat coil.

We measured the modulus of the time-varying magnetic field produced by the figure-of-eight coil by means of a custom-made isotropic triaxial probe consisting of single-turn shielded coils of 1 cm in diameter. The probe was placed in air at one cm from the surface of the figure-of-eight coil, and it measured simultaneously the three components of magnetic field with temporal resolution.

We analysed the cTBS protocols in two different ways. First, we evaluated the intensity of the three pulses of the first burst to check if stimulators/coils are able to deliver the same intensity in the three burst components. Second analysis consisted of analysing the three pulses of the burst throughout the whole protocol (600 pulses/200 bursts) to check if stimulators/coils are able to maintain the same intensity over time.

The magnetic field produced by the first pulse at 100% MSO was 1.96 T for MagProX100.

First burst analysis

At 40% and 50% of MSO, the second and the third pulses of the first burst were within 1% of the first (see Figure and supplementary Table). Magstim-Rapid2 at 50% MSO produced similar results. However, at 100% MSO, the second pulse of the first burst diminished with respect to the first pulse by 0.28 T (14.3%) for MagProX100. The third pulse of the first burst diminished to 1.48 T (24.7% of the first pulse).

More in details, the second pulse of the first burst was diminished with respect to the first pulse at intensity of 60–90% MSO for MagProX100 as follows: 60% MSO, 0.03 T; 70% MSO, 0.09 T; 80% MSO, 0.16 T; 90% MSO, 0.23 T; 100% MSO, 0.28 T. Thus, compared to the first pulses, the intensity of second pulse decayed depending on the MSO used (from 14.3% for 100% MSO to 2.4% for 60% MSO). At an intensity of 60%–90% MSO, the third pulse of the first burst diminished with respect to the first pulse for MagProX100 as follows: 60% = 0.05 T, 70% = 0.16 T, 80% = 0.27 T, 90% = 0.39 T, 100% = 0.48 T. Compared to the first pulses, the intensity of third pulses decayed depending on the MSO used (from 24.7% for 100% MSO to 4.3% for 60% MSO).

cTBS protocol analysis

The first pulse was virtually unchanged at the end of the 200 bursts. The last first pulses (pulse 598) were: 100% MSO = 1.95 T; 90% MSO = 1.77 T; 80% MSO = 1.57 T; 70% MSO = 1.35 T; 60% MSO = 1.19 T. Compared to the first pulses (pulse n 1) the variation of pulses over time was less than 1%.

Overall, the second and third pulses diminished over the course of the TBS protocol (Fig. 1 and supplementary Table). Pulse 599: 100% MSO = 1.63 T; 90% MSO = 1.51 T; 80% MSO = 1.38 T; 70% MSO = 1.24 T; 60% MSO = 1.14 T. Compared to the second pulse, the intensity of magnetic pulses decayed over time depending on the MSO used (from 3% for 100% MSO to 1.8% for 60% MSO). For the last pulse in the last burst (pulse 600), the intensities were: 100% MSO = 1.40 T; 90% MSO = 1.34 T; 80% MSO = 1.26 T; 70% MSO = 1.16 T; 60% MSO = 1.11 T. Compared to the third pulses of the first burst (pulse n 3), the intensity of magnetic pulses decayed over time depending on the stimulator intensity used (from 5.4% for 100% MSO to 2.5% for 60% MSO).

We show that at 50% of MSO both MagProX100 and Magstim-Rapid2 are suitable for cTBS for at least 40 sec, with a constant intensity of all the pulses (600 pulses/200 bursts tested). At intensities above the 50% of the MSO, MagProX100 (Magstim-Rapid2 not tested) delivers bursts that are composed by pulses that do not have the same intensity. The third pulse of each burst is the most affected. These decreases in pulse amplitude likely arise from technical limitations of the stimulator electrical

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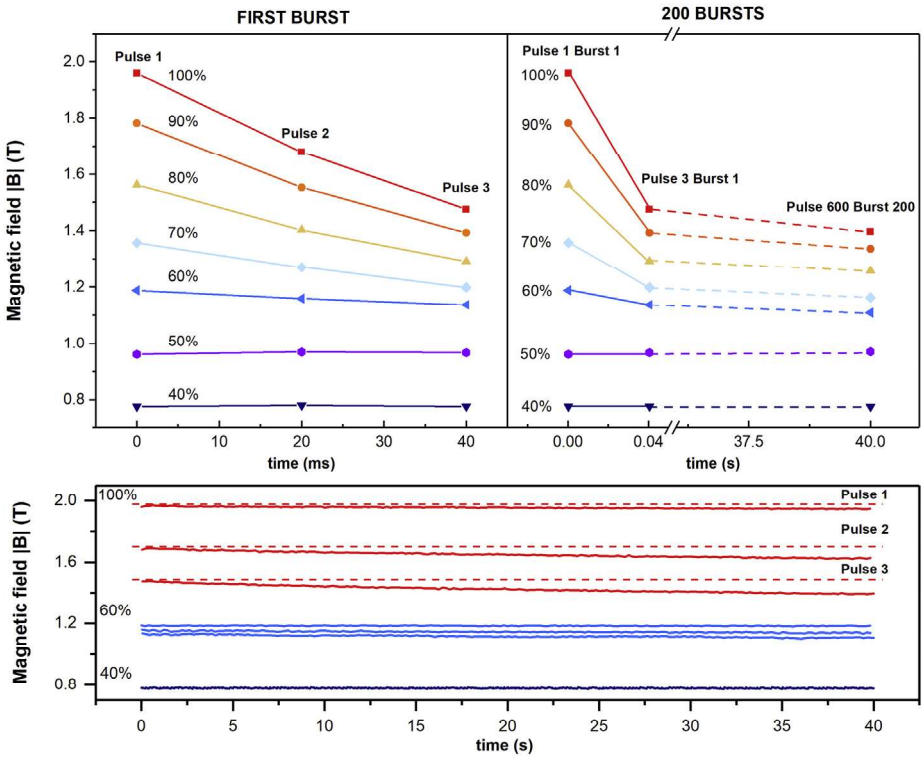

Fig. 1. Upper left panel. First burst measurements at different stimulator output intensities. The magnetic field of the three components of the burst (pulses) are showed. **Upper right panel.** The magnetic field of the first and third pulses of the first burst and third pulses of the last burst are shown with different stimulator output intensities. **Lower panel**: time course of the three pulses composing the burst showed separately at three representative stimulation intensities. At 40% MSO, the pulses are not changing over time and at 60% MSO, the pulses are slightly reduced over time. At 100% MSO, the pulses are slightly reduced over time (dotted lines show the magnetic field of the pulses of the first burst).

components. The manufacturers report some of these limitations, but here for the first time we quantified the intensity of the delivered magnetic pulses across a range of intensities and for each pulse in a burst.

The majority of studies using TBS apply stimulation intensities around 50% of MSO. At this intensity range, all pulses have a consistent intensity. On the other hand, the reduced intensity of the second and third pulses of each burst may limit the uses of the TBS protocols at higher intensities. The effects of TBS depend on the fact that the neural elements are stimulated by the burst [1–5]. Neural structures stimulated well above their thresholds probably will be "burst stimulated" even with an intensity decay of the later components of the burst. On the other hand, with intensity variation of up to 25–30% between the first and third pulse in a burst, proportional variation in the neural response to the second and third pulses seems likely. Speculatively, this may add variability to the TBS effects at intensities above 50% of the MSO.

Declaration of competing interest

We confirm that there are no known conflicts of interest associated with this manuscript and there has been no significant financial support for this work that could have influenced its outcome.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.brs.2020.01.002.

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