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E-Field Orientation during Theta Burst Stimulation Modulates Changes in Motor Evoked Potential Amplitude

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Background

Transcranial magnetic stimulation (TMS) is a noninvasive method for brain stimulation employed in an increasing range of diagnostic and therapeutic settings (6,7). Although TMS-based neuromodulation (NM) protocols are utilized in the treatment of neuropsychiatric and other conditions, the underlying neurophysiological processes remain insufficiently understood (3). One thus far unexamined factor to optimize TMS NM outcomes is the orientation of the stimulating coil relative to individual cortical anatomy, which has been recognized as a relevant factor in single-pulse stimulation (8). We present preliminary findings from healthy participants in whom we investigated the impact of e-field orientation during continuous theta burst stimulation (cTBS) on NM regarding motor evoked potentials (MEPs).

Methods

8 healthy participants (average age: 23 ± 3 years, 4 females) underwent T1-weighted (T1w) imaging at 3 Tesla to obtain images for neuronavigated TMS (nTMS). Three nTMS sessions separated by at least 14 days were conducted per subject to assess the impact of the e-field orientation during cTBS on the MEP amplitude. After identification of the abductor pollicis brevis muscle hotspot and the coil orientation for maximum MEP generation within the dominant hemisphere, the resting motor threshold (rMT) was determined and 30 MEPs were elicited at 150% rMT (2,4). Afterwards, cTBS with conventional parameters (40 s, 600 stimuli, 3 stimuli with 50 Hz every 200 ms*)* (5) was performed at 70 % rMT (2,4) at the same site using one out of three protocols (OPT: stimulation with optimal coil direction; 90°: anterior coil end rotated 90° upwards from OPT; SHAM: stimulation with a 7.3-cm spacer). Subsequently, we elicited 3 sets of 30 MEPs at increasing intervals after cTBS (0-5 min, 5-10 min, 10-15 min). The MEPs were analyzed to evaluate the influence of the e-field orientation on MEP amplitudes.

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Results

After adjusting for a family-wise error rate, MEP amplitudes pre- and post-TBS differed significantly between the measured time points, with the observed differences varying by e-field orientation of cTBS (Figure 1A-C). On a group level, cTBS in both OPT and SHAM conditions demonstrated heightened MEPs compared to baseline (OPT: post-cTBS 3553±1999 µV vs. pre-cTBS 2923±2460 µV, $p<0.05$; Figure 1A; SHAM: post-cTBS 3174±2160 µV vs. pre-cTBS 2235±1703 µV, $p<0.0001$; Figure 1C). Here, SHAM demonstrated significantly higher increases of MEP amplitudes compared to the other two conditions (SHAM-cTBS 698±1249 µV vs. OPT-cTBS 321±1293 µV vs. 90°-cTBS 293±1240 µV, $p<0.05$). Results on the group level did not reflect pronounced and heterogenous NM effects as observed on the single-subject level.

Discussion

On a group level, counter to the classical assumption of MEP suppression, we observed MEP facilitation following cTBS in both OPT and SHAM conditions, potentially highlighting the need to further elucidate sham-derived effects in TMS NM (1). These findings add to research questioning the consistency of TMS NM (3). Changes in NM response based on e-field orientation were more pronounced for some subjects compared to others, stressing the inter-individual variability in NM responses (3).
Our results may underscore the complexity and variability of cTBS effects on cortical excitability. Additionally, we provide first evidence implying e-field orientation during TMS NM as a factor influencing NM outcome. Individual optimization of e-field orientation could improve NM outcomes in other settings, e.g. therapeutic applications.

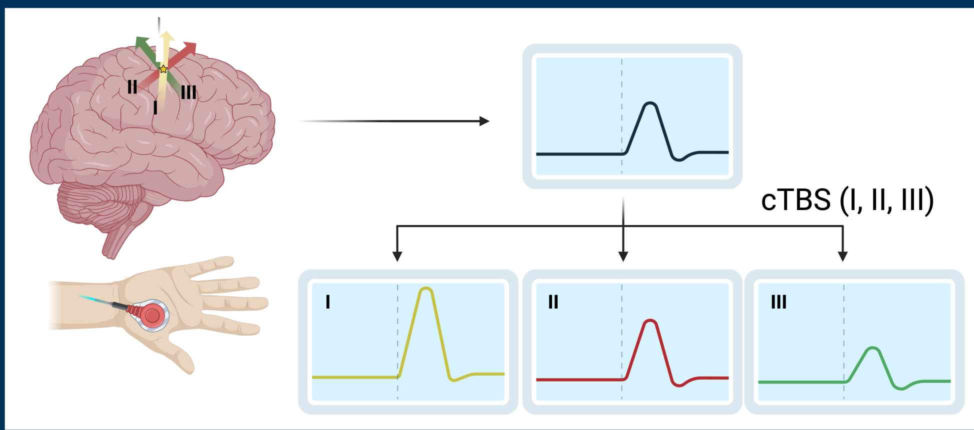

Figure 1:
I: SHAM; II: OPT; III: 90°. *V*arying E-field orientation in continuous theta burst stimulation significantly affects MEP amplitudes, suggesting that E-field orientation influences neuromodulation results. MEPs were measured at the abductor pollicis brevis (APB) muscle. Comparing all three conditions (x-axis: OPT, 90°, SHAM) on group level, MEP facilitation after SHAM was significantly higher both in the 0-5 min interval compared to 90° and in the 5-10 min interval compared to both OPT and 90°.

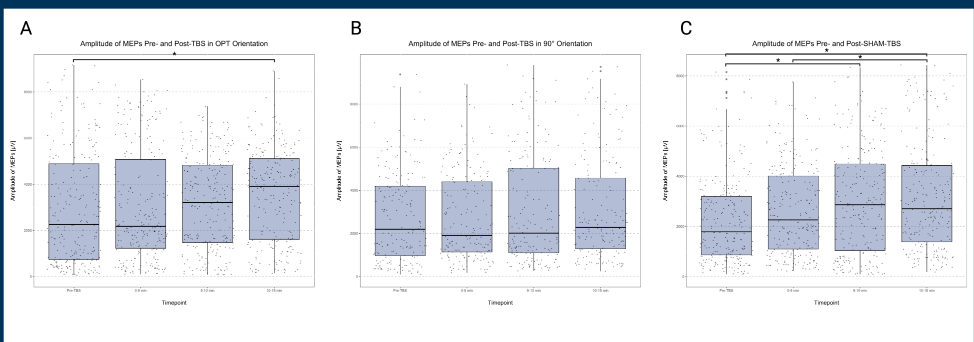

Figure 2:
A-C: Change of motor evoked potential (MEP) amplitudes (y-axis) pre- and post-continuous theta burst stimulation (cTBS) across three short-term intervals (x-axis; 0-5 min, 5-10 min, 10-15 min) for all three conditions (OPT [A]: stimulation with previously determined optimal direction; 90° [B]: stimulation with anterior coil end rotated 90° upwards from OPT; SHAM [C]: stimulation with a 7.3 cm spacer) on group level. OPT (A) and SHAM (C) cTBS led to significantly heightened MEPs compared to baseline.

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