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Research article

Current direction-dependent modulation of human hand motor function by intermittent theta burst stimulation (iTBS)

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HIGHLIGHTS

- Uni-directional iTBS was applied to the left primary motor cortex.
- Finger-tapping with the left hand was disturbed after posteroanterior iTBS.
- Current direction of iTBS had an impact on human motor behaviour.

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ABSTRACT

Background: Transcranial magnetic stimulation (TMS) with different current directions can activate different sets of neurons. Current direction can also affect the results of repetitive TMS.
Objective: : To test the influence of uni-directional intermittent theta burst stimulation (iTBS) using different current directions, namely posteroanterior (PA) and anteroposterior (AP), on motor behaviour.
Methods: In a cross-over design, PA- and AP-iTBS was applied over the left primary motor cortex in 19 healthy, right-handed volunteers. Performance of a finger-tapping task was recorded before and 0, 10, 20, and 30 min after the iTBS. The task was conducted with the right and left hands separately at each time point. As a control, AP-iTBS with reduced intensity was applied to 14 participants in a separate session (AP_{weak} condition).
Results: The finger-tapping count with the left hand was decreased after PA-iTBS. Neither AP- nor AP_{weak}-iTBS altered the performance.
Conclusions: Current direction had a significant impact on the after-effects of iTBS.

1. Introduction

Transcranial magnetic stimulation (TMS) can activate different populations of neurons in the primary motor cortex (M1) by applying so-called "monophasic" pulses with different current directions. Indeed, a single-pulse TMS with predominantly posteroanterior (PA) induced-current elicits motor evoked potentials (MEPs) of shorter latencies than one with an anteroposterior (AP) current [1,2]. This is perhaps caused by different compositions of the descending volleys representing cortical outputs produced by TMS [3]. Furthermore, a decreased amplitude of a later component of the volleys was related to transient post-operative paresis of the hand, suggesting that each of the descending volleys plays a specific role in hand function [4]. The difference between the thresholds of PA and AP monophasic stimulation for eliciting MEPs also supports the notion that a particular group of neural components is activated in a current-direction dependent manner [5,6].

Theta-burst stimulation (TBS) has been introduced as a rapid, effective intervention to induce neuroplasticity-like effects in various regions of the human brain, including M1. Depending on the protocols with up to several minutes of stimulation, it can have after-effects lasting 20–60 min [7,8]. Not only physiological measures such as MEP, but also behavioural parameters includ-

Abbreviations: AMT, active motor threshold; ANOVA, analysis of variance; AP, anteroposterior; cTBS, continuous theta burst stimulation; cTMS, controllable pulse parameter transcranial magnetic stimulation; FDI, first dorsal interosseous; FT, finger tapping; iTBS, intermittent theta burst stimulation; M1, primary motor cortex; MEP, motor evoked potential; PA, posteroanterior; TMS, transcranial magnetic stimulation.

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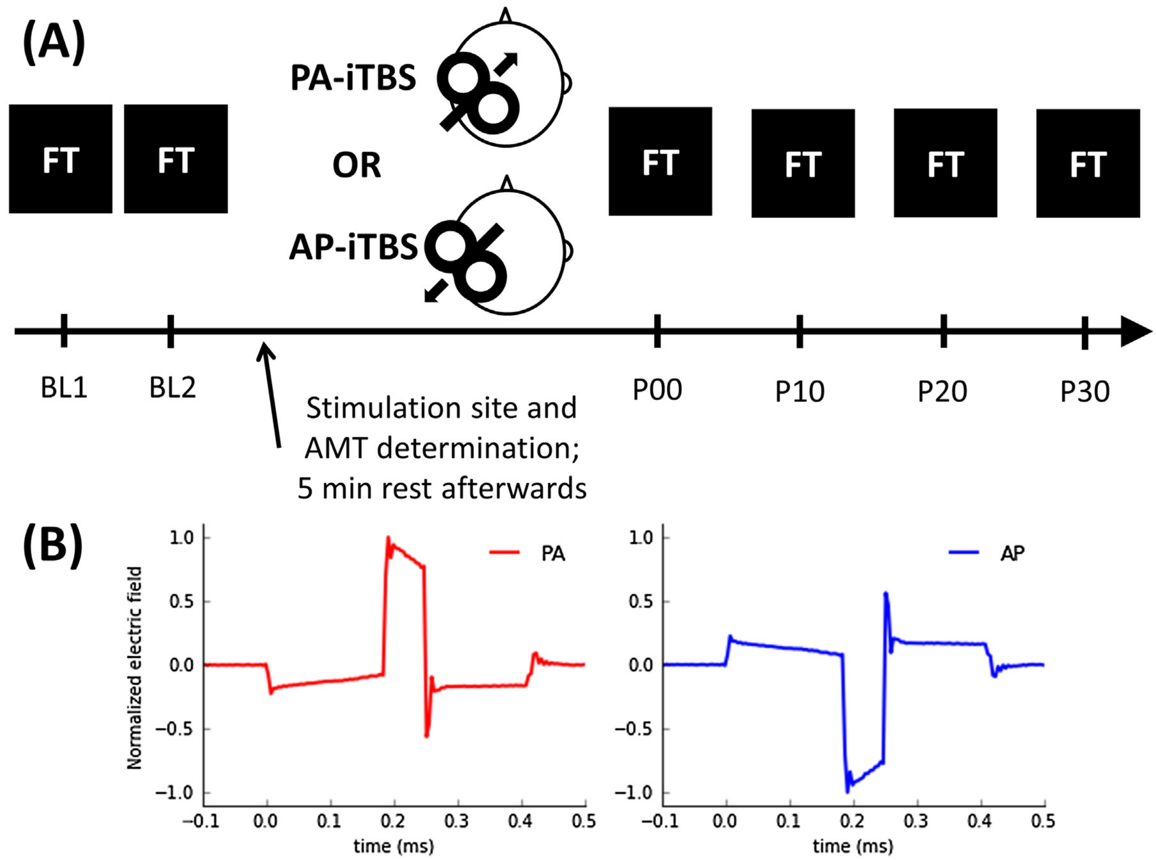

Fig. 1. Experimental design.
(A) Timeline for the experiment. Baseline performance was measured twice (BL1 and BL2). The stimulation site and AMT were determined, followed by a five-minute break to allow the participants to relax. Post-stimulation measurements were performed at 0, 10, 20, 30 min after the iTBS (P00, P10, P20, and P30). (B) Pulse shapes used for PA (red) or AP (blue) iTBS. Positive values indicate PA currents. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)
AMT, active motor threshold; AP, anteroposterior; iTBS, intermittent theta burst stimulation; PA, posteroanterior.

ing motor learning can be modulated by TBS [9]. There are two main TBS protocols: intermittent TBS (iTBS), which was originally reported to increase the MEP size on average, and continuous TBS (cTBS), which decreased it [7].

Since conventional TBS uses biphasic, *i.e.* more symmetrical, TMS pulses, any role played by the putative PA- and AP-sensitive neurons in M1 might have been obscured in TBS studies. In fact, the results from two publications that investigated physiological effects of current direction of TBS applied with a conventional biphasic stimulator are not completely congruent [10,11]. A recent technological advance has enabled us to address this issue with more uni-directional TBS pulses using a controllable pulse-parameter TMS (cTMS) stimulator [12–15]. Such uni-directional pulses are more similar to monophasic pulses than biphasic ones both physically (Fig. 1B) and physiologically [5,6,16]. Further evidence has been obtained regarding the influence of current direction in M1 stimulation with this device [17]. The influence of the current direction on the after-effects of TBS has not been well studied, although it was recognized as a potentially important moderator [18]. Furthermore, functional meaning of this physiological distinction between the PA and AP currents is not elucidated yet.

The aim of the study was to investigate the influence of the current direction induced by iTBS on human motor performance. More specifically, predominantly uni-directional PA-iTBS and AP-iTBS were applied in a cross-over design, and the motor performance was tested before and after the intervention using a finger-tapping (FT) task.

2. Methods

2.1. Participants

Nineteen healthy, right-handed (mean ± standard deviation of the Edinburgh Handedness Inventory (EDI) score was 83.3 ± 19.1) volunteers participated in the study (7 men and 12 women, mean age ± standard deviation was 27.2 ± 6.0 years). All participants were free from any neurological or psychiatric disorders, took no centrally-acting medications, and had no contraindications for TMS [19,20]. Informed consent was obtained from each before participation. The study protocol, which conformed to the Declaration of Helsinki, was approved by the local ethics committee of the University Medical Center Göttingen.

2.2. Overall study design

This study was conducted using a cross-over design with two arms: PA-iTBS and AP-iTBS. The interval between the sessions was at least three days, and the order of the two arms was randomly determined. Care was taken to start the sessions for each participant either in the morning or the afternoon as much as possible. After a short practice session with the motor task (*see* below), the participants performed two sets of baseline measurements (BL1 and BL2 in Fig. 1A). iTBS was then applied as described below. Post-stimulation measurements took place at 0, 10, 20, and 30 min after the iTBS (P00, P10, P20, and P30 in Fig. 1A).