Comparing motor-evoked potentials through paired pulse transcranial magnetic stimulation and intermittent theta burst stimulation at the supplementary motor area

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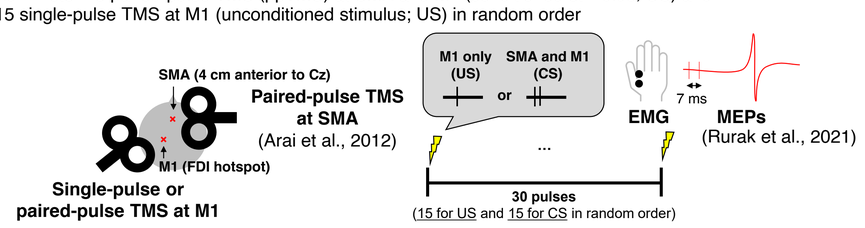
Introduction

- Non-invasive brain stimulation techniques, such as transcranial magnetic stimulation (TMS), have been shown to modulate the excitability of the corticospinal tract, which is the pathway connecting the motor cortex to the spinal cord and controls voluntary movements.
- Some studies reported that corticospinal excitability (i.e., motor-evoked potential (MEP)) increased when TMS at the supplementary motor area (SMA) preceded TMS at the primary motor cortex (M1) (Arai et al., 2012; Rurak et al., 2021).
- Huang et al. (2005) revealed that the delivery of three pulses at 50 Hz, repeated every 200 milliseconds (i.e., 5 Hz as the theta frequency), can influence MEP amplitude.
- This study investigated the connectivity between SMA and M1 using paired-pulse transcranial magnetic stimulation (ppTMS) (Experiment 1) and intermittent theta-burst stimulation (iTBS) (Experiment 2).

Methods

Experiment 1

1 Administer 15 paired-pulse TMS (ppTMS) at SMA and M1 (conditioned stimulus; CS) and 15 single-pulse TMS at M1 (unconditioned stimulus; US) in random order

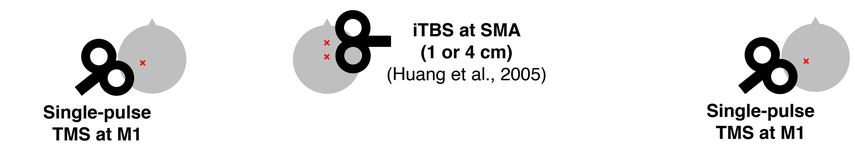


- 52 undergraduate students
- 35 females and 17 males
- **Mean age:** 20.03 (*SD*: 1.45)

- **Orientation:** 45 (M1) and 270 (SMA) degrees
- **rMT:** minimum intensity to evoke 0.05 mV
- **Intensity:** 110% of rMT at M1, 140% at SMA

Experiment 2

1 Baseline measure 2 Intermittent theta-burst stimulation (iTBS) at 1 or 4 cm anterior to Cz 3 Post-measures at 5 min, 15 min, and 25 min after iTBS



- 33 undergraduate students
- 18 females and 15 males
- **Mean age:** 21.64 (*SD*: 1.06)

- **Orientation:** 45 (M1) and 270 (SMA) degrees
- **rMT:** minimum intensity to evoke 0.05 mV
- **Intensity:** 110% of rMT at M1, 80% at SMA

Results

Experiment 1

- Only 34 individuals received SMA stimulation at 4 cm anterior to Cz in the 10-20 system (**Fig. 1**).
- The other 18 individuals received it at 5, 6, or 7 cm anterior to Cz (**Fig. 1**).
- Facilitation was observed in 25 of the 34 participants, representing 73.53% of the participants (**Fig. 1**).
- It is worth noting that systematically moving the site of stimulation of SMA during ppTMS in an anterior fashion along the midline removed the facilitatory influence of SMA on M1 (p = .033) (**Fig. 1**).
- Stimulation at 4 cm was associated with a robust facilitatory effect, manifested as a 21.22% increase in mean peak-to-peak MEP amplitude for the conditioned stimulus compared to the unconditioned trials (p = .004) (**Fig. 2**).

1. The **conditioned stimulus** (SMA prior to M1 stimulation) **induced larger MEPs** compared to the unconditioned stimulus (M1 only).

2. Application of **iTBS at 1 cm** anterior to Cz **facilitated MEPs**, whereas **iTBS at 4 cm did not**.

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Results (cont.)

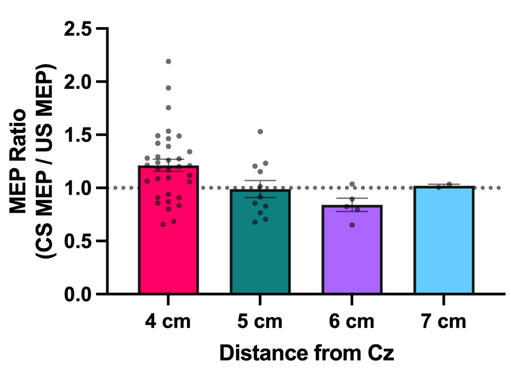

Fig. 1. CS:US MEP ratio by distance. Values greater than 1 indicate facilitation. Error bars represent standard errors.

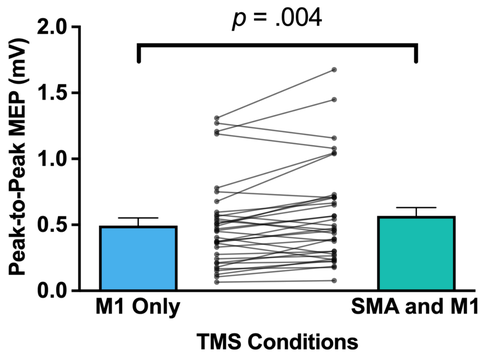

Fig. 2. MEP when TMS applied at M1 only and both SMA and M1 (ppTMS). Error bars represent standard errors.

Results (cont.)

Experiment 2

- When iTBS was applied 1 cm anterior to Cz, MEPs were consistently facilitated (5 min, p = .010; 15 min, p = .008; 25 min, p = .049) (**Fig. 3**).
- No such facilitation was observed when iTBS was applied at 4 cm anterior to Cz (**Fig. 3**).
- 13 of 16 participants (81.25%) receiving iTBS at 1 cm exhibited facilitation.

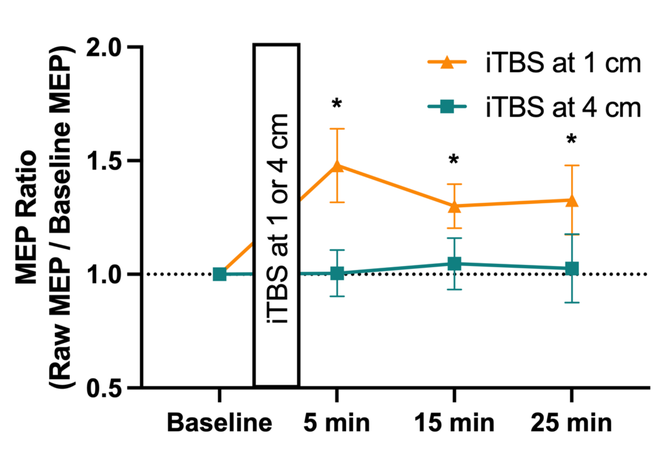

Fig. 3. MEP ratio changes after iTBS at 1 or 4 cm anterior to Cz. Error bars represent standard errors.

Discussion

- In general, these data are congruent with a recent claim that SMA exerts a facilitatory influence on M1 (Rurak et al., 2021) but raise concerns about how to target SMA-M1 connectivity precisely.

Limitations

- Measurement error may have occurred when locating the site of stimulation of SMA.
- In Experiment 1, placement of coils is limited by coil size (2 x 30 mm) and location of individual FDI hotspot.
- In Experiment 2, the increased MEP may be because iTBS directly influenced the M1.

References

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- Huang, Y. Z., Edwards, M. J., Rounis, E., Bhatia, K. P., & Rothwell, J. C. (2005). *Neuron*, 45(2), 201-206.
- Rurak, B. K., Rodrigues, J. P., Power, B. D., Drummond, P. D., & Vallence, A. M. (2021). *Neuroscience*, 472, 11-24.

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