# Effects of intermittent theta burst pattern median nerve stimulation on cortical excitability


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## Background

### Intermittent theta burst stimulation (iTBS)

- iTBS involves applying bursts of high-frequency stimulation in a set pattern (Fig.1).
- iTBS is typically delivered using transcranial magnetic stimulation (TMS) (hence forth iTBS-TMS) and has been shown to produce sustained increases in cortical excitability.
- Consequently, iTBS-TMS has been proposed as a treatment for disorders associated with dysfunctional cortical inhibition, such as depression [2].
- However, there are practical limitations to the therapeutic use of iTBS-TMS. An alternative approach may be median nerve stimulation (Fig.3).

### Median nerve stimulation (MNS)

- MNS is a non-invasive brain stimulation technique, where low intensity electrical stimulation is applied to the wrist with afferent signals ascending to cortex (Fig. 2).
- Replicating a TMS stimulation pattern using MNS can lead to comparable cortical responses:
  - E.g. Rhythmic (but not arrhythmic) TMS can entrain parietal alpha oscillations [3] and comparable entrainment of mu-alpha cortical oscillations has been observed with delivery of rhythmic (but not arrhythmic) MNS [4].
- MNS has recently been shown to deliver clinically meaningful improvements in the symptoms of Tourette syndrome [5].

**Figure 1:** Intermittent theta burst stimulation


(Huang et al., 2005 [1]).

**Figure 2:** Median nerve stimulation

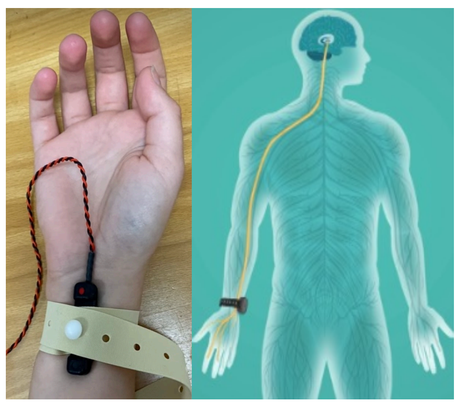


**Figure 3:** Relative advantages of MNS compared to TMS

| TMS | MNS |
|---|---|
| Trained professional must deliver stimulation – often requires multiple visits to clinic. | Can be successfully delivered at home by patients or their carers [5]. |
| May require MRI scan to determine target location – expensive and not always accessible. | Placement of electrodes is determined visually. |
| Subset of recipients report moderate-severe side effects [6]. | No severe side effects documented [7]. |

## Aims

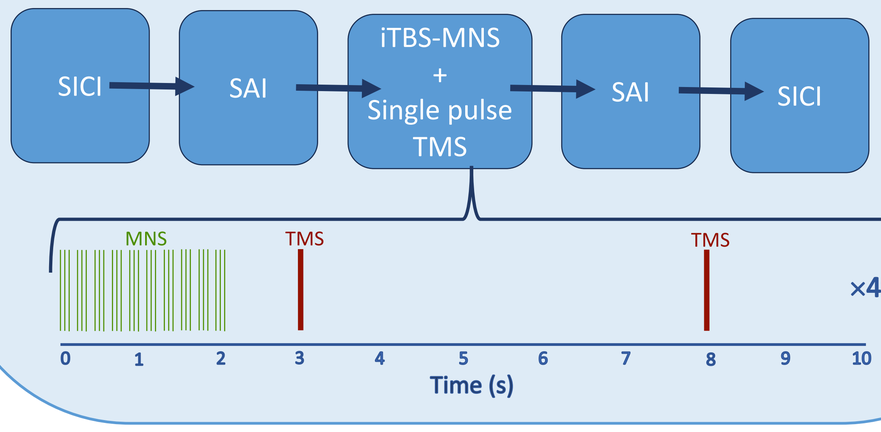
1) Determine if median nerve stimulation delivered using an intermittent theta burst stimulation pattern (iTBS-MNS) can modulate cortical excitability assessed by changes in motor evoked potentials (MEPs).

2) Investigate time course of potential changes.

## Methods

- 26 healthy individuals (17F, mean age=25 years (range=18-34), 1 left-handed) participated.
- 2 session study (within-subjects design, counterbalanced).
  - Active session: iTBS-MNS (40 cycles) delivered at 100% MNS motor threshold (lowest intensity to elicit a visible thumb twitch).
  - Sham session: iTBS-MNS (40 cycles) delivered at 50% MNS motor threshold.
- TMS resting motor threshold: minimum intensity required to elicit MEPs (50-100$\mu$V peak-peak amplitude) in 5/10 trials.
- TMS measures of cortical excitability and inhibition were taken before and after iTBS-MNS procedure:
  - Short-interval intracortical inhibition (SICI): Subthreshold (65/75%) conditioning stimulus → 3ms ISI → suprathreshold (120%) test stimulus. 30 conditioned trials and 30 unconditioned trials.
  - Short-latency afferent inhibition (SAI): Motor threshold MNS pulse → 20ms ISI → 1mv TMS test pulse. 20 conditioned trials and 40 unconditioned trials.
- Single pulse unconditioned TMS measures were also collected between bursts during the iTBS-MNS procedure (80 trials total, see Figure 4).

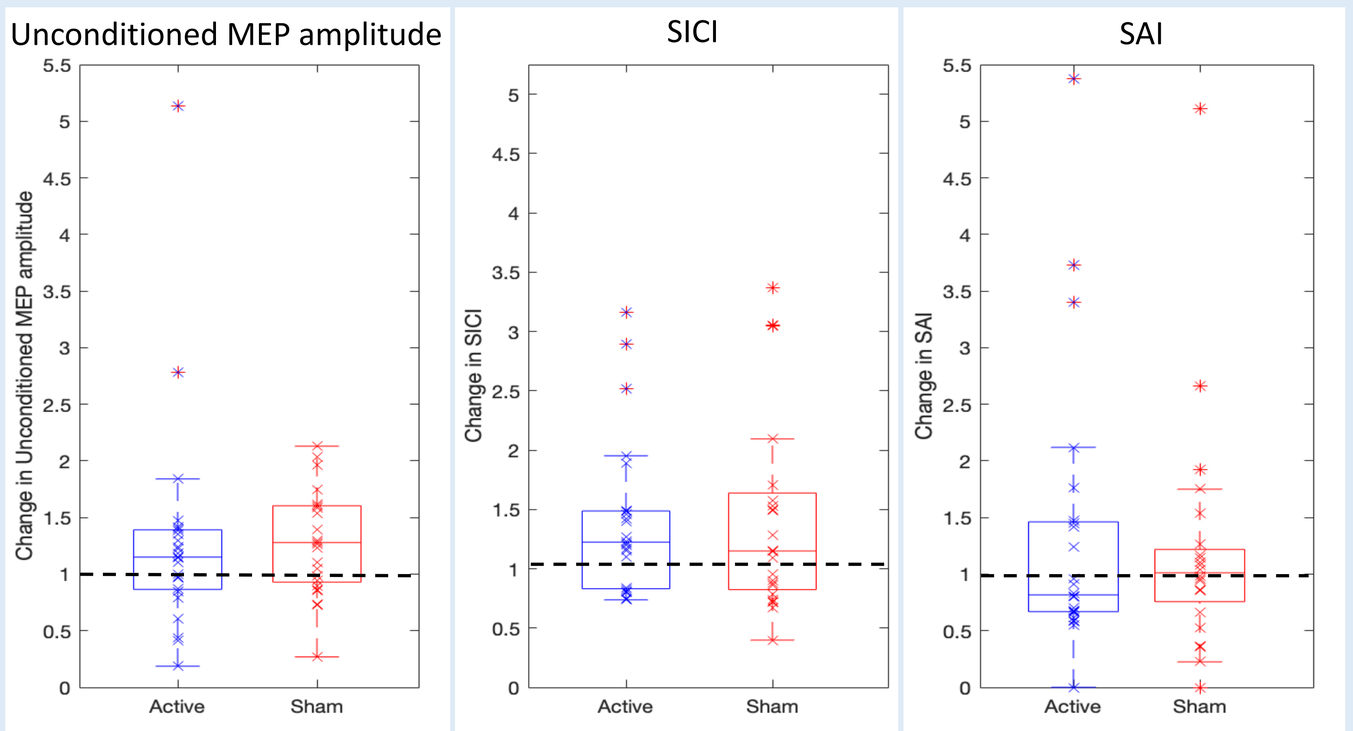
**Figure 4:** Study procedure




## Results

- Fig. 5 shows change from baseline ( $\frac{post\ iTBS-MNS}{pre\ iTBS-MNS}$ ) in active and sham conditions for: unconditioned MEP amplitude (evoked by 120% RMT single pulse TMS trials in SICI protocol); SICI and SAI.
- Active and sham iTBS-MNS led to a slight increase in unconditioned MEP amplitudes and a slight reduction in SICI (Fig. 5).
- No significant differences between active and sham conditions for any measures.
- Analysis also revealed no significant changes in cortical excitability (measured by unconditioned MEP amplitude) emerging over the duration of the iTBS-MNS procedure.

**Figure 5:** Changes in cortical excitability/inhibition measures following iTBS-MNS




Key: Active Sham (1) = No change from pre to post iTBS-MNS.

## Conclusion

iTBS-MNS does not replicate effects seen following iTBS-TMS and therefore is not currently a viable replacement for iTBS treatment options. The measures of cortical excitability and inhibition investigated in this study were not significantly different between the sham and active iTBS-MNS conditions. Further study into the effects of repetitive MNS paradigms is required.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