Exploring short-interval intracortical inhibition (SICI) using transcranial magnetic stimulation-electroencephalography (TMS-EEG): a potential diagnostic tool for MND

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1 Introduction

The diagnosis of MND relies on detection of both upper & lower motor neuron (UMN and LMN, El Escorial Criteria).
An objective measure of UMN is lacking.

TMS may provide a solution (Menon 2015) though the output - a motor evoked potential or MEP - is a measure of both UMN and LMN function.

TMS in MND is limited by its dependence on a peripheral output due to muscle wasting.

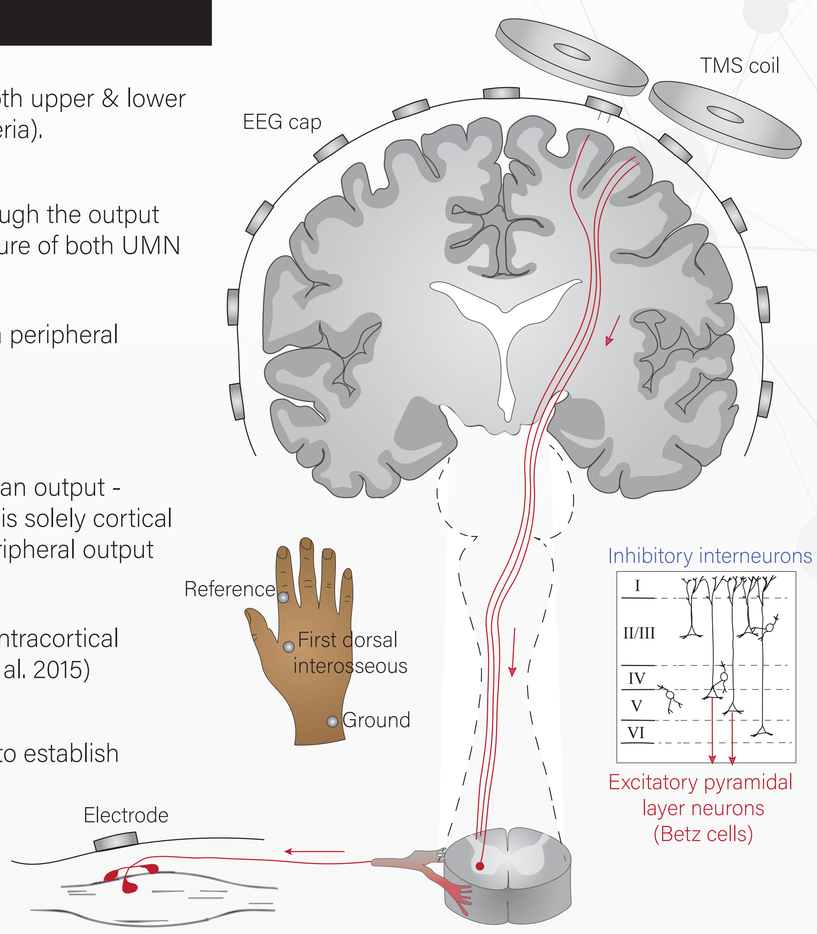
Is TMS with EEG (TMS-EEG) the solution?

By combining TMS with EEG we can produce an output - called the TMS evoked response or TEP - that is solely cortical in origin. This circumnavigates the lack of a peripheral output in people living with MND.

While previous work has shown short-interval intracortical inhibition (SICI) is reduced in MND (Menon et al. 2015) plwMND without a MEP were excluded.

Before applying this to plwMND we first need to establish the response in healthy volunteers.

Hypothesis: A paired pulse protocol (SICI) will result in a TEP that is significantly inhibited compared to an unconditioned TEP.



2 Methods

TMS was delivered to the left motor cortex in 13 participants (9 female, mean age 24.3 yrs old)

Stimulation was given in two paradigms:

1. **Single pulse TMS** – at an intensity required to evoke a peripheral MEP of 1mV peak-to-peak amplitude. This is a reflection of baseline central and peripheral excitability.

2. **SICI TMS** – a preconditioning pulse is given 2ms prior to the single pulse TMS. This preconditioning pulse is subthreshold (70, 80 & 90% of resting motor thresold). The decrease in amplitude of the resulting MEP is an index of central and peripheral inhibition.

Eighty stimuli were randomly delivered per condition (single pulse, paired pulse of either 70, 80 & 90% of resting motor thresold + single pulse) in four blocks, resulting in a total of three-hundred and twenty TMS pulses per session.

EEG was recorded using the 64-channel actiCHamp device. Surface EMG was recorded over the right FDI.

Preprocessing of TMS-EEG data followed the established pipeline by Rogasch et al. using the TESA MATLAB toolbox.

MEPs were processed in Signal (CED, Cambridge, UK).

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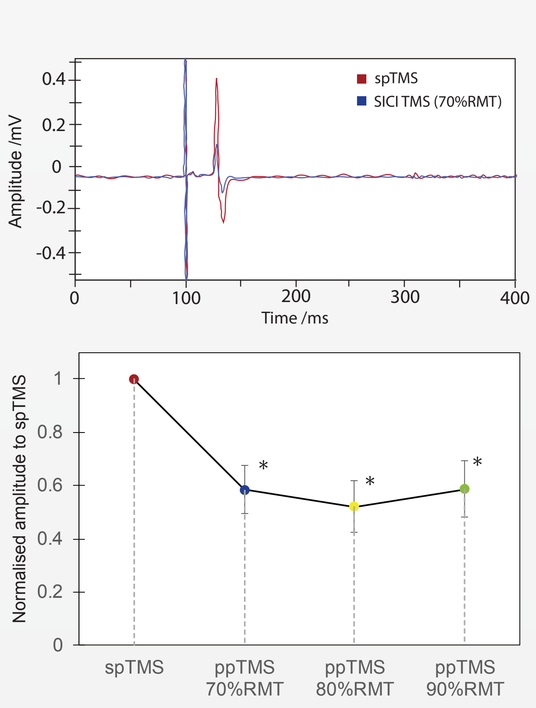
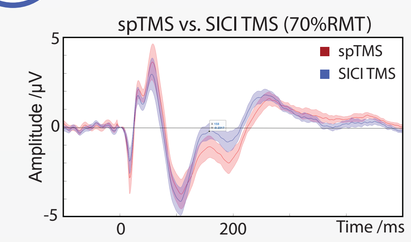
3 Peripheral SICI TMS

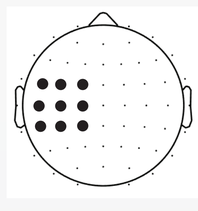
MEP amplitudes are normalised to single pulse TMS.

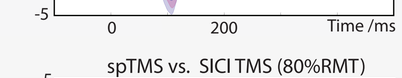
As expected SICI is present in all three conditions.

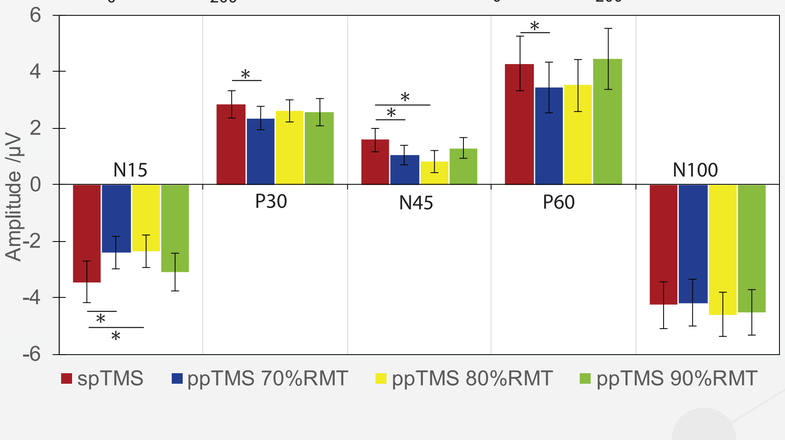


4 Central SICI TMS: TEP peaks are reduced







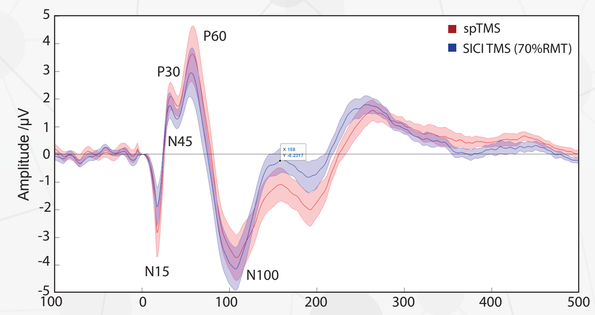


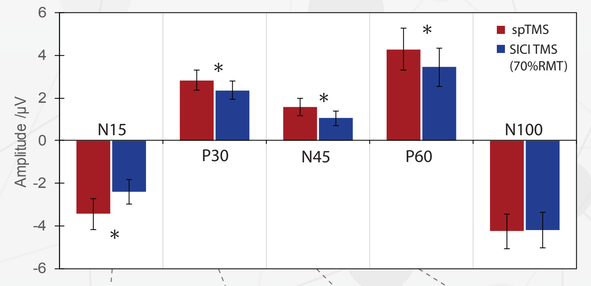
TEPs are averaged for each condition for a cluster of nine electrodes surrounding the motor cortex. This TEP reflects activity occurring at and around the local vicinity of the motor cortex.

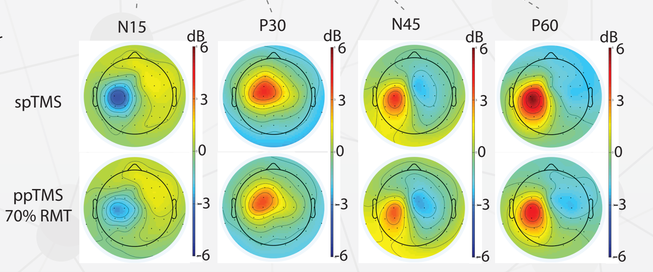
The amplitude of characteristic peaks (N15, P30, N45, P60 and N100) of the motor cortex. TEP response are measured for each subject.

Motor cortex TEP peaks are smaller for SICI conditions than single pulse TMS. The size of this effect is greatest for SICI 70. Hence, **we focus on the SICI 70 condition for further analyses**.

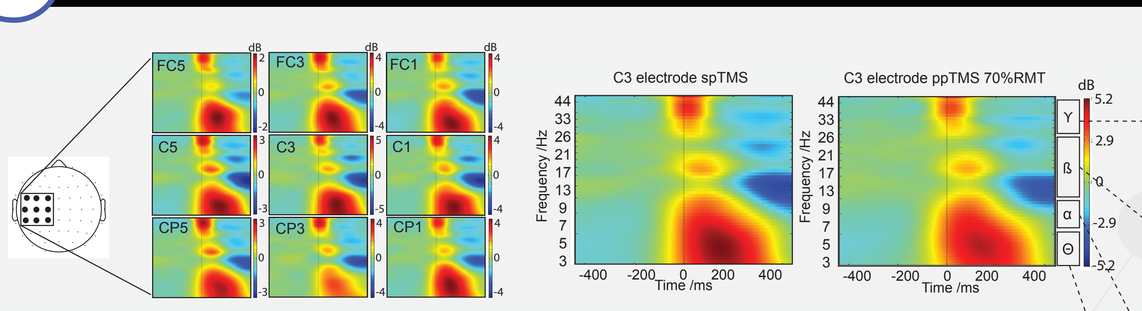
When comparing the peaks for the SICI 70 vs single pulse TMS condition, statistical significance ($p<0.05$) is reached for peak comparisons (N15, P30, N45 and P60).

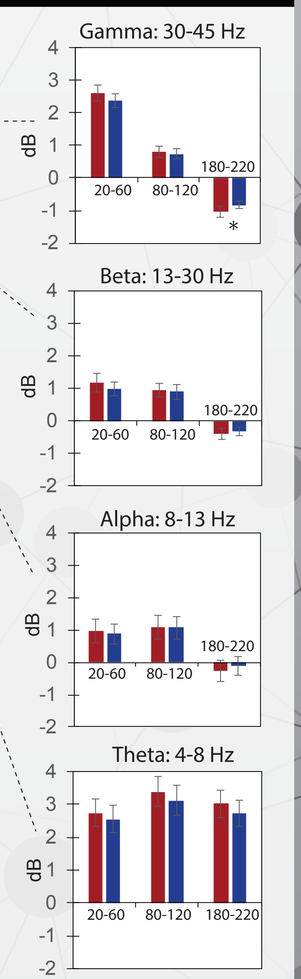






5 TMS evoked cortical oscillations





TMS has been known to induce oscillatory activity, which can be measured using EEG.

These cortical oscillations can occur in distinct frequency bands: theta (4-8Hz), alpha (8-13Hz), beta (13-30Hz) and gamma (30-45Hz).

Here we analyse the strength of these evoked cortical oscillations in these distinct frequency bands for both single pulse TMS and SICI 70 TMS, during three distinct time points after TMS (20-60ms, 80-120ms and 180-220ms).

We find that power of cortical oscillations induced during SICI 70 TMS are smaller than single pulse TMS.

Gamma power (30-45Hz) from 180-220ms is significantly different from single pulse TMS ($p<0.05$)

6 Conclusions and future directions

It appears that cortical inhibition can be measured using TMS-EEG.

TMS-EEG shows promise in objectively identifying UMN involvement while being entirely independent of peripheral output which is critical in people living with MND.

The central TEP measure of cortical inhibition is distinct from the combined central and peripheral measure (MEP) of inhibition.

Future directions

In order to apply this to people living with MND we need to;

- explore the relationship of TEPs with age and reproducibility.

- establish a fully automatic platform for TMS-EEG.

- apply this to people living with MND at an early stage.

TMS-EEG has potential to aid early diagnosis and to further understand central and peripheral pathophysiology in MND.

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7 References

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