

## INTRODUCTION

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- Non-invasive brain stimulation has received a lot of attention as potential pain therapy<sup>1</sup>.
- No studies have proven whether decreased pain sensitivity could be maintained several days after multiple sessions of repetitive 10 Hz transcranial magnetic stimulation (rTMS) to the left dorsolateral prefrontal cortex (L-DLPFC).
- The mechanisms underlying 10 Hz rTMS-induced analgesia are still unclear and may be mediated by the activation of descending pain control systems<sup>2</sup> or neuro-modulatory effects on the intracortical motor excitability<sup>3</sup>.
- A new paradigm of rTMS, called theta-burst stimulation (TBS), has been recently developed<sup>4</sup>.

## AIM

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This study aimed to compare the analgesic effects of 3 days of consecutive sessions of 2 rTMS protocols and investigated whether:

- 1) L-DLPFC TBS produced a stronger reduction in pain sensitivity compared with the "classical" 10 Hz L-DLPFC rTMS
- 2) Analgesic effect lasted beyond the last day of stimulation
- 3) Increase in pain thresholds was associated with changes in the descending pain control system and/or in intracortical excitability

## METHODS

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16 participants were recruited in this randomized cross-over study. Pain detection thresholds to pressure (PPT), heat (HPT), Conditioned Pain Modulation (CPM) with mechanical and heat supra-pain threshold test stimuli and the cold pressor test as conditioning, and intracortical excitability assessment were collected before (Day 1), 3 (Day3) and 4 days (Day4) after the 3-day session of rTMS LDPFC (Figure 1).

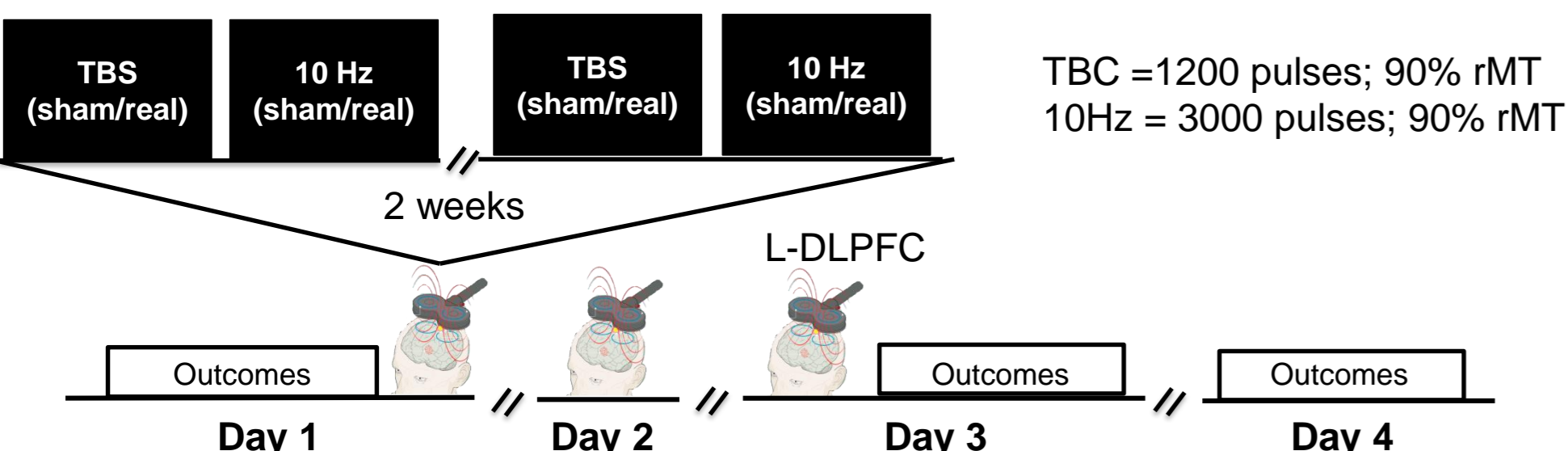
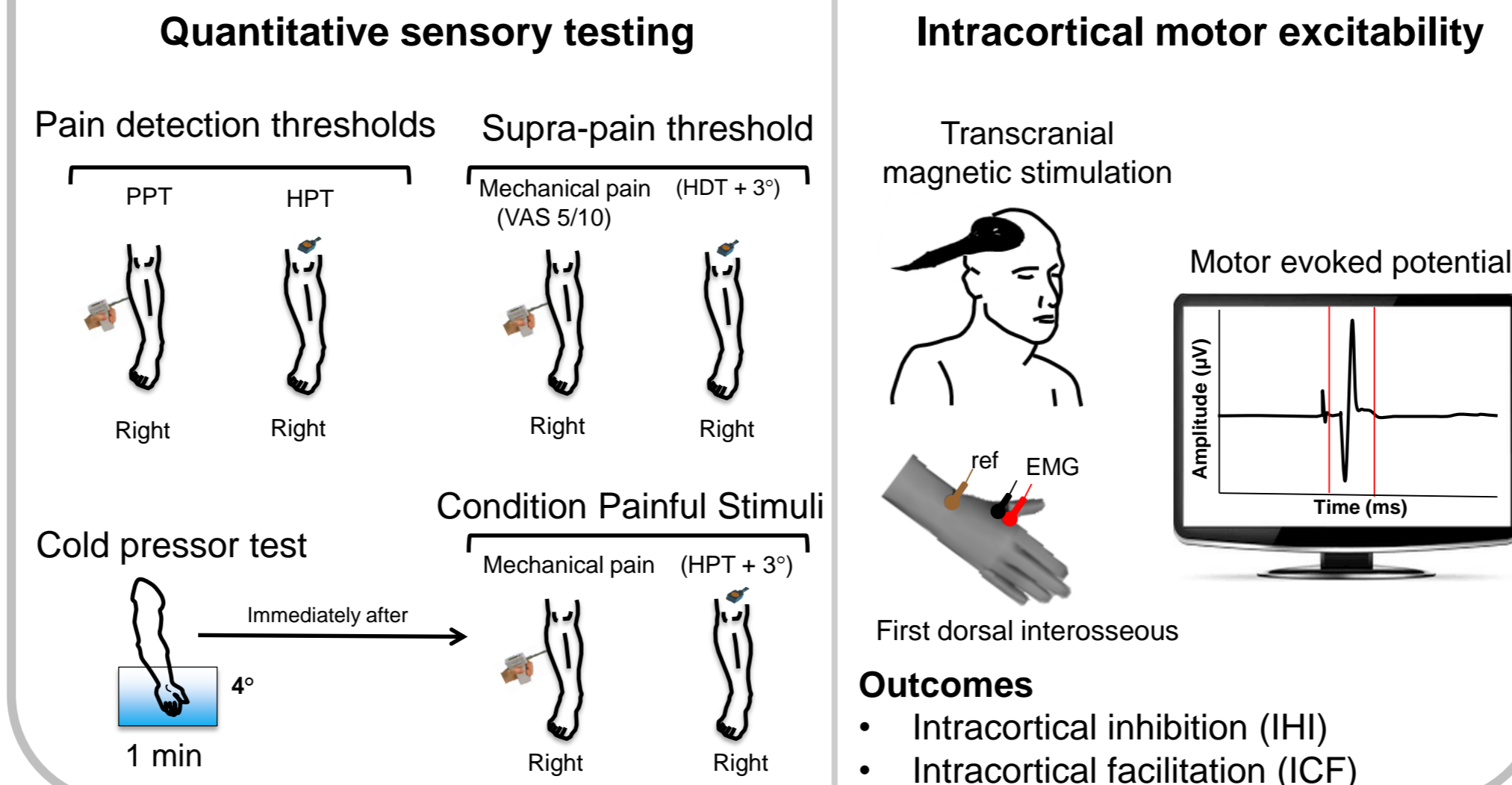


Figure 1. Study design

## METHODS (CONT.)

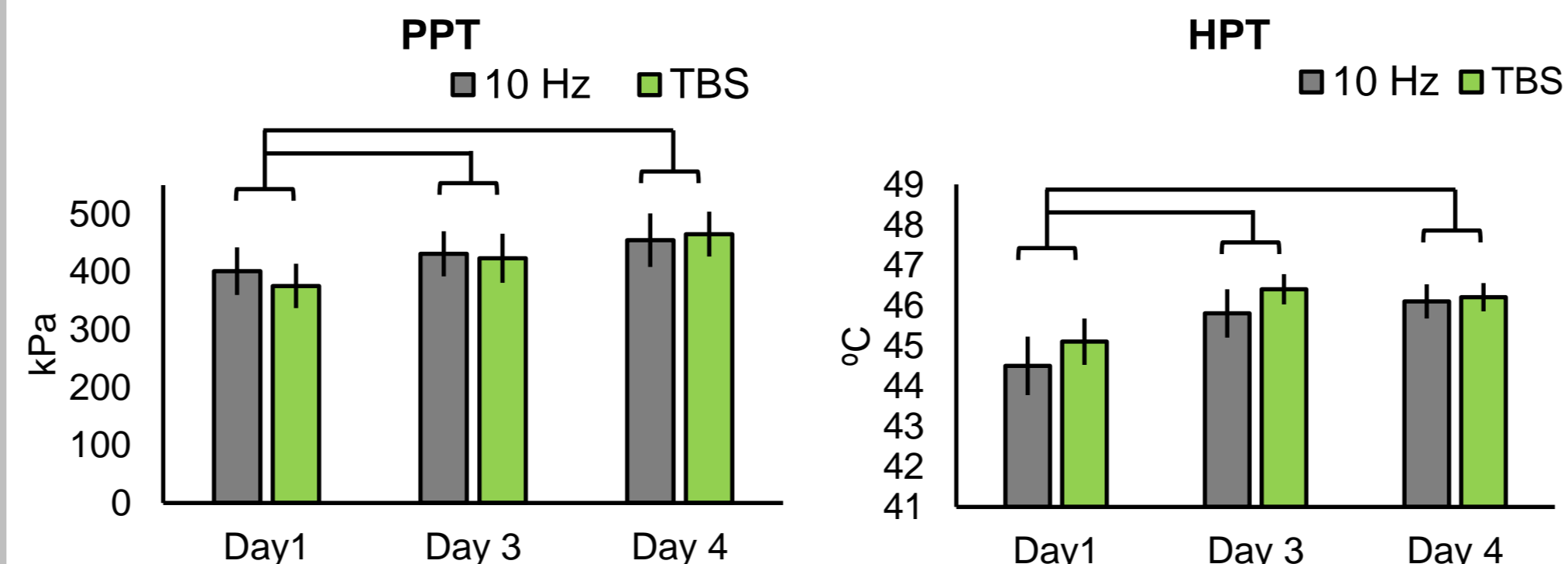
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## RESULTS

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- PPT (Figure 2) and HPT (Figure 3) increased with 10 Hz-rTMS and TBS at Day 3 and Day 4 compared with Day 1 (both  $P < 0.005$ ). No main effect of Protocol and Protocol\*Day interaction was found.



- No main effect of Day, Protocol, and Day\*Protocol interaction in conditioned pain modulation and intracortical excitability across Day and Protocol (all  $P > 0.05$ ).

## RESULTS (CONT.)

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- Based on pooled data from TBS and 10 Hz-rTMS, the increased PPTs correlated with increased efficacy of CPM at Day3 ( $P = 0.008$ ; Figure 4).

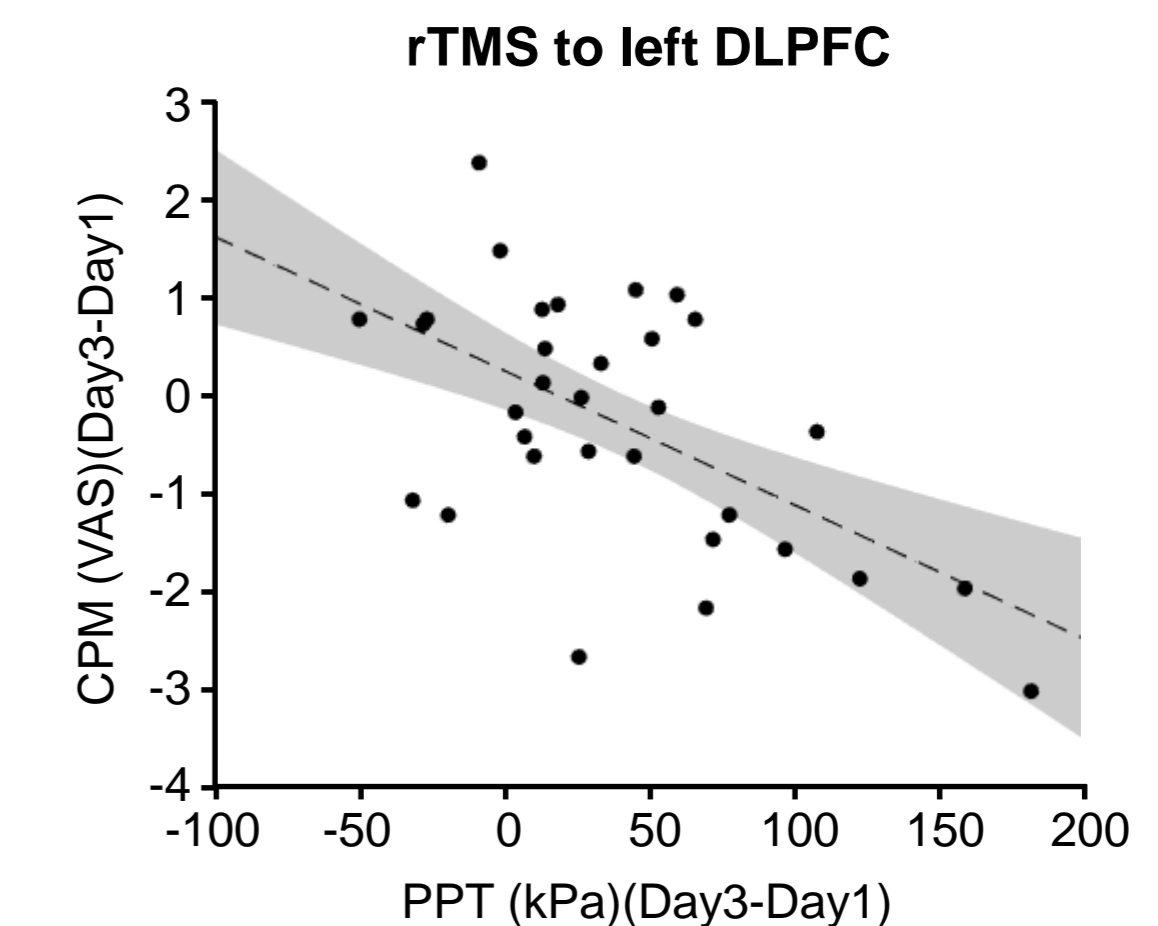


Figure 4. Correlations between changes in PPT and CPM (mean value of VAS reduction across heat and pressure test stimuli) at Day3.

- No correlation was found between increased PPTs and intracortical excitability.

## CONCLUSIONS

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- The current results did not show stronger pain sensitivity reduction by TBS compared with 10 Hz L-DLPFC rTMS.
- Both protocols maintained increased pain thresholds up to 24-hours after the last session.
- Pain sensitivity reduction was partially associated with modulation of CPM efficacy but not with the intracortical motor excitability changes.

## REFERENCES

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1. Lefaucheur JP et al. Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS). Clin Neurophysiol, 2014
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4. Huang Y et al. Theta burst stimulation of the human motor cortex. Neuron, 2005