Pre-stimulus high and low beta phase coherence modulates the impact of TMS entrainment modulating conscious visual perception

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INTRODUCTION

Published evidence from our laboratory supported a causal association between the entrainment of high-beta (**30 Hz**) oscillatory activity driven trial-by-trial by short bursts of Transcranial Magnetic Stimulation (**TMS**) delivered to the right Frontal Eye Field (**FEF**) and bilateral improvements of conscious visual perception for lateralized near-threshold visual stimuli [1]. Nonetheless, responses to neurostimulation rely heavily on baseline neural activity at the moment of stimulation [2] raising the question whether **visual improvements induced by right frontal high-beta rhythmic TMS bursts on conscious perception** could have been **influenced by ongoing pre-stimulus patterns of frequency specific oscillatory activity**, operating in **fronto-parietal systems**, well before the onset of stimulation patterns.

METHODS

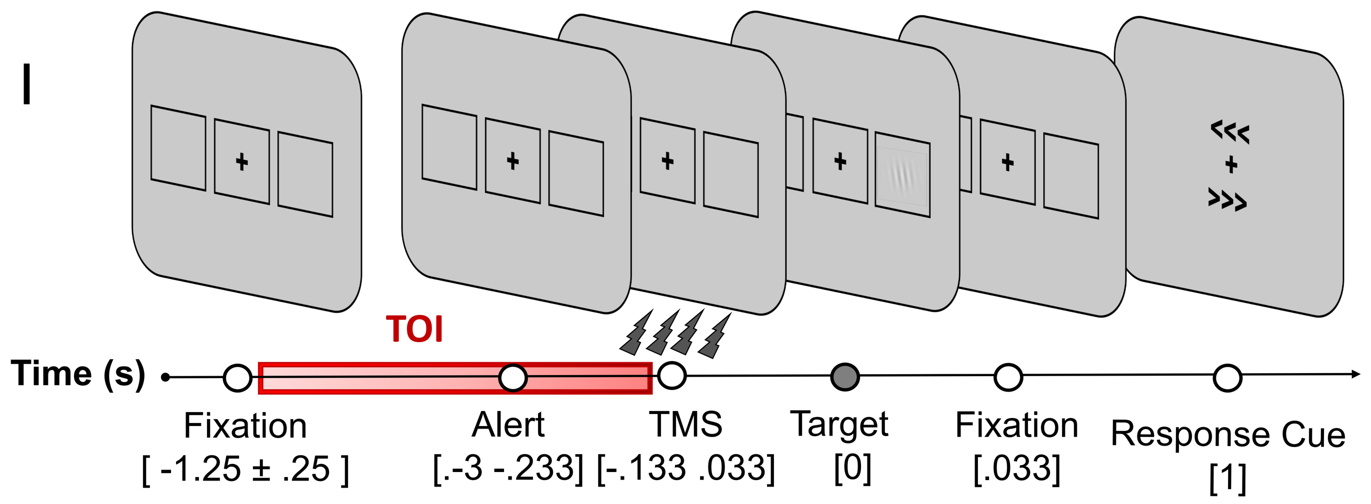
Here we reanalyzed an existing dataset [1] of recorded scalp **EEG** signals (64 channels) obtained in a cohort of healthy **right-handed** participants (n=14) while performing a visual detection task on lateralized near-threshold stimuli. On every trial, participants received prior to the onset of a visual target active/sham **high beta rhythmic (30 Hz**, 4 pulse bursts) bursts of **TMS**, or **active/sham control random bursts** of equal duration and identical number of pulses delivered to the **right FEF,** a key region of the dorsal attention network. In order to examine the influence of pre-stimulation neural activity,

we investigated potential differences in ongoing EEG correlates:

- in the beta band [15 45 Hz] for a time window [-0.5 to -0.3 s]
- and across bands [2 45 Hz] for a time window [-0.8 to -0.2 s]

prior to the onset of the visual stimulus [0 0.033 s] and active/sham TMS bursts [-0.133 -0.033 s] for trials leading to **'hits'** or **'misses'**. **Permutation tests** across channels were used to account for the **statistical difference** of pre-stimulus inter-trial phase coherence (**ITC**) between EEG features leading to 'misses' or 'hits' for either active TMS patterns (**rhythmic vs. random**) **vs. sham** TMS patterns for contralateral (**left**) or ipsilateral (**right**) **targets**.

Figure 1

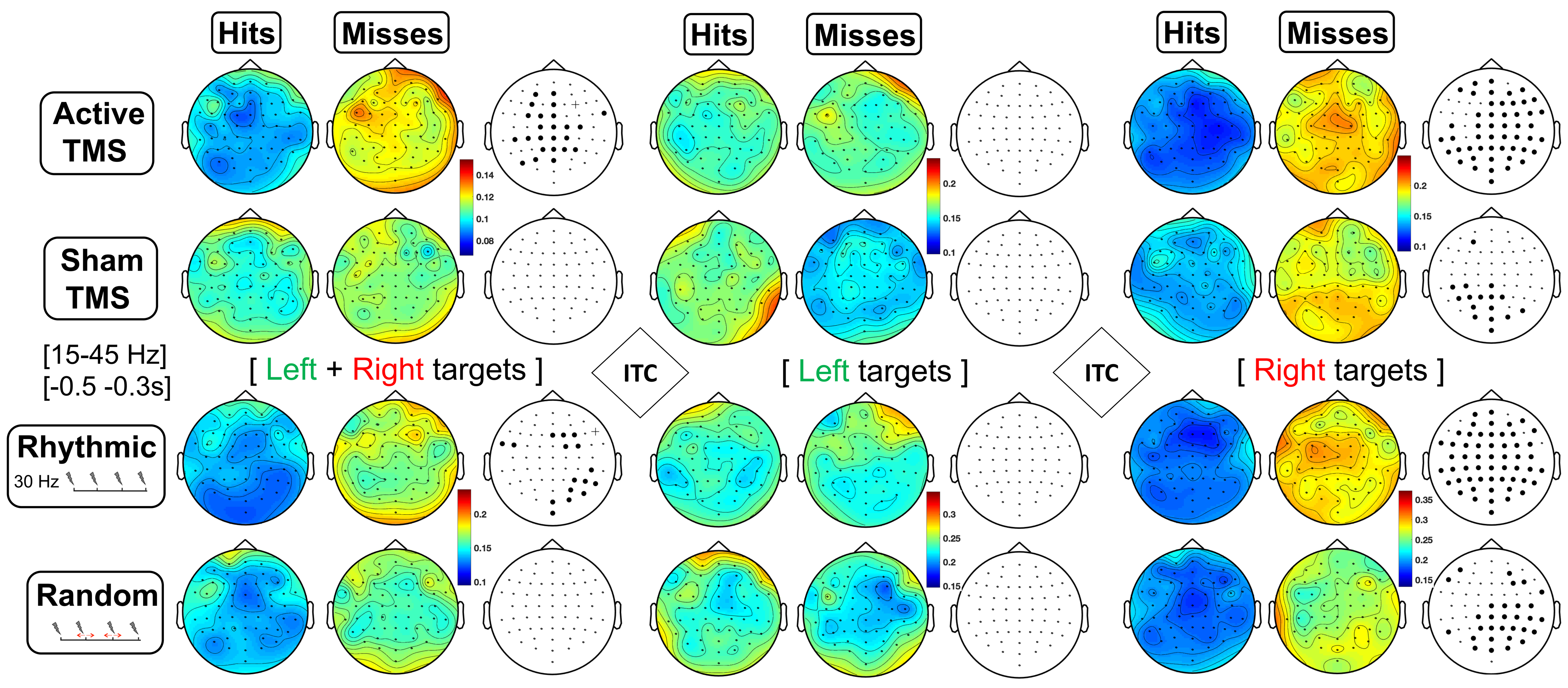


RESULTS

Our analyses revealed **statistically significant differences in ITC** between trials leading to **'hits' or to 'misses'** :

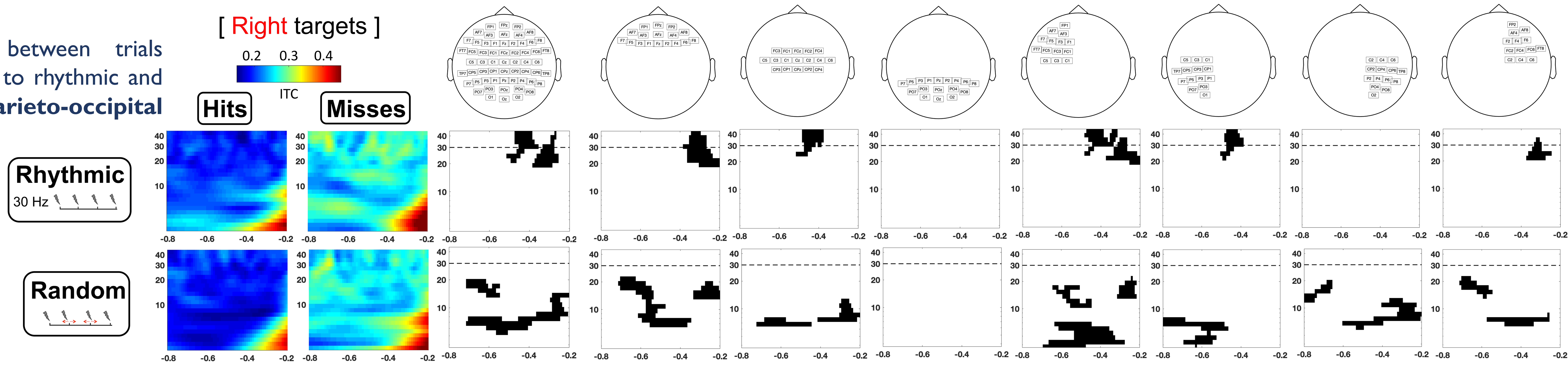
- **decreases of pre-stimulus/stimulation ITC in frontal and central locations** for trials leading to **hits**, specifically within a broad beta-band [**15-45 Hz**] (Fig. 2 left)
- **decreases more consistent and more widely distributed** for trials preceding **rhythmic** rather than **random** active TMS bursts (Fig. 2 bottom rows)
- these differences reached significance **only for right targets** but not for left targets (Fig. 2)

Figure 2



- **ITC decreases** in the time-frequency domain centered around the 30Hz stimulation pattern [~20 40 Hz] for a time-window [-0.5 -0.2 s] for trials prior to the **rhythmic** TMS bursts leading to **hits** (Fig. 3 upper row)
- Sustained **decreases** in **ITC** for the **theta/alpha band** for [-0.7 -0.2 s] and several **decreases** in the **low beta band** across [-0.8 - 0.2 s] for trials prior to the **random** TMS bursts leading to **hits** (Fig. 3 lower row)
- **no statistical differences** between trials leading to hits and misses prior to rhythmic and random stimulation for **parieto-occipital channels** (Fig.3 middle column)

Figure 3



CONCLUSIONS

Our findings show that **ongoing neural activity** at the time of stimulation **influences the ability of active TMS stimulation** delivered to the right FEF to **facilitate the detection** of near-threshold lateralized visual targets. These findings support well-established models of state dependency of TMS modulatory effects and extend such to the domain of oscillatory activity and frequency specific phase synchrony [2].

We are currently working on elucidating both the reasons why we **only** observe differences in **ITC** between trials leading to hits and misses for **right targets** (Fig. 2), and how pre-stimulation activity differs with relation to **rhythmic and random** patterns of TMS stimulation (Fig. 3). For the latter, our current hypothesis considers that our findings are broadly consistent with a growing body of evidence showing the **periodicity of visual information** sampling at low frequencies [3, 4], which could **explain the differences** in trials leading to hits and misses prior to **random TMS** bursts.

Lastly, our results open new venues, which by manipulating pre-stimulus oscillatory patterns via afferent sensory inputs or TMS, could facilitate the efficacy of neuromodulation. Future work will focus on the **deep learning classification of EEG features** (e.g. ITC) differentiating successful from failed visual perception for prospective use in **closed-loop neuromodulation adapting the stimulation intensity and timing according to ongoing neural activity**.

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