Investigating early neural responses during transcranial magnetic stimulation (TMS) in a non-human primate model

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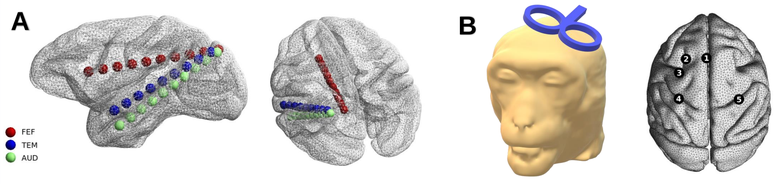
Introduction

Transcranial Magnetic Stimulation (TMS) is a non-invasive brain stimulation method which is used in human neuroscience and has shown promise as a treatment option for a range of neuropsychiatric disorders. Despite its widespread use, its mechanisms are still poorly understood. To this end, we study TMS mechanisms using in-vivo recordings in non-human primates (NHP) model.

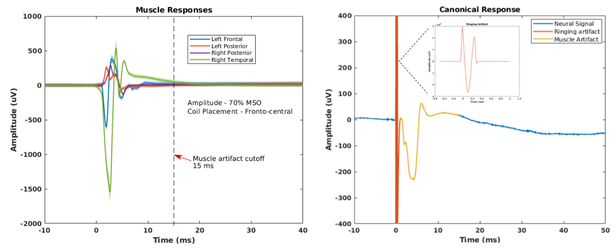
Methods

A macaque was implanted with three depth electrodes spanning from occipital cortex to frontal eye field (FEF) region, auditory cortex (AUD) and temporal (TEM) region. TMS was delivered to the anesthetized monkey at 5 stimulation intensities as a percentage of maximum stimulator output (MSO) with inter-pulse interval of 5-10 seconds. Concurrent EMG activity was recorded from cranial muscles using needle electrodes. A sham protocol was executed by tilting the coil away from the scalp to mimic auditory response. We processed the neural data by removing the ringing and muscle artifacts, removing noisy channels, filtering and time-locked averaging. We performed statistical analyses to ascertain effects of stimulation intensity on physiological response. We also generated head models by pre-surgical MR images and used SimNIBS to run electric field simulations.



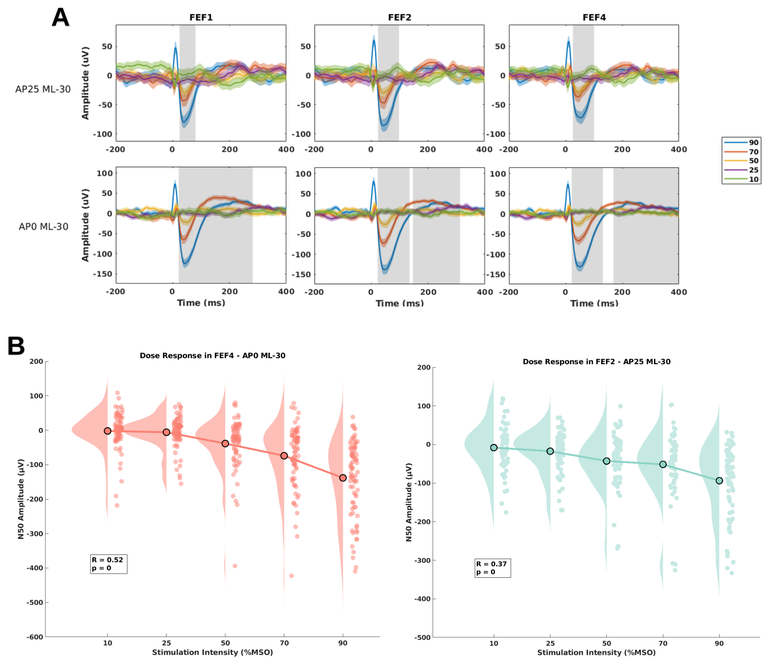
(A) The locations of implanted depth electrodes and (B) stimulation locations. ***In B, 1 – AP35 ML0, 2 – AP35 ML-20, 3 – AP25 ML-30, 4 – AP0ML-30, 5 – AP0ML30***

Muscle Artifact Rejection



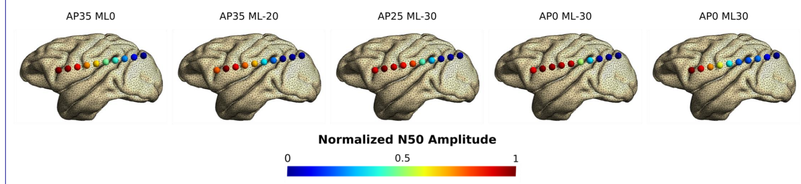
Muscle artifacts obtained by 4 locations on the head showing the duration of the muscle activity (left) and TMS evoked signals with the time window used for artifact interpolation (right)

Dose Dependent Effects



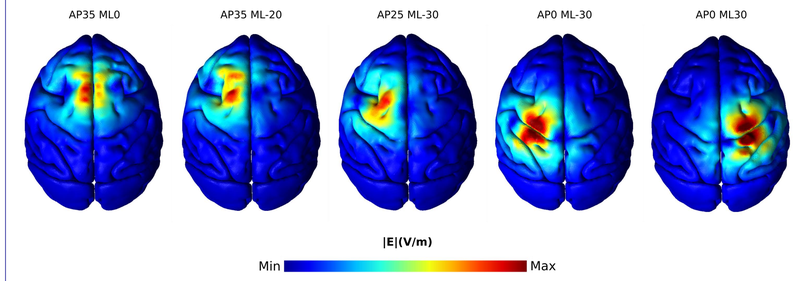
(A) Neural signals as a function of stimulation intensity. Shaded regions indicate significant differences calculated by cluster-based ANOVA test. The prominent deflection at ~50 ms is observed in all contacts (N50). (B) Regression analysis of one contact from each coil location 3 and 4, showing physiological dose response.

Location Dependence



The spatial distribution of the physiological response characterized by N50 amplitude. The hotspot and the effect size of the physiological response moves posterior, when the coil location moves posterior

Electric field modeling



Simulated TMS induced electric fields for the studied coil locations. Stimulation location 4 elicits the highest electric field magnitude as well as the highest physiological response

Conclusion

We demonstrate that there is a dose-response in electrophysiological recordings characterized by an early TMS-evoked potential component (N50). Furthermore, clear differences across different TMS sites point to the spatial specificity of TMS.

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