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Investigating cortical motor representations in response to intermittent theta burst stimulation (iTBS) using 7T fMRI

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Introduction

- Functional representations within the motor cortex are stable over time [**1**], yet dynamic and susceptible to input. For instance, rapid and long-term functional changes can be seen in response to removal or introduction of input (e.g. digit fusion, sensory stimulation, cortical lesions) [**2**].
- High-frequency repetitive transcranial magnetic stimulation (hf-rTMS) is a method recently found to alter functional cortical maps. Specifically, recent animal research has demonstrated that hf-rTMS to the visual cortex can induce a brief destabilisation of functional cortical representations with enhanced cortical excitability and increased spontaneous activity [**3**].
- Using voltage-sensitive dye, weakened intracortical inhibitory mechanisms were demonstrated in response hf-rTMS, which were proposed to result in increased cortical excitability and early plasticity processes. Moreover, functional maps became malleable and sensitive to visual input, suggesting hf-rTMS may prime the cortex ready for plasticity and learning [**3,4**].
- However, it is unclear if hf-rTMS can alter or induce destabilisation of human functional cortical maps.

Methods

Participants

- 21 healthy right-handed participants (4M,17F – mean age 23.1 years, range 19.9 - 34.1). 2 participants were removed due to poor data quality.
- 11 participants were assigned to the active condition and 8 participants were assigned to the control condition.

Parameters

- MRI parameters **(7T Philips, Achieva; 32-channel head coil)**
  - **PSIR** anatomical scan
    - 224 slices, TR = 6.3 ms, TE = 2.7 ms
  - **fMRI** single-shot 2D T2*-weighted GE-EPI sequence
    - 26 slices (1.5 mm thickness), TR = 2 s, TE = 25 ms
    - Travelling-wave finger tapping task, right hand
- iTBS **(Magstim Rapid² system (Dyfed, UK), 70mm figure-of-8 coil)**

Analysis

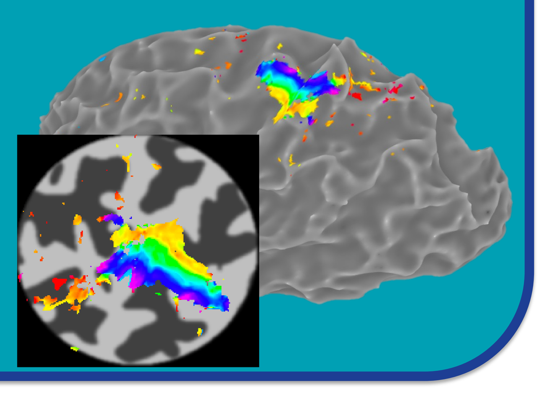
- Pipeline developed by O'Neill et al. [**5**] using mrTools [**6**]
- Travelling-wave scans for the right hand were combined to cancel the haemodynamic delay [7].
- Calculated the following metrics and analysed using t-tests:

Blurring metric [8]	Figure of merit [9]
How well digit regions of interest from each participant overlap in a standard space - Complete overlap of digit areas = 0	How well each subject's digits match to the standard probabilistic atlas of digit representations [6]. - Doesn't match atlas (spread) = 0 - Complete match of atlas = 1

fMRI Travelling Wave Tapping task

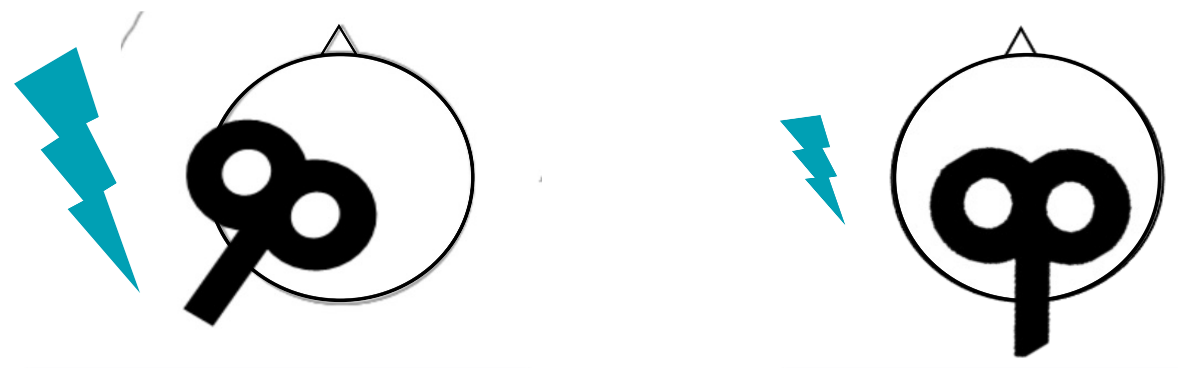
Participants made right-hand tapping movements from digits 1 (thumb) to digit 5 (pinky). This occurred in order (D1-D5) and in reverse (D5-D1) for 8 cycles

Forward	D1	D2	D3	D4	D5
Reverse	D5	D4	D3	D2	D1



iTBS

3 pulses every 200ms (5Hz), frequency of 50Hz, repeated 20 times (10s inter-stimulus interval) = total of 600 pulses

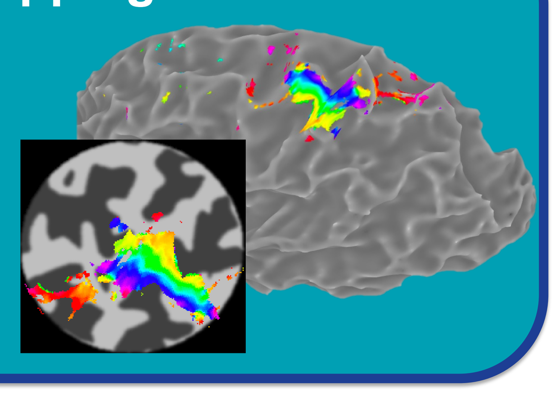


Active
M1 stimulation
70%RMT

Control
Vertex stimulation
30%RMT

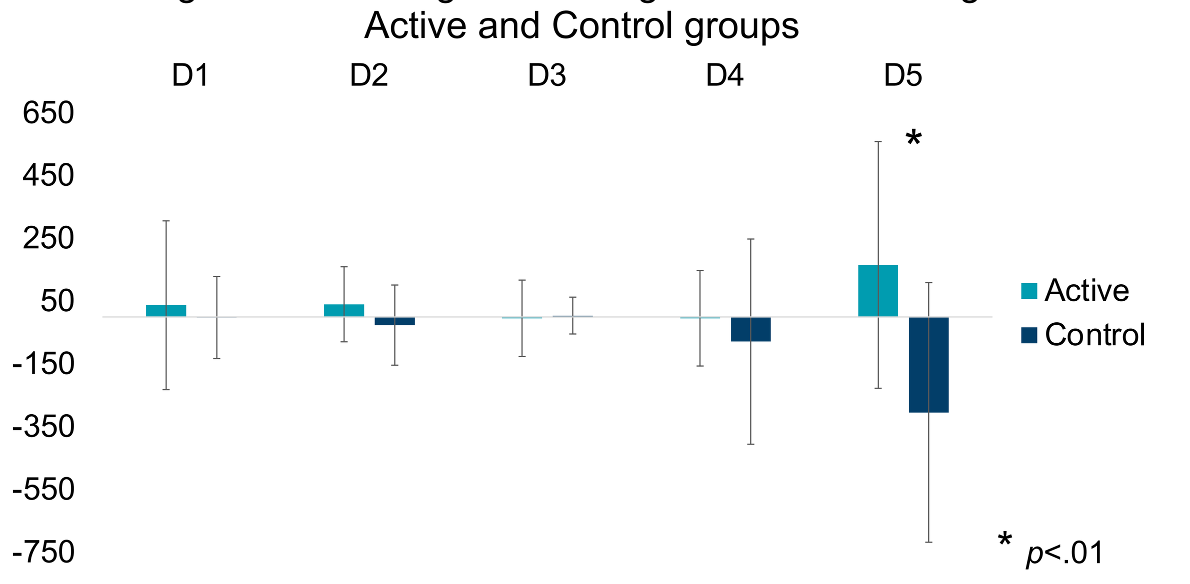
Repeat of fMRI Travelling Wave Tapping task

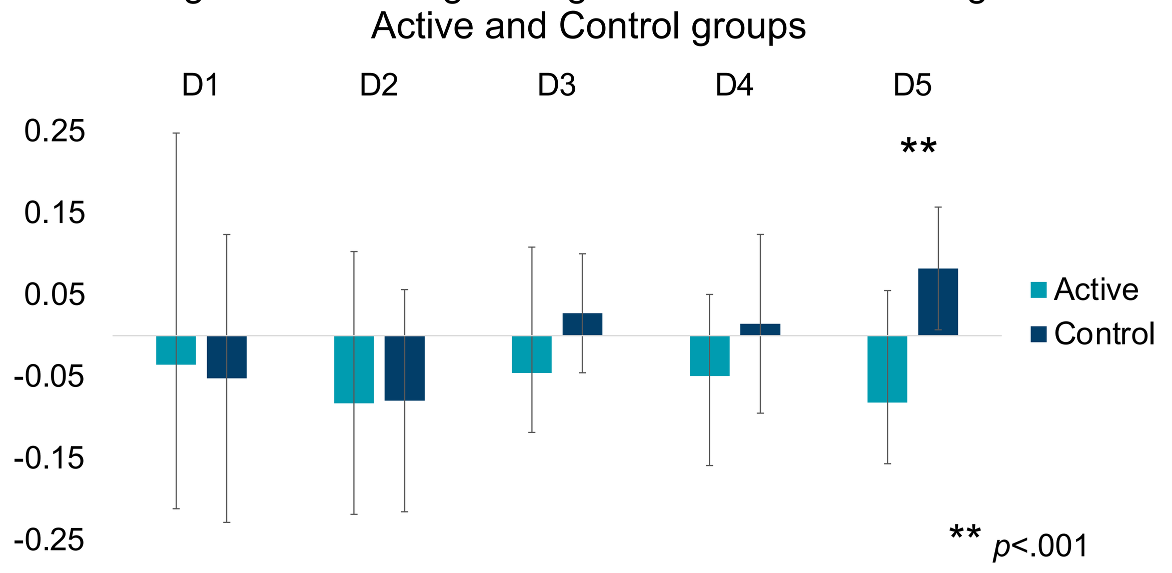
Forward	D1	D2	D3	D4	D5
Reverse	D5	D4	D3	D2	D1



Results

Blurring metric	Figure of merit
- No significant differences before and after iTBS for each digit in active or control groups - No significant differences between the magnitude of change in each group in digits 1-4 - Significant differences between the magnitude of change in each group in digit 5 (p<.01)	- No significant differences before and after iTBS for each digit in active or control groups - No significant differences between the magnitude of change in each group in digits 1-4 - Significant differences between the magnitude of change in each group in digit 5 (p<.001)





Conclusions

- Preliminary data suggest iTBS has no influence on how well motor cortical digit representations match to a standard atlas and overlap in standard space
- Only D5 showed significant differences in blurring and figure of merit between active and control groups
- However, not clear if due to stimulation effects or because the D5 cortical representation is highly variable [**5**]

References

[**1**] Sánchez-Panchuelo RM et al., (2012). *Journal of Neuroscience* 32:15815-15822; [**2**] Kaas JH (1991). *Ann. Rev. Neurosci* 14:137-167; [**3**] Kozyrev V et al., (2014). PNAS 111:13553-13558; [**4**] Kozyrev V et al., (2018). PNAS 115:6476-6481; [**5**] O'Neill GC et al., (2020). *NeuroImage* 217:116880; [**6**] Gardner JL et al., (2018). *Zenodo*; [**7**] Besle J et al., (2013). *Journal of Neurophysiology* 109:2293-2305; [**8**] Fischl B et al., (1999). *Hum. Brain Mapp.* 8:272-284; [**9**] O'Neill GC., (2017). *NeuroImage* 146:667-678