Prefrontal stimulation alters hippocampo-striatal responses during motor memory acquisition and consolidation

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Introduction

Motor memory consolidation is the process that supports the retention of new motor behaviors. Importantly, activity and connectivity in hippocampo-cortical and striato-cortical networks during initial motor sequence learning (MSL) critically condition the subsequent consolidation process [1]. We have recently shown that theta-burst stimulation (TBS) applied on the dorsolateral prefrontal cortex (DLPFC) prior to initial MSL can alter learning-related hippocampo-frontal as well as striatal responses [2]. **Here, we investigated whether such stimulation-induced modulations of brain responses can influence subsequent motor memory consolidation**.

Methods

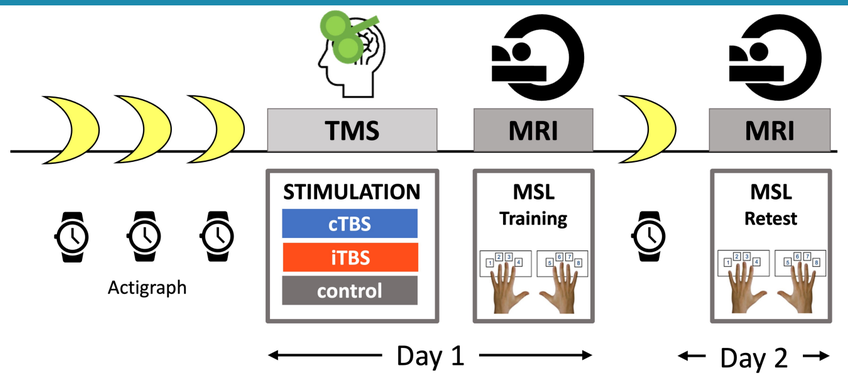

Fig. 1. Experimental design. Participants (N=69, age 19-29ys) received TBS on the DLPFC prior to initial MSL (self-initiated, bimanual, 8-element sequence) on day 1 (Training, TR) and were retested on day 2 (RT) after a night of sleep.

- 3 groups: inhibitory cTBS (N=24); facilitatory iTBS (N=24); control (N=21)
- TBS applied on DLPFC (-30 22 48mm [2]) at 80% (active TBS: cTBS/iTBS [3]) or 40% (control) active motor threshold
- fMRI data (TR=2s, voxel size=2.5x2.5x2.5mm) were analysed using SPM12 as in [4].

Behavioral results

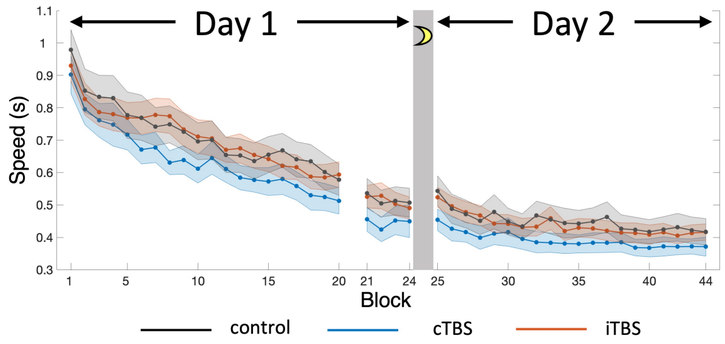

Fig. 2. Speed (i.e., inter-trial interval in s) as a function of practice. On day 1, performance plateaued earlier under cTBS as compared to iTBS (blocks 21-24) (block x group, p=.021). This effect did not carry over to day 2. Performance changes from day 1 (blocks 21-24) to day 2 (blocks 25-28) did not differ across groups.

fMRI results

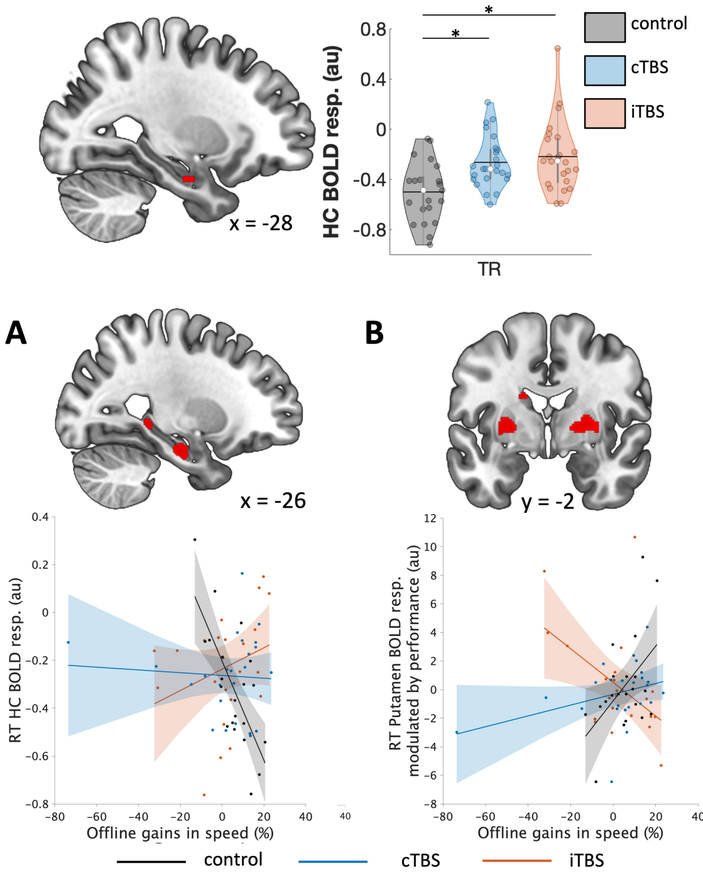

Fig. 3. Main effect of group on brain activity during initial MSL training (TR). Stimulation resulted in less deactivation of the hippocampus (HC) and caudate during task practice (i.e., less activity during inter-practice rest periods) as compared to control stimulation. This suggests that stimulation compromised micro-offline consolidation processes taking place during the inter-practice rest intervals [5,6].
Colored circles represent individual data. White circles represent medians, black lines represent means. Asterisk (*) indicates significance at p<.05. resp: response, au: arbitrary unit.

Fig. 4. Main effect of group on the relationship between brain activity during retest (RT) and overnight offline gains in performance speed. (A) Greater hippocampal deactivation during retest (i.e., higher activity during inter-practice rest intervals) was related to larger gains in controls as compared to the stimulation groups. This suggests that micro-offline processes during retest benefit performance but that this relationship is abolished after active stimulation. (B) Offline gains in performance were associated to a progressive decrease in basal ganglia activity during retest (higher value: more decrease) in the control group while they were related to a practice-related increase in the iTBS group. This link was abolished in the cTBS group.
Circles represent individual data, solid lines represent linear regression fits, shaded areas depict 95% prediction intervals of the linear function.

Conclusion

Our data showed that active, as compared to control, stimulation disrupted brain responses in deep brain regions such as the hippocampus and the caudate nucleus during initial motor sequence learning. While the different stimulation conditions did not modulate consolidation at the behavioral level, brain-behavior regression analyses showed that active stimulation interrupted the link between offline gains in performance and task-related activity in the hippocampus and the striatum.

References & Acknowledgements

[1] Albouy et al., 2013, Hippocampus. [2] Gann et al., 2021, NeuroImage. [3] Huang et al., 2005, Neuron. [4] Dolfen et al., 2021, Cerebral Cortex. [5] Jacobacci et al., 2020, PNAS. [6] Buch et al., 2021, Cell Reports. | This work and MG are supported by the Belgian FWO Research Foundation Flanders (grant number G099516N; predoctoral fellowship 1141320N).