

# Interleaved TMS/CASL: State Dependence of Repetitive TMS Effects on the Dorsal Premotor Cortex

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## Introduction

We have recently demonstrated the technical feasibility and the potential advantages of combining transcranial magnetic stimulation (TMS) with multi slice continuous arterial spin labeling (CASL) imaging (1). Here, we use this novel approach to assess the effects of repetitive TMS applied to the left dorsal premotor cortex (PMd) on rCBF (regional cerebral blood flow). Motivated by prior studies demonstrating that the effects of rTMS protocols depend on the activation state of the stimulated cortex (e.g., 2, 4), we compare the effects of stimulation during different motor states (i.e., at rest and during sequential finger tapping with the left hand [FT]).

## Methods

Interleaved TMS/CASL was performed on 9 subjects (3T Siemens TIM Trio). The stimulation site above the left PMd was determined offline (2 centimeter anterior and 1 centimeter medial to the motor "Hot Spot" of a particular finger muscle in the motor cortex; see 2, 3). Inside the scanner, the TMS coil was positioned over the "Hot Spot", the resting and active motor thresholds (rMT and aMT) were determined and then the coil was repositioned over the left PMd. A 2 x 2 factorial block design was used with motor state (finger tapping vs. no finger tapping) and TMS over left PMd (TMS high = 110% rMT, TMS low = 70% aMT) as experimental factors. During one run (3 blocks, one block consisting of 60 seconds of experimental factor followed by 120 seconds of rest) only one experimental condition was tested and the subjects were informed prior to each run whether they had to perform the task or not. Each subject underwent 8 experimental runs, 2 runs for each experimental factor. The order of the measurements was counterbalanced among subjects. TMS was applied as short 10Hz rTMS trains (5 pulses per train, 4 sec gap between trains).

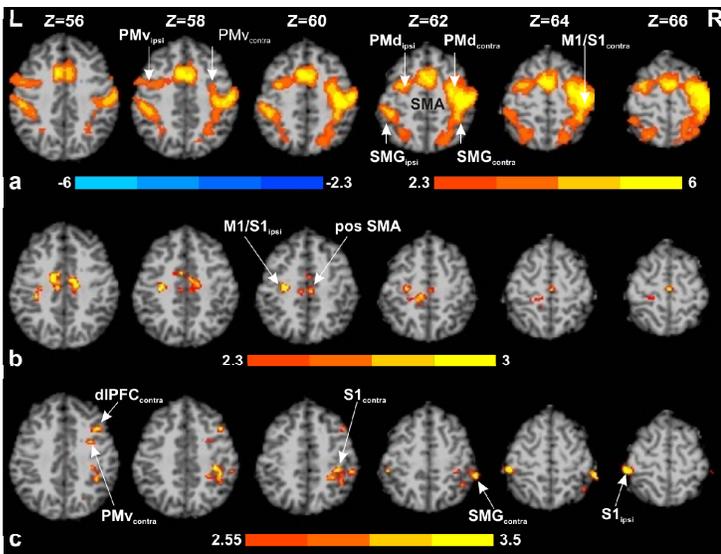
During the blocks, subjects viewed a randomized sequence of 5 geometrical figures. In the finger tapping condition, each figure instructed a response with a specific finger. These arbitrary cues were presented at a rate of 0.8 Hz and subjects were trained on the task before the TMS/CASL experiment. Reaction times as well as the accuracy of the finger tapping were recorded throughout the whole experiment. During the rest periods the subjects had to fixate a white cross presented in the central visual field.

## Results

The group rCBF activation map of the task main effect (finger tapping > no finger tapping) shows significant rCBF increases in cortical motor areas: contralateral (to the site of stimulation) M1/S1, CMA/SMA, ipsi- and contralateral PMv, PMd and SMG (Fig. 1a). The TMS rCBF main effects (TMS high > TMS low) revealed increases in perfusion in ipsilateral M1 and posterior SMA (Fig. 1b). Movement related perfusion changes were significantly modulated by TMS intensity in several sensorimotor areas, especially in the right hemisphere (Fig. 1c).

## Conclusion and Outlook

The task main effect revealed the expected activation pattern for finger tapping paced by arbitrary cues, with a strong involvement of premotor and supplementary motor areas (5). The state-dependent effects of left PMd rTMS on rCBF, as demonstrated by the interaction between TMS and motor state, is in concordance with previous results using BOLD imaging and a different task (2). Unlike BOLD imaging, CASL allows the investigation of slow modulations of rCBF. Thus, as a next step, we will analyze the time dependence of the observed TMS effects across the 3 experimental blocks. This will allow us to determine whether rTMS in the prior block pre-conditioned the effects in the following block (resulting, e.g. in a stabilization of the rTMS effects).



**Figure 1** a) Main effect of finger tapping (9 subjects, voxel threshold  $z=2.3$ , cluster threshold  $p=0.05$  corrected, FSL FLAME mixed effects analysis, MNI space) b) TMS main effect (same threshold level as for finger tapping) c) Interaction between TMS and task ([TMS low, no FT] - [TMS low, with FT] - [TMS high, with FT]); voxel threshold  $z=2.55$ , cluster threshold  $p=0.05$  corrected)

## References

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