Visualizing virtual brain lesions: Simultaneously combining fMRI and TMS

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Introduction:

Transcranial magnetic stimulation (TMS) of the human brain can lead to a reversible impairment of behavioral performances [1]. This non-invasive virtual lesion technique has been used to investigate the causal relationship between a stimulated brain region and a specific behavioral or cognitive function [2]. However, TMS cannot illuminate the brain activity changes underlying the virtual lesion. Recently, it was demonstrated that interleaved TMS and functional magnetic resonance imaging (fMRI) is feasible [3, 4]. Here we show the physiological consequences of a virtual brain lesion by simultaneously combining fMRI and TMS during the execution of behaviorally controlled visuospatial tasks. This approach enabled us to visualize the physiological effects of a TMS-induced functional lesion as measured by the induced changes of BOLD responses.

Methods:

MRI was performed at 3T (Siemens TRIO) on 6 healthy subjects. During the fMRI experiments subjects had to discriminate angles of hands from a displayed clock (ANGLE TASK) or to classify the color of the displayed hands (COLOR TASK), respectively. TMS was applied during two successive fMRI sessions, centering the TMS coil above the right or left parietal cortex with the coil producing an initial medio-lateral current orientation. During both sessions in half of the trials, a train of five TMS pulses (inter-pulse-interval = 75 ms) was applied to the superior parietal lobe (SPL) which had a priori been identified [5] as being activated during this task. The TMS pulses were time-locked to the presentation of the stimulus and applied with stimulation parameters known to induce a functional lesion.

Results:

Behavioral effects of left parietal TMS: The left parietal TMS had no effect on the behavioral performances. The reaction times during left parietal TMS were almost identical to the reaction times without TMS and did not differ significantly from baseline.

Behavioral effects of right parietal TMS*:* The reaction time in the ANGLE task was significantly increased during TMS (functional lesion), while the reaction time in the COLOR task showed no significant effect. This task-related differential behavioral effect of TMS was further supported by a significant interaction between task (ANGLE versus COLOR) and TMS (with versus without) within a two-factorial ANOVA.

fMRI effects of left parietal TMS: Comparing BOLD changes during task execution with versus without left parietal TMS, we found significant TMS-induced BOLD signal increases in bilateral auditory (AC) and predominantly right motor areas. The superior occipital gyrus and the left and right SPL showed similar neuronal activation levels during both task conditions. None of the brain areas showed an interaction between task (ANGLE versus COLOR) and TMS (with versus without), nor did any of the areas show a significant correlation between the TMS-induced changes in brain activity and changes in behavioral performances.

fMRI effects of right parietal TMS: Right parietal TMS induced BOLD signal reductions in the right (stimulated) SPL, the right postcentral gyrus, and the right middle frontal gyrus (MFG) during the ANGLE task (Fig.2 top). No such effect was prominent during the COLOR task (Fig. 2 bottom). This difference in TMS-induced reduction of neuronal activity between both tasks was particularly pronounced in the right SPL (Fig. 2). Accordingly, a two-way ANOVA revealed a significant interaction between task (ANGLE versus COLOR) and TMS (with versus without) only in the SPL and MFG of the right hemisphere.

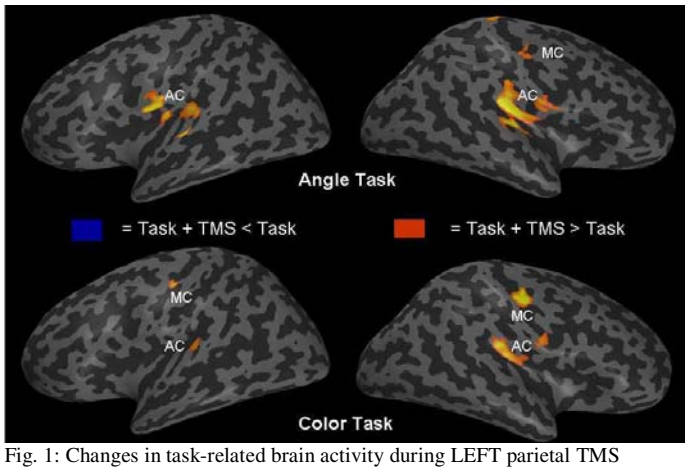

Fig. 1: Changes in task-related brain activity during LEFT parietal TMS

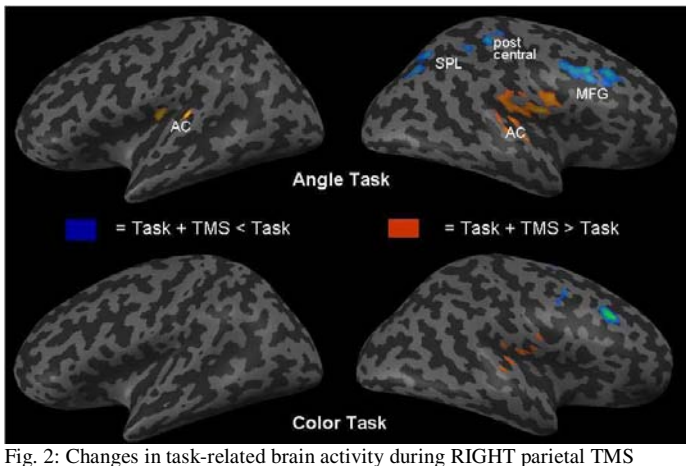

Fig. 2: Changes in task-related brain activity during RIGHT parietal TMS

Discussion

This is the first study combining the concept of functional lesions induced by TMS with simultaneously applied fMRI. A functional lesion resulted in reduced BOLD signals in the stimulated cortex as well as in involved remote brain structures. The TMS-induced reduced neuronal activity correlated with respective behavioral impairments. While functional lesions by TMS already offer a new modality in brain imaging, the combination with fMRI provides a chance to visualize the specific neuronal effects of the functional lesions, and holds the potential to investigate alternative mechanisms used to bypass the lesioned cortical pathway.

References

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