

## Behavioral correlates of negative BOLD signal changes in the primary somatosensory cortex

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### Introduction

Aside from positive BOLD signal changes there is converging evidence that neuronal responses within various cortical areas also induce negative BOLD signals [1,2,3]. Although it is commonly believed that these negative BOLD signal changes reflect suppression of neuronal activity direct evidence for this assumption is sparse. Since the somatosensory system offers the opportunity to quantitatively test sensory function [4] during concomitant activation and has been well-characterized with fMRI in the past, the aim of this study was to determine the functional significance of ipsilateral negative BOLD signal changes during unilateral sensory stimulation by means of correlating them with a change in the sensory perception threshold of the contralateral unstimulated finger.

### Methods

**Subjects:** A total of 9 healthy subjects were included in our studies. All subjects gave their written formal consent prior to the experiment. The study was approved by the local Ethics committee and was in line with the Declaration of Helsinki.

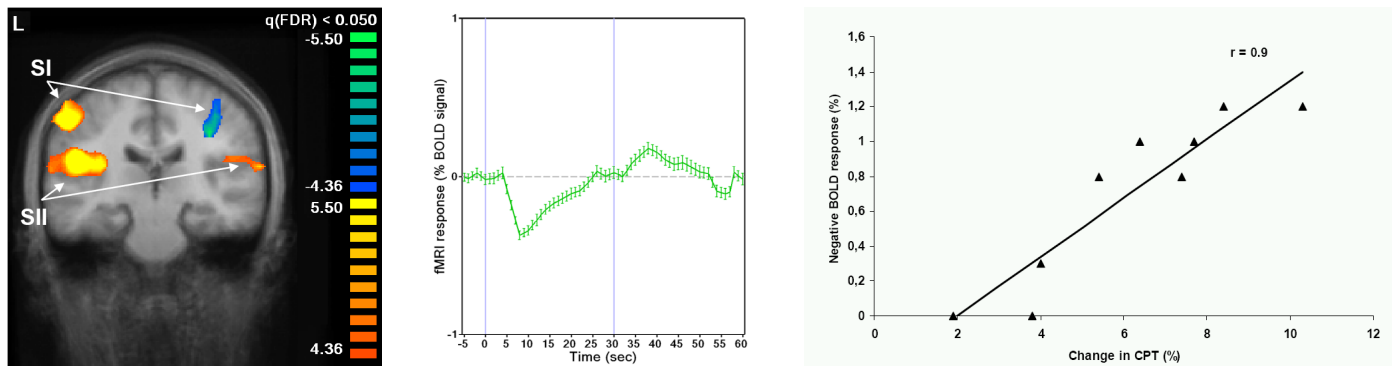
**Electrical Stimulation:** Based on previous results [5] a stimulus frequency of 40 Hz of the right median nerve at the wrist was chosen for this study. The current was individually adjusted to the level of motor threshold, defined as the lowest current that caused a visible contraction. No subject experienced a sensation of pain. The electrical stimulation apparatus did not cause any artefacts in the fMRI images. The stimulus protocol was a typical block design alternating 6 times rest periods (30 s) with stimulation periods (30 s) resulting in a duration of 6.5 minutes. A second functional measurement was started approximately one minute later with the same parameters.

**fMRI Data Acquisition and Analysis:** BOLD fMRI was performed at 3 Tesla (Siemens TRIO, whole-brain EPI, TR 2000ms, TE 36ms, 2x2x4mm<sup>3</sup>). For each of the two experimental runs a total of 195 volumes were recorded. A random effects analysis was chosen for the statistical group-analysis and the false discovery rate (FDR) at a level of 5% was used to threshold group activation maps. Finally, the signal intensity time-course was calculated to delineate the temporal pattern of BOLD signal change across the whole group.

**Psychophysiological Experiments:** In order to measure sensory function quantitatively, the perceptual threshold to electrical stimulation of the left index finger (current perception threshold, CPT) was tested during concomitant electrical stimulation of the right median nerve. These additional experiments were performed using the identical stimulation equipment and protocol as in the fMRI studies. The CPT is the minimum amount of a transcutaneously applied current that an individual consistently perceives as evoking sensation and has recently been proposed as a unique method for investigating sensory function. In order to link the results from the fMRI and psychophysical experiment, the same stimulus as in the MR-setting was administered. During both stimulus and pause, the CPT of the left index finger was measured with the same protocol as described above. This was repeated 6 times as it was done during one run of the fMRI experiments. Comparable to the analysis of the BOLD signal change, the difference in perception threshold during simultaneous contralateral stimulation was calculated as percent change compared to the non-stimulus condition and correlated with the percent change of the BOLD decrease.

### Results

During electrical stimulation of the right median nerve all subjects demonstrated significant increases in BOLD signal (red) in the contralateral primary and bilateral secondary somatosensory areas (left figure). In contrast to these areas with positive BOLD signal changes a decreased BOLD signal (blue) was observed in the ipsilateral SI in 7 of the 9 subjects. The averaged time course of the negative BOLD signal changes (middle figure) was characterized by a transient initial decrease, followed by a gradual return towards baseline within the stimulation period as well as a subsequent poststimulus overshoot.



CPT values increased significantly ( $p < 0.001$ ) by  $6 \pm 3\%$  (range: 2-10%) across the whole group. The individual ipsilateral negative BOLD signal changes correlated extremely well ( $r = 0.9$ ,  $p < 0.01$ ; Pearson correlation coefficient) with the percent change of the CPT of the left index finger during right median nerve stimulation (right figure).

### Conclusion

We used fMRI and electrical median nerve stimulation to study the functional significance of ipsilateral negative BOLD signal changes during unilateral sensory stimulation. Significant BOLD signal decreases were identified in the primary somatosensory cortex ipsilateral to median nerve stimulation. More importantly, additional psychophysiological experiments revealed that these focal cortical fMRI signal decreases reflect a functionally effective inhibition in the somatosensory system, resulting in a measurable increase in perception threshold of the non-stimulated contralateral finger.

### References

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