Dependencies of the negative BOLD signal in primary somatosensory cortex on stimulation intensity and duration

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Introduction

Unilateral stimulation of the somatosensory system induces activation of neurons in the contralateral primary somatosensory cortex (SI) that is accompanied by an increased blood oxygenation level dependent (BOLD) signal. Studies report an additional negative BOLD signal in the ipsilateral SI during mechanical or electrical stimulation [1, 2]. As declines in BOLD signal have been shown to be associated with decreases in neuronal activity [3], this indicates inhibition of the ipsilateral SI. Since it is not clear which representations of the body are affected, we show here that during high intensity stimulation of the somatosensory system another, spatially extensive negative BOLD signal in the parietal and occipital cortex forms that has not been mentioned before. These results seem to indicate inhibition of the whole sensory map of the body, implying an increase of sensory thresholds. Low intensity stimulation in contrast results in short term adaptation of the contralateral activity in SI that causes the BOLD signal to change from positive to negative with prolonged stimulation.

Methods

8 healthy subjects (2 female, 6 male, average age: 29) took part in this study, which was approved by the local ethics committee.

Protocol/ Paradigm: Electrical stimuli were applied through ring electrodes (anode proximal, distance to cathode ~1 cm) to the left index finger as single monophasic square-wave current pulses (pulse duration 0.2 ms) in blocks of 21 s or 3 s, alternating with 21 s of rest. 5 and 8 number of blocks and two different frequencies (2 and 60 Hertz) were used. Total length of paradigms were 7, 13 and 14 min. Stimulation intensity was uncomfortable but below pain threshold and determined by method of limits and forced choice.

MR Imaging: MR imaging was performed in a 3.0 T Philips Intera Achieva scanner (Philips Medical Systems, Best, The Netherlands) using an eight-element phased-array receive head coil. Anatomical images were acquired using a T1-weighted 3D turbo field echo sequence (170 sagittal slices 1 mm thickness; in-plane resolution 1x1 mm; repetition time 9.9 s; echo time 4.6 ms; flip angle 8°). Functional imaging utilized a gradient echo EPI sequence (22 slices 4.0 mm thickness; slice gap 0.1 mm; field of view 230x230 mm; in-plane acquired resolution 2.9x2.9 mm; repetition time 3.0 s; echo time 35 ms; flip angle 90°; SENSE factor 1).

Analysis:

Data was analysed using Brain Voyager QX. Slice time correction, 3d motion correction and temporal high pass filtering were applied, as well as spatial smoothing (3d Gaussian, FWHM 4mm). Functional datasets were co-registered to the anatomical datasets and transformed into Talairach space. They were further analysed using the general linear model. Activated voxels were determined requiring a False Discovery Rate (FDR) of less than 0.02. Regions of interest in SI for left index finger (Brodmann area 3) were determined anatomically.

Results and Discussion:

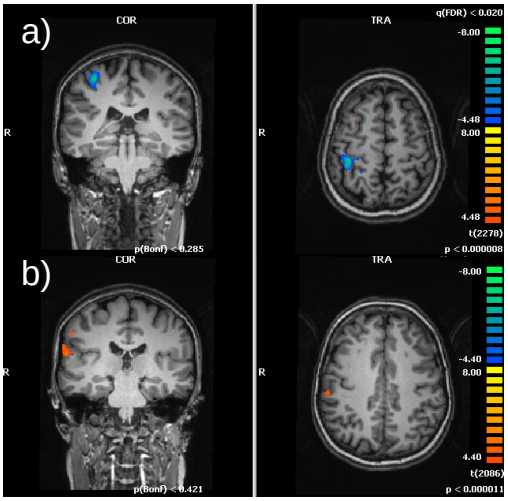


Figure 1: Low intensity stimulation (2 Hz) for a) 21 s and b) 3 s elicits contralateral BOLD signals in SI and b) SII. 8 subjects.

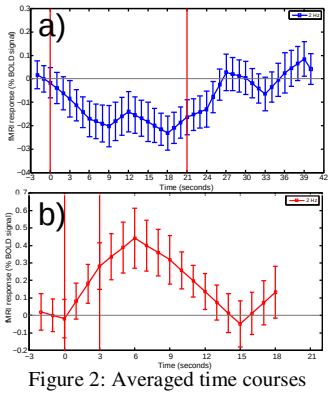


Figure 2: Averaged time courses (mean ± SE) of the contralateral BOLD response during low intensity stimulation (2 Hz) for a) 21 s and b) 3 s.

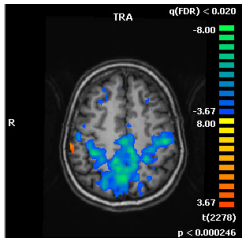
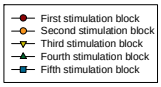


Figure 3: High intensity stimulation (60 Hz) for 21 s elicits a positive BOLD signal in contralateral and a negative BOLD signal in ipsilateral SI and parietal cortex. 8 subjects.



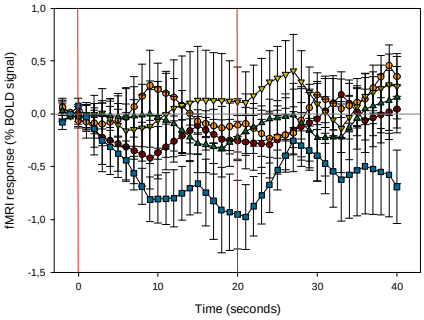


Figure 4: Low intensity stimulation (2 Hz) for 21 s, averaged (mean ± SEM) over 8 subjects. Shown are BOLD signals over time during five consecutive stimulation blocks.

Low intensity stimulation (2 Hz) elicits a contralateral BOLD signal, which changes from positive (Figures 1b and 2b) for short stimulation duration (3 s) to negative (Figures 1a and 2a) for long stimulation duration (21 s). This is presumably caused by neuronal adaptation and subsequent inhibition representing gating mechanisms of innocuous stimuli. Analysis of BOLD signals during five consecutive stimulation blocks does not show stepwise decrease (Figure 4). However, the most negative BOLD signal can be found during the last stimulation block. High intensity stimulation (60 Hz) elicits a positive contralateral BOLD signal and a negative ipsilateral BOLD signal in SI (Figure 3). These signals are accompanied by a spatially extensive negative BOLD signal in the parietal and occipital cortex. This negative BOLD signal seems to represent functional inhibition, either of the sensory map representing the body, or of downstream association cortices [4]. Insufficient perfusion pressure may also lead to attenuation of the BOLD signal [5]. Further measurements including more subjects are required to improve statistical evidence. This work shows that stimulation duration and stimulation intensity have great impact on BOLD signal changes in SI.

References

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