Consistent negative BOLD responses in SI of primate cortex produced by tactile stimulation

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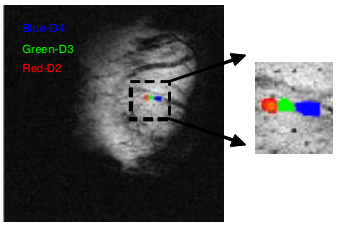
Introduction: Positive BOLD signals have been measured with sub-millimeter resolution in the cortex of non-human primates at high field during subtle tactile stimulation [1, 4]. The resulting fMRI maps correlate very well spatially with intrinsic optical imaging and electrophysiology maps. In studies of SI of squirrel monkeys, we have detected consistent negative BOLD signals in motor area and sensory areas near to SI, which also respond to tactile stimulation.

Fig.1. Topology map of 3 Digits



Method: Squirrel monkeys were anesthetized with ketamine hydrochloride and maintained with isoflurane anesthesia. Animals were intubated and artificially ventilated. The physiological states (respiration rate, temperature, SpO2, heart rate, ET-CO2) of the animals were carefully monitored. All scans were performed on a 9.4T 21-cm bore Varian INOVA magnetic using a 3cm surface transmit-receive coil secured over the sensory cortex. Gradient echo images (512x512 matrix) and GE-EPI (64x64 matrix) were used to acquire anatomical and functional images respectively. A custom-designed MR cradle with ear bars and eye bar was also used to reduce motion. The monkey's fingers were secured, leaving the glabrous surfaces available for vibro-tactile stimulation by a rounded plastic probe (2mm diameter) connected to a piezioelectric device. Piezos were driven by Grass stimulators at a rate of 8Hz. Stimuli were synchronized to the image acquisitions. A block-designed stimulation pattern was used in this study (30s on/ 30s off). The repetition time TR on individual scans was adjusted (1.5s or 2s) to match the ventilator rate to minimize respiration-induced signal variations in the functional time-courses. Matlab was used for data analysis. A polynomial model was used for time course drift correction. The data were then spatially and temporally smoothed. Functional maps were generated by calculating the correlation of each functional time-course with a reference waveform.

Fig.2. Positive and Negative BOLD at D2 (day1, run 1)

a) Topology map **b) Averaged BOLD over ROIs**

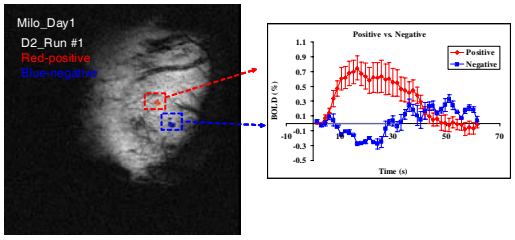
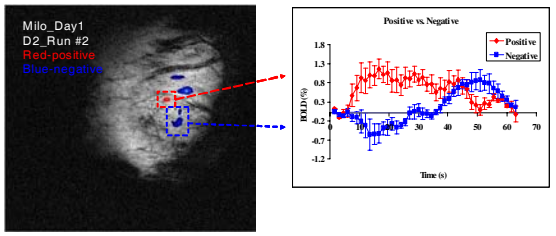


Fig. 3. Positive and Negative BOLD at D2 (day1, run2)

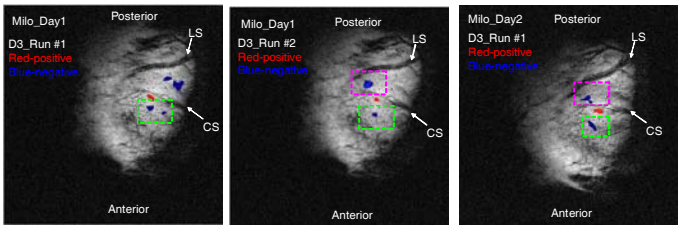
a) Topology map **b) Averaged BOLD over ROIs**



Results: One monkey was scanned on two different days. On day one, 3 digits (D2, D3, D4) were stimulated separately. Consistent positive BOLD signals at SI were observed for each single digit revealing fine topographic maps of fingerpads with high spatial resolution, as shown in Fig. 1. This result is consistent with previous reports [1, 4]. In addition to the positive BOLD signals, we also observed consistent focal negative signals nearby. An example is shown in Fig. 2 (a). As digit 2 was stimulated, the usual focal positive BOLD signal (the same red spot as shown in Fig.1) was seen in area 3b, while a negative BOLD signal (blue spot) was also observed nearby. ROIs were chosen to measure the average time course of the positive and negative BOLD signals (percent signal changes), which are shown in Fig. 2 (b) (error bars +/- 1 s.d. across ROI voxels). On the same day, another run with D2 digit stimulation showed a similar pattern and the results are shown in Figs. 3 (a) and (b). The time course of these two negative BOLD signals showed that at the blue marked positions, BOLD signal decreased during the stimulation, returned to baseline right after the cessation of stimulation and showed a positive overshoot during the early stimulation "off" period. Consistent negative BOLD signals were also found for D3 stimulations, as shown in Fig. 4 (a,b,c), and similar results were also found for D4 (data not shown).

Fig.4. Positive and Negative BOLD at D3 for animal scanned

a) day 1 run 1 **b) day 1 run 2** **c) day 2 run 1**



Discussion: Based on the literature on cortical organization [5], we can classify the location of the negative BOLD signals into two distinct areas. The first category is the motor area; examples are the negative BOLD in Fig. 4 that is marked with a green square, where the negative BOLD signal position is more anterior to the central sulcus (cs in Fig. 4) and SI position. Another category is the sensory area; an example is shown in Fig. 4 (b)-(c) marked with a pink square. We have shown that with mild tactile stimulation, focal negative BOLD signals with millimeter scale resolution were found for different digits. The results were consistent and highly reproducible as shown across runs and on different days. These mm scale positive and negative BOLD responses to physiologically realistic stimuli, in an area that is accessible for both optical imaging of intrinsic signal and electrophysiological measurements, offer an opportunity to examine the neurovascular coupling mechanisms underlying negative BOLD signals in future studies. Finally, these data suggest that inhibitory responses (or suppressed excitability) occur in motor and other somatosensory areas (area 1/2) while primary sensory area 3b is activated during tactile stimulation. This experimental model in combination with single cell electrophysiology can be further studied to provide a test bed for understanding the neural basis of the negative BOLD signal.

References: 1. Turner G.H., Chen L.M., Friedman R.M., Gore J.C., Roe A.W., Avision M.J. ISMRM 2006, # 2134, p420.

2. Nelson A, Staines W, Graham S, McIlroy W. *Cogn Brain Res.* 2004;**19**:174–184.

3. Arthurs O, Williams E, Carpenter T, Pickard J, Boniface S.. *Neuroscience.* 2000;**101**:803–806.

4. Chen L.M., Turner G.H.. Markus T.M., Friedman R.M., Gore J.C., Avison M.J., Roe A.W. sfN 2006, #212.2, p75

5. Wu CW-H, Kaas. JH Neurosci. 1999 19: 7679-7697.