Tight Coupling of Resting-state BOLD fluctuations with Intracortical DC Changes in Rat Somatosensory Cortex during Prolonged Medetomidine Sedation

W-J. Pan[1], M. Magnuson[1], G. Thompson[1], D. Jaeger[2], and S. Keilholz[1]
[1]Biomedical Engineering, Emory University/ Georgia Institute of Technology, Atlanta, GA, United States, [2]Biology, Emory University, Atlanta, GA, United States

Introduction: The neural processes underlying low-frequency BOLD fluctuations in resting-state fMRI have not been fully investigated [1]. We hypothesized that the neural activity reflected in slow potential changes (DC; < 1 Hz) may be the origin of resting-state BOLD signal fluctuations. To test the hypothesis, simultaneous fMRI and intracortical recording were conducted in rat somatosensory cortex. The BOLD fluctuations were compared with concurrent DC as well as regular local field potentials (LFP; 1-100 Hz). The dynamic signal properties of prolonged medetomidine administration over 6 hours were examined as well.

Materials and methods: Simultaneous fMRI and intracortical recording, which has been described elsewhere [2], were conducted in 5 male SD rats (200~300 g) under medetomidine sedation. Briefly, a pair of glass microelectrodes was implanted in somatosensory cortex (S1FL) of the left and right hemispheres and DC/LFP activity was recorded during the resting state fMRI scan. All imaging was performed on a 9.4T animal MRI system (Bruker, Germany). A 2-cm house-made surface coil was used, which allows the recording electrodes to protrude from the center. The electrophysiological signals were filtered < 100 Hz, amplified (x 500) by an DC/AC amplifier located just outside the scanner room, and digitized at 12 KHz. A coronal slice over the somatosensory cortex was imaged with GE-EPI (TR/TE=500 ms/15 ms, slice thickness 2 mm). The resting-state fMRI scan lasted 8.33 minutes and repeated every ~30 minutes during medetomindine sedation up to 4-6 hours [3]. The artifacts in the electrical recordings due to gradient switching during scans were removed [2]. Cross correlation analysis was performed between DC (or LFP power) and BOLD across image voxels with various time lags.

Results: The scans acquired at different time points (up to 6 hours after switching to medetomidine from isoflurane) indicated dynamic changes in BOLD low-frequency power. Within the first hour of medetomidine administration, the BOLD power was highest at < 0.1 Hz, as previously observed in human resting-state studiesl. However, the power of <0.1-Hz decreased and a peak at ~0.2-Hz increased over time (Fig. 1). The 0.2-Hz peak was observed for the rest of the experiment (up to 5 hours). The correlation between the BOLD signal and neural activity was further estimated for both peaks (<0.1-Hz, 0.2-Hz and 0.4-Hz as the control, Fig. 2A, B and C). We found the time-lagged BOLD signals at the voxels near the recording site showed significant correlation with DC signals at frequency of both <0.1-Hz and 0.2-Hz (Fig. 2). Interestingly, the 0.2-Hz peak exhibited stronger coherence with BOLD fluctuations at same frequency range (Fig. 2B). The LFP (theta/delta) powers also exhibited correlation with the BOLD signal, but less than DC.

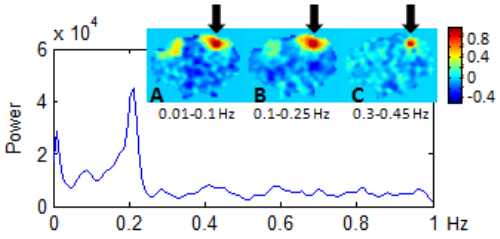

Fig. 1 BOLD power spectrum and functional connectivity. The region of interest at SI (arrow) showed high power and interhemispheric connectivity for <0.1-Hz (A) and ~0.2-Hz (B) but not the neighboring ~0.4-Hz (C).

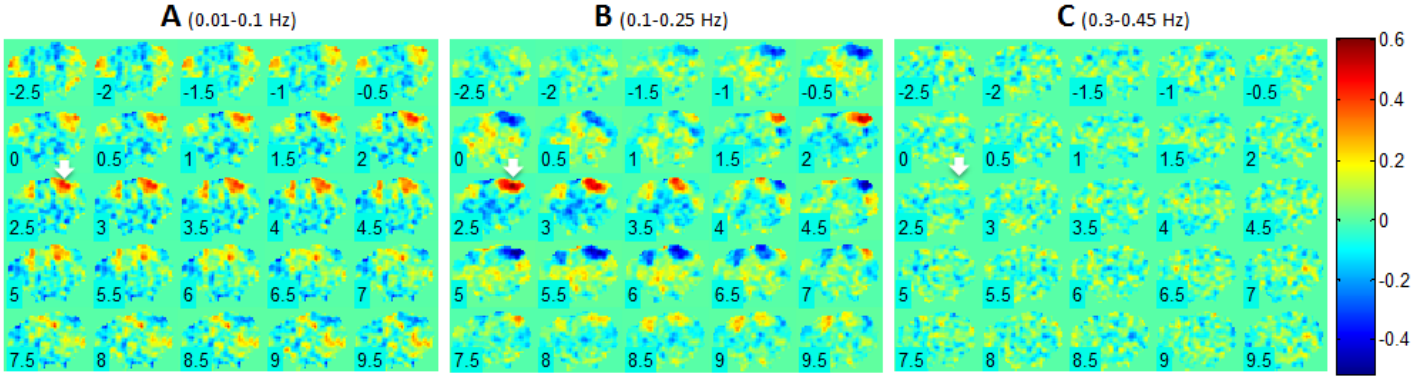

Fig. 2 Cross correlation between BOLD and DC in different frequency ranges. The DC signal from right S1LF (arrow) was compared with BOLD of all voxels of the imaging slice in frequencies of <0.1-Hz (A), ~0.2-Hz (B) and ~0.4-Hz (C). The different BOLD lags from -2.5 to 9.5 s are labeled at left-bottom corner of each correlation map. The DC signal correlated significantly with BOLD in voxels near the recording site (arrow) with ~2.5-s lag in the frequency < 0.25 Hz. Interestingly, the correlation at ~0.2 Hz (B) is stronger than that of <0.1 Hz (A).

Discussions: To our knowledge, this is the first examination of the relationship between resting-state BOLD signalfluctuations and the intracortical DC signal. This study demonstrates tight coupling of BOLD with slow neural processes in the resting state. The findings of dual peaks (<0.1-Hz and 0.2-Hz) of the BOLD signal in the rat cortex during prolonged medetomidine sedation was reproducible across all electrode-implanted rats. We also imaged one control rat (without any surgery) at the same time points used for the combined imaging and recording experiments. The 0.2-Hz peak was observed in the control after a few hours of medetomidine administration. This 0.2-Hz peak is prominent in CBV-weighted fMRI resting-state scans [4]. Our findings demonstrated the BOLD signals of both commonly-used <0.1-Hz and 0.2-Hz components, observed in prolonged medetomidine sedation, correlate to neural activity, especially slow changes (DC) in resting state.

References: [1] Logothetis N. K., et al., Nature, 2008, 453(7197):869-878 [2] Pan W.J., et al., J Vis Exp, 2010, 42 [3] Pawela, C.P., et al., Neuroimage, 2009, 46(4): 1137-1147 [4] Magnuson, M., et al., J Magn Reson Imaging 32(3): 584-592