Spontaneous fluctuations of BOLD signal: effect of anesthesia and functional significance

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INTRODUCTION

Spontaneous fluctuations in BOLD signal are used for functional connectivity [1]. It has been suggested that these spontaneous fluctuations may influence trial-to-trial variability of the evoked BOLD response [2]. Taken together, these studies suggest that the *amplitude* of the spontaneous fluctuation has significance for the strength of the functional connectivity (between symmetric points in two hemispheres) and the *phase* of the BOLD signal fluctuation just preceding the stimulus can affect the trial-to-trial variability of the evoked BOLD response. We measured the BOLD signal spontaneous fluctuations and whisker functional responses in rat cortex with two slightly different baseline states (lightly anesthetized and awakened animals) to investigate these suggestions.

METHODS

Pre-experimental procedure: Long Evans rats (n=5) were habituated to restraint and scanner noise. Once they tolerated restraint and sat quietly they were surgically prepared for head post implantation. After recovery from surgery, they were re-acclimated to restraint. ***Experimental procedure:*** On the experiment day, animals were anesthetized with domitor (0.1 mg/kg/hr) and fixed to the holder via the implanted head post. Anatomical images, whisker stimulus evoked functional images with 8 Hz air-puffs, and resting state fluctuations in BOLD signal were acquired. The anesthetic was stopped and whisker stimulated evoked functional images, and resting state fluctuations in BOLD signal were acquired at several time points after the anesthetic wore off. ***fMRI:*** All fMRI data were obtained on a modified 11.7T Bruker/Varian horizontal-bore spectrometer using a ^{1}H surface coil (Ø = 1.4 cm). The functional images were acquired with gradient echo EPI sequence (TR/TE = 1000/15 ms). Spontaneous BOLD data were obtained using TR of 200 ms with NR of 4200 and TE 15 ms. ***Analysis:*** The stimulus evoked BOLD response was measured in both the awake and the anesthetized animal (Figure 1). The localization of the functional response was identified by Student's t-test. The power spectra of the BOLD fluctuations in the low frequencies (to 1 Hz) was computed for both domitor anesthetized and awake animal. The t-score of the BOLD responses were compared voxel by voxel to the last baseline value of the signal. The value of the resting BOLD signal just before stimulus onset was determined and the evoked response was measured. The variability of the evoked BOLD responses as function of the baseline amplitude was plotted (Fig. 2). Statistical analysis was calculated using repeated measure ANOVA.

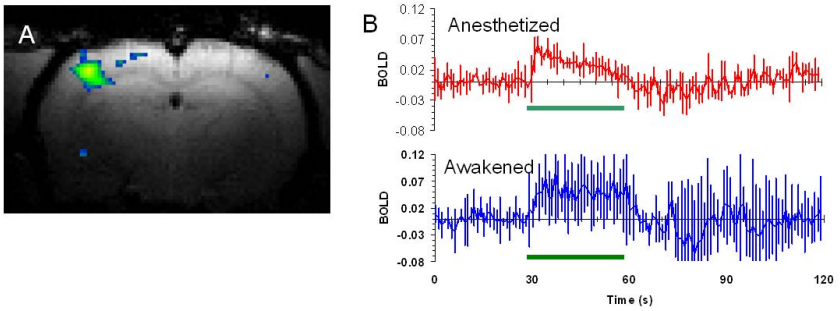

Figure 1. Functional responses in the barrel cortex. **A.** The t-map of the evoked response. **B.** The averaged time series of responses in the same animal under anaesthesia (red) and in awakened (blue) state. The timing of the stimulation is labeled by a green bar. The error bars show that the response to whisker stimulation is variable, and changes with arousal state of the rat.

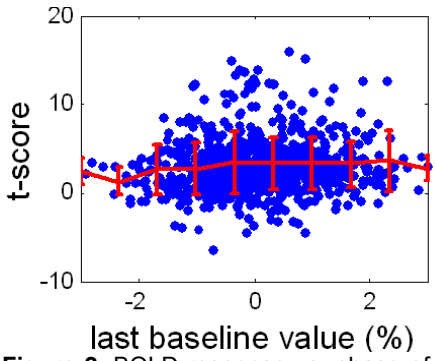

Figure 2. BOLD response vs. phase of pre-stimulus BOLD signal. The phase of the pre-stimulus BOLD signal has little impact on the predictability of the BOLD response.

RESULTS and DISCUSSION

Spontaneous fluctuations in the BOLD signal have the same frequency distributions in the domitor anesthetized and awakened state. The frequency analysis of the awake and anesthetized animals shows high power in the range of 0.05-1Hz fluctuation and this power does not show significant difference across states (p=0.19). If we shrink the analysis to the lower frequency range (0.1-0.5 Hz) the difference between the powers was even smaller (0.51±0.2 vs. 0.54±0.3, p=0.89). The time series of evoked BOLD responses were collected according to activated voxels (Fig. 1A), and the variability of the BOLD responses were estimated from their standard deviation. The variability of the awakened BOLD responses was significantly higher than in the anesthetized state (0.05 vs. 0.15), although the magnitude of evoked BOLD responses were similar (Fig. 1B). We also found that the pre-stimulus BOLD values did not predict the BOLD response amplitude or the rate of rise of the evoked BOLD response (Fig. 2). Our results show that while there is a significant difference in the variability of the functional responses during whisker stimulation between anesthetized and awakened animals, the spontaneous fluctuations show no significant difference in their frequency power and the trial-to-trial variability of functional responses could not be explained by the phase of the spontaneous fluctuations in BOLD signal.

REFERENCES

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