Power of spontaneous BOLD signal and neural activity fluctuations is baseline-dependent

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INTRODUCTION

Evoked responses in functional studies show baseline dependence [1], i.e. in higher metabolic baseline state the functional response is smaller but delocalized, whereas lower metabolic baseline shows higher amplitude localized responses. Other human studies [2] showed that spontaneous fluctuations in BOLD signal seem to be important in local variability or trial-to-trial reproducibility of the functional response. In this study we examined high and low energy baselines of light (Domitor) and deep (α-chloralose) anesthesia, respectively, to compare whether high or low energy baselines are related to fluctuations in neural activity and baseline BOLD signals.

METHODS

Sprague-Dawley rats were tracheotomized and artificially ventilated (70% N_2O, 30% O_2) with 55-80 beat/minute rates. The anesthesia was switched to i.p. α-chloralose (80mg initial dose, then 40 mg/kg/hr) or s.c. Domitor (0.1mg/kg/h) from Isoflurane (1-2%) after the surgery. A femoral arterial line was used for monitoring blood pressure, acid-base balance and blood gases throughout the experiment. ***fMRI:*** All fMRI data were obtained on a modified 11.74T Bruker horizontal-bore spectrometer (Billerica, MA) using a ^{1}H resonator/surface coil RF probe (Ø = 1.4 cm). All images were acquired with gradient echo EPI (TR/TE=200/12.53 ms). Resting state BOLD data were obtained with NR of 4200. All fMRI data were subjected to a translational movement criterion analysis [3], animals with movement larger than 0.25 voxels were excluded from further analysis (Fig. 1A). ***Neural measurements:*** The rat was placed in a stereotaxic holder on a vibration free table inside a Faraday cage. Tiny burr holes were made above left and right somatosensory regions (S1) [4.4 mm lateral and 1.0 mm anterior to bregma] and tungsten microelectrodes (FHC inc, Bowdoinham, ME) were inserted up to layer 4 (1mm depth) with stereotaxic manipulators. All signals were then digitized (>20 kHz) with a μ-1401 interface using Spike2 software. The multi-unit activity (MUA) was extracted from the raw signal with a band-pass (300-3000Hz) electronic filter (Krohn-Hite, Inc) ***Analysis:*** fMRI signals were analyzed voxel by voxel. Only those voxels from collected GE-EPI images were analyzed where the signal to noise ratio was higher than 50. The sampling frequency of time series was 5Hz, but we applied an 8 octave Butterworth filter with 0.9 Hz cutoff frequency (Fig. 1B), since the artificial ventilation produced a large artifact in the signal ~1Hz. The fluctuations of the signals were estimated using standard deviation (SD), where the larger value means larger fluctuation (Fig. 1C). The SD of the voxel based time series were calculated, and then averaged by individual experiments. The SDs of the two groups (n=15 for α-chloralose and n=11 for Domitor) were tested with Student's t-test. The temporal fluctuation of MUA signal (denser and rarer regions in the signal) was transformed into amplitude fluctuation with root mean square (RMS) method with 1s binning (Fig. 2). The RMS method calculates the mean of the square of the data within the selected bin, then takes its square root [4]. The SDs of the RMS time series were calculated for 210s intervals in Domitor (n=15) and alpha-chloralose (n=14) groups.

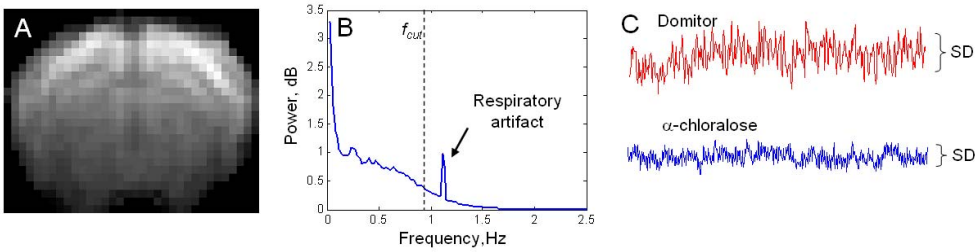

Figure 1. Analysis of the spontaneous BOLD signal. **(A)** Typical BOLD image. **(B)** Low pass filtered BOLD data at f_{cut} = 0.9 Hz to remove the respiratory artifact. **(C)** The *SD* of the BOLD signal characterizes fluctuations in α-chloralose (bottom) and domitor (top).

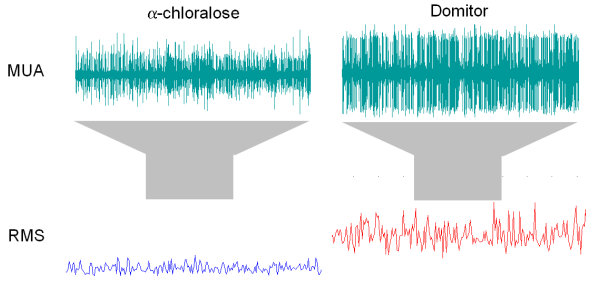

Figure 2. Analysis of the neural signals. The MUA time series (top) are converted into RMS series (bottom) to characterize fluctuations in α-chloralose (left) and domitor (right) states.

RESULTS AND DISCUSSION

In our study we characterized the spontaneous fluctuations in BOLD (Fig. 1) and neural (Fig. 2) signals and measured their respective standard deviation (SD). The high cortical activity under light anesthesia produces higher frequency signaling measured by MUA (or LFP) which is converted into large amplitude RMS fluctuations. These RMS fluctuations were significantly different in the two anesthetized states (p=0.007). The SDs were 0.0085±0.003 and 0.0049±0.003 in light and deep anesthetized states, respectively. Similar results were observed with the BOLD data for the two baseline states (p<0.0001), with SDs of 0.013±0.001 and 0.008±0.001 in light and deep anesthetized states, respectively. Therefore the power of the baseline neural activity is correlated with the magnitude of the BOLD signal fluctuations. A plausible explanation of these results is that with light anesthesia and higher metabolic activity [1], the fluctuations in neural activity is larger due to high frequency signaling. These fluctuations in neural activity seem correlated with the BOLD signal fluctuations. A transfer function analysis, which can convert the baseline neural activity to BOLD signal, similarly as during functional activity [5,6], possibly can provide further insight into the origins of the spontaneous BOLD fluctuation.

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