Tightly Coupled Spontaneous EEG and CBF Signals in the Anesthetized Rat Brain

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Introduction The neurovascular coupling is always one of the most important topics for the functional magnetic resonance imaging (fMRI), because the blood-oxygenation-level dependent (BOLD) contrast of the fMRI technique originates from the vascular dynamic response to neural activity. However, the direct measure[1] of neurovascular coupling between electrophysiological signals and BOLD signals is difficult to carry out in the human brain due to the technical requirements. It is well known that other than the cerebral blood volume (CBV) and the metabolism rate of oxygen ($CMRO_2$), the cerebral blood flow (CBF) is the dominant factor contributing to BOLD signals; and the fMRI study has also demonstrated the strong linear correlation between regional CBF and BOLD changes[2]. Therefore, the coupling between the electrophysiological signals and CBF signals can serve as an alternative way to study the mechanism of BOLD signals associated with the underlying neuronal activity. The purpose of the present study is to study the neurovascular coupling in the anesthetized rat brain by examining the simultaneously-recorded EEG and CBF signals. Strong correlation was found between them, indicating a tight neurovascular coupling between CBF fluctuation and spontaneous neuronal activity in the resting brain. We also found strong temporal correlations between the left and right hemispheres (in somatosensory cortices) for both EEG and CBF signals, which could be linked to the coherent BOLD fluctuations at the resting state which were recently observed in human and animal brains. Therefore, our results may provide supports for the neural origin of the resting coherent BOLD fluctuations phenomenon.

Methods Four Sprague-Dawley rats were first anesthetized with ~2% (v/v) isoflurane (ISO) in a mixture of O_2 and N_2O gases (2:3). Femoral artery and vein were catheterized for physiologic monitoring and/or blood sampling. The ground EEG electrode was inserted into the nose, and the other two EEG electrodes were inserted into the somatosensory cortices on two hemispheres symmetrically through two small holes on the skull. Dual-channel OxyLab LDF/OxyFlo instrument (Oxford Optronix, UK) was used to measure the CBF simultaneously with EEG. Two Laser Doppler flowmetry (LDF) probes were inserted into the somatosensory cortices just under the EEG electrodes through the same holes. The experiment configuration is shown in Fig.1.a. The sampling rate of the EEG recording was 1000 Hz, and the band-pass (0.5~30 Hz) filter was applied during the data acquisition; the sampling rate of the LDF was 10 Hz. The simultaneous CBF/EEG recordings were performed when the physiological condition of the rats approached the steady-state. Then, the isoflurane concentration was switched to ~2.2% and ~1.8%, respectively, for the simultaneous EEG/CBF measurements under these anesthesia levels.

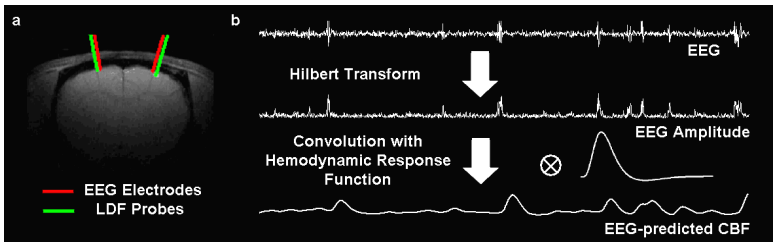

Fig.1. Scheme of the experiment. (a) the locations of EEG electrodes and LDF probes; (b) the generation of EEG-predicted CBF time course.

EEG signals were first down sampled to 10 Hz, and then its amplitude was extracted by Hilbert transformation. The result was convoluted with the canonical hemodynamic response function (hrf) to get the EEG-predicted CBF time course as demonstrated in Fig.1. b. The simultaneously measured CBF data were band-pass filtered (0.005-0.1 Hz) in the Fourier domain to remove the baseline drafting and high-frequency noises.

Result The EEG, EEG-predicted CBF, and measured CBF time courses under three anesthesia conditions are shown in Fig.2 (from one representative rat). The EEG signals show a large number of spontaneous "bursts"; but their appearing frequency decreased as the anesthesia level increased and almost disappeared at the condition of 2.2% ISO. We found that such "burst" in EEG signals was always followed by a "bundle" in the simultaneously-recorded CBF signals with a delay. The excellent similarity between the measure CBF and the EEG-predicted CBF suggests a strong neurovascular coupling between CBF fluctuation and spontaneous neuronal activity in the resting brain. It also implies that canonical hrf provides an appropriate link function between EEG and CBF. Moreover, we also observed the strong inter-hemispheric CBF/EEG temporal correlations between the left and right hemispheres.

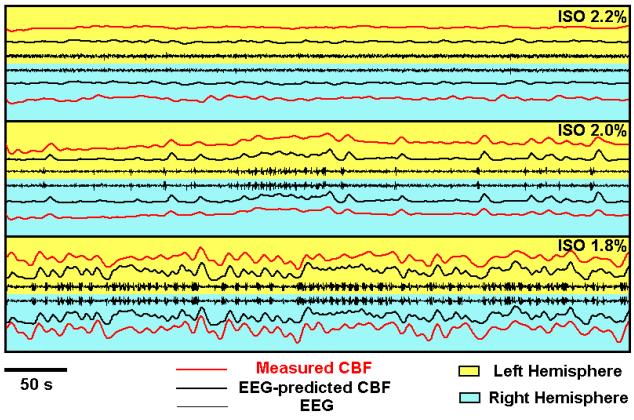

Fig. 2. Comparison of EEG, EEG-predicted CBF, and measured CBF time courses.

The correlation coefficients were calculated (based on 500s and 5000 points segments) to quantify correlations. The results from all rats are summarized in Table 1. We note that the CBF and EEG coupling, as well as the inter-hemispheric correlation of CBF signals, dropped significantly at the 2.2% ISO condition. This could attribute to the disappearing of EEG "bursts" at deep (2.2% ISO) anesthesia.

Table 1. Summary of Correlation Coefficients (*r*)

	Anesthesia Level		
	2.2% ISO	**2.0 % ISO**	**1.8% ISO**
Measured CBF vs. EEG-predicted CBF (left hemisphere)	0.23±0.11	0.73±0.07	0.59±0.01
Measured CBF vs. EEG-predicted CBF (right hemisphere)	0.17±0.08	0.72±0.09	0.62±0.01
Left vs. Right Hemispheric Measured CBF	0.71±0.06	0.91±0.06	0.92±0.05
Left vs. Right Hemispheric Measured EEG	0.82±0.11	0.81±0.15	0.89±0.09

Discussion and Conclusion There are two major conclusions for this study. First, the strong correlation between spontaneous "bursts" of EEG and "bundles" of CBF indicates the strong neurovascular coupling in the resting rat brain: the increase of neural activity causes the vascular response reflected by the increased CBF. We also showed that the canonical hrf can serve as a very good link function for this neurovascular coupling relationship. It is likely that a similar coupling should exist between BOLD fluctuation and spontaneous EEG due to the fact that CBF dominates the BOLD signal at normal physiological condition.

Secondly, the strong correlation between the CBF signals from the left and right somatosensory cortices could be linked to the coherent BOLD fluctuations observed in human and animal brains, especially those observed in isoflurane-anesthetized monkeys[3] showing the similar EEG patterns as observed in our study. Therefore, our results provide supports for the neural origin of the coherent BOLD fluctuation phenomenon at the resting brain, although further investigation is needed to consolidate this important conclusion.

Finally, the strengths of the neurovascular correlation and as well inter-hemispheric correlation are sensitive to the depth of anesthesia.

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References 1. *Logothetis NK. et al. Nature 2001;* 2. *Zhu XH. et al. Magn Reson Med 1998;* 3. *Vincent JL. Et al. Nature 2007;*