Strong correlation of spin-echo BOLD signal with neuronal activity in rat cortex during forepaw stimulation

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Introduction

The relation between signal in neuroimaging techniques and the neuronal activity is essential to investigate brain function. The hemodynamic response follows the neuronal activity and a number of studies have demonstrated that cerebral blood flow (CBF) is linearly correlated to neuronal activity [1-3]. However, the correlation of the BOLD signals which relate to the CBF responses is still unclear [4,5]. Thus, to investigate the correlation between the BOLD signals and neuronal activity, we performed both measurements of the spin-echo (SE) BOLD signals and the somatosensory evoked potentials (SEP) in the anesthetized rat cortex during forepaw stimulation as a function of stimulus current and frequency.

Materials and Methods

Animal preparation: Male Sprague-Dawley rats (n=9) were used for both measurements. Animals were initially anesthetized by isoflurane and tracheotmized. Femoral catheters were placed in artery for blood sampling (blood pH, pO_2, pCO_2) and blood pressure monitoring, and in vein for injection of pancuronium bromide (2 $mg \cdot kg^{-1} \cdot hr^{-1}$). Alpha-chloralose anesthesia (initial 80 $mg \cdot kg^{-1}$, supplement 40 $mg \cdot kg^{-1} \cdot hr^{-1}$, i.p.) was given after surgery and isoflurane was discontinued. *Stimulation:* A pair of needle electrodes was inserted beneath the skin of a forepaw. Forepaw stimulations (4 s) were applied with various currents (0.5 to 2.0 mA) at a frequency range from 1 to 10 Hz. *SEP measurements:* The SEP was measured with silver ball electrodes on the surface of somatosensory area. The differential amplitude between P1 and N1 was averaged and integrated (i.e. averaged amplitude × number of SEP) during the entire stimulation period. *MRI measurements*: MRI experiments were performed on a horizontal 7 T/11cm magnet (Oxford instruments, Oxford, UK) interfaced to a Varian^{INOVA} console (Palo Alto, CA) with a single turn 10 mm transmit/receive surface coil. FMRI data were acquired using a single-shot SE EPI sequence with scan parameters as follows: TR/TE = 1000/40 ms, slice thickness = 2 mm, FOV 20 × 20 mm^2, matrix size = 32 × 32. Each SE-BOLD signal was analyzed to three values: the average within entire stimulation, the maximum of the BOLD signals, and the integration of the BOLD signals (i.e. area of the time course).

Results and Discussion

The average and integration of SEP amplitudes increased with an increase in the stimulus current for each stimulus frequency. On the other hand, the average of the SEP amplitude decreased with an increase in the stimulus frequencies and the integration of the SEP amplitude has a peak at 3-5 Hz. The SE-BOLD signals showed the similar trends with the integration of the SEP amplitude. Figures show the correlation of the integration of the SE-BOLD signals with the integration (Fig. 1) and the average (Fig. 2) of the SEP amplitudes for all stimulus conditions (triangles 0.5 mA; squares 1.0 mA; circles 2.0 mA; black 1 Hz; blue 3Hz; green 5 Hz; red 10 Hz). The integration of SEP amplitude linearly increased with the average (R = 0.87), maximum (R = 0.97) and integration (R = 0.98 [Fig. 1]) of the SE-BOLD signal over all stimulus conditions but the average of SEP amplitude did not (R = 0.07, 0.20, and 0.18 [Fig. 2], respectively). The SEP amplitude is attributed to the synchronized extracellular currents—which are related to the release of neurotransmitters [6,7]—and astrocytic somatic Ca^{2+} signaling that correlated with the uptake of glutamate [8] in the primary somatosensory cortex. Thus, our findings suggest that the SE-BOLD signals reflect the activation-dependent release of glutamate and the glutamate–glutamine cycles during cortical activation [9].

Conclusion

In the rat forepaw model, the SE-BOLD response measured at high magnetic field strongly correlates with neuronal activity.

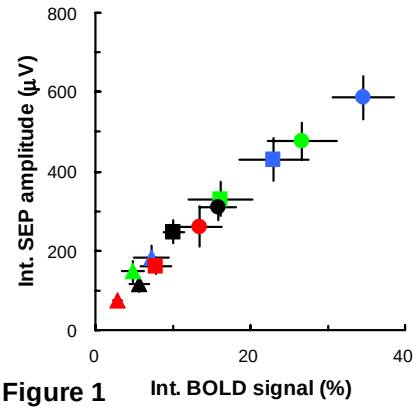

Figure 1

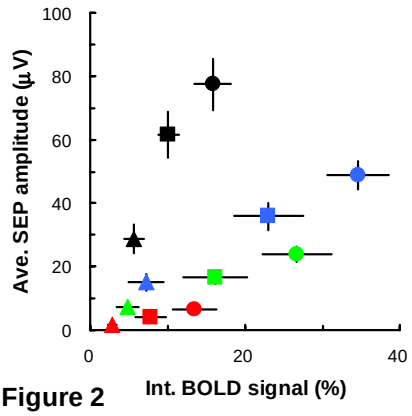

Figure 2

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