Stimulus Frequency Dependence of the Relationship between BOLD Signal and Somatosensory Evoked Potential in Rat Cortex

I. Kida[1], M. Tamura[2], T. Yamamoto[3]

[1]Graduate School of Dental Medicine, Hokkaido University, Sapporo, Hokkaido, Japan, [2]Research Institute for Electronic Science, Hokkaido University, Sapporo, Hokkaido, Japan, [3]School of Medicine, Hokkaido University, Sapporo, Hokkaido, Japan

Introduction

Since BOLD fMRI signal does not provide direct measurements of neural events, the relationship between neuronal events and BOLD fMRI signal is still controversial to interpret the neuroimaging. To clarify this relationship, the rat forepaw electrical stimulation model has been well studied for fMRI and other methods such as Laser Doppler Flowmetry (LDF) and optical imaging (1-4). However, especially for stimulus frequency, there is a conflicting result between BOLD signal by fMRI and CBF change by LDF or deoxygenated hemoglobin by optical imaging. BOLD signal increases with lower frequency of forepaw stimulation (1), whereas the hemodynamic signals measured by LDF and optical imaging have a peak with the stimulation at 3-5 Hz (2-4). Since the BOLD fMRI signals correlate with deoxygenated hemoglobin content, the stimulus-frequency dependence should match both for BOLD fMRI and optical imaging. In this study, we investigated whether the BOLD signal correlates with hemodynamic changes or neuronal events (i.e. somatosensory evoked potential (SEP)) for the various stimulus frequencies in rat forepaw stimulation model.

Materials and Methods

Animal preparation: Male Sprague-Dawley rats (n=6) were initially anesthetized by isoflurane with N_2O/O_2 (70/30%) and tracheotmized. An femoral arterial and vein catheters were placed for blood sampling (blood pH, pO_2, pCO_2) and blood pressure monitoring, and for immobilization by pancuronium bromide (2 mg/kg/hr), respectively, throughout the experiment. After surgery, isoflurane was discontinued and α-chloralose anesthesia (initial 80 mg/kg, supplement 20 mg/kg/1/2hr, i.p.) was given. A pair of needle electrodes was inserted beneath the skin of a forepaw. Forepaw stimulations were repeated with different stimulus frequencies, 1, 3, 5, 10Hz of intensity 2 mA and duration 0.3ms for 4 second. In additional experiment, SEP was measured with silver ball electrode on the surface of somatosensory area. *MRI measurements*: All fMRI experiments were carried out 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 spin echo EPI sequence with scan parameters as follows: TR/TE = 1000/40 ms, slice thickness = 2 mm, FOV 25×25 mm^2, matrix size=64×32.

Results and Discussion

Figure 1 shows the BOLD signal changes during forepaw stimulation averaged over animals (n=6). The BOLD signal increased even after offset of stimulation and peaked at 6 seconds except for the stimulation at 10Hz. The averaged BOLD signals were 0.7±0.2%, 1.6±0.3%, 1.8±0.4% and 0.8±0.2% (mean±SD, n=6) for the period of stimulation at 1, 3, 5, 10 Hz, respectively. No significant difference of the signals between 3Hz and 5Hz was observed. The stimulus-frequency dependence of BOLD signals in this study is in good agreement with the CBF changes by LDF (2,3) and deoxygenated hemoglobin changes by optical imaging (4) but not the aforementioned gradient-echo BOLD signal (1). Amplitude of SEP was defined as differential amplitude between the positive and negative peaks and this amplitude was normalized in each animal by the initial peak following the onset of stimulation. Figure 2 shows the integrated (closed triangles) and the averaged (opened triangles) SEP amplitudes within entire stimulation period. The averaged SEP declined with increasing stimulus frequency. In contrast, the integrated SEP amplitude has a peak at 3-5 Hz, which is a similar tendency with the BOLD signals shown in Figure 1. The correlation of the BOLD signal with the integrated SEP amplitude was much better than with the averaged one (R^2=0.98 vs. 0.03). This result is supported by the recent fMRI study (5) and the other methods (2-4).

Conclusion

In the BOLD fMRI of rat forepaw model, there is a good correlation between the BOLD signal and the "integrated" SEP amplitude, which have a peak at 3-5 Hz of stimulus frequency. Methodological differences between the current and the previous study (1) such as a sequence (spin echo vs. gradient echo) may lead to the different results.

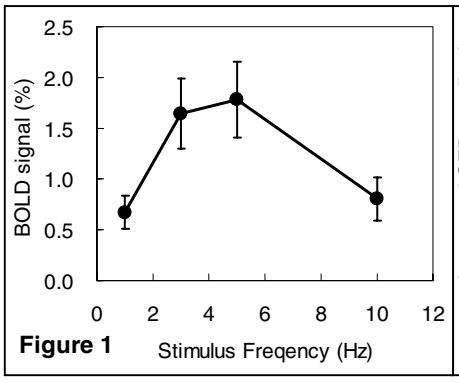

Figure 1

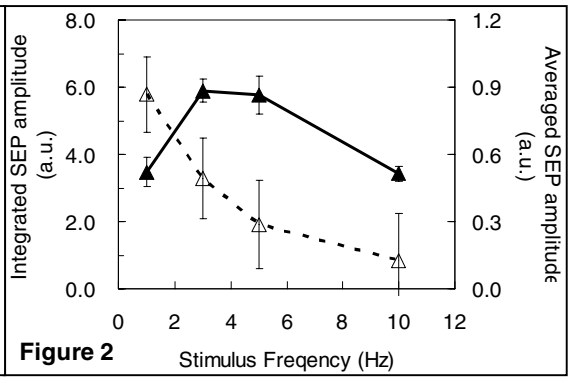

Figure 2

References

1. Brinker et al., MRM 41:469(1999)
2. Ngai et al., BR 837:221(1999)
3. Ureshi et al., Neurosci Res 48:147 (2004)
4. Nemoto et al., J Neurosci 24:3850 (2004)
5. Logothetis et al., Nature 412:150 (2001)

Supported by The Akiyama Foundation, Takeda Science Foundation and The Mitsubishi Foundation (IK).