Correspondence between Changes in BOLD Contrast, Cerebral Blood Flow and Tissue Oxygenation In Response to Forepaw Stimulation and Blood Pressure Changes

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Introduction

Functional magnetic resonance imaging (MRI) studies are widely used to map various cognitive, sensory and motor functions based on changes in blood oxygenation-level dependent (BOLD) MR contrast. In normal brain, the changes in MR contrast detected in response to neuronal activation are primarily a result of a local increase in cerebral blood flow(CBF) and oxyhemoglobin (oxyHb) and a decrease in deoxyhemoglobin (dHb) (1-3). Clearly, the 'activation' detected with fMRI studies will depend on factors such as the coupling between CBF and metabolism, the efficacy of the autoregulatory response to blood pressure changes and the relationship between CBF and BOLD/dHb changes in the tissue. Understanding these is key to interpreting BOLD fMRI results particularly as applications are expanding to include assessments of function in diseased or injured brain. Thus in the present study, we investigated the effect of forepaw stimulation and transiently induced increases in blood pressure on the intensity changes in BOLD signal using MRI. We compared these responses to the effect of these manipulations on changes in cortical blood flow measured with laser Doppler flowmetry and cortical oxygenation changes measured with near-infrared (IR) spectroscopy.

Material and Methods

Functional MRI or near IR experiments were performed in 19 adult rats prepared as described previously for fMRI studies under alpha-chloralose anesthesia (4). Body temperature, respiration and the blood gases of the rats were controlled and arterial blood pressure was monitored. For each functional MRI scan using a 9.4T/21cm MRI system, a set of 32 gradient echo T2* images (TR/TE=70/10ms, flip angle=20°, matrix=128x128, slice thickness=1.5mm) were acquired and a number of experiments were performed investigating the 'activation' response to: 1.forepaw stimulation, 2. an increase in arterial blood pressure or 3. a combination of an increase in blood pressure and forepaw stimulation. Images were collected with electrical stimulation of the forepaw either off or on (6 off, 7 on, 6 off, 5 on, 8 off) or during arterial blood pressure increases of 0, 30-45 or >60 mm Hg produced by the intravenous injection of norepinephrine (0.15-1.2μg/kg). A cross-correlation analysis ($p<0.001$) to either the stimulation paradigm or the time course of blood pressure changes was used to identify voxels of apparent activation in the sensory motor cortex from which their maximum intensity changes relative to initial baseline values was determined. Near IR experiments (n=5) were performed on the bench and had procedures identical to the MR experiments except that the skull was thinned and laser Doppler flowmetry (Perimed) probes were placed over the sensory motor cortex. A single near IR transmit probe was positioned against the skull along the midline to conduct near-IR radiation from a near-IR source (Oriel) to the skull. A receiver probe was placed ~5 mm away to collect radiation conducted through the skull/brain and transmit it to a near-IR spectrometer (Control Development Inc.). Near-IR spectra were acquired every second during each paradigm, and subsequently curve-fit (least squares) with the component absorptivity spectra of oxyHb, dHb, and water.. The absorption feature of water at 840 nm was used to estimate of the optical pathlength (assuming the brain to be 80% water), so that quantitative changes in oxyHb and dHb could be estimated throughout. Similarly, maximal changes in cortical blood flow relative to baseline in response to forepaw stimulation or blood pressure increases were determined from the Doppler flow traces. Results were grouped according to forepaw stimulation and the range of blood pressure changes and compared using ANOVA followed by a Duncan's multiple comparison test.

Results

In experiments with no stimulation or BP changes the measures in MR signal intensity, blood flow or tissue oxygenation were stable. With electrical stimulation of the forepaw alone, activation was detected within the sensory motor cortex and the R signal intensity increased by approx. 6% (Fig.1 B). Correspondingly, forepaw stimulation resulted in increases in cerebral blood flow and oxyHb and decreases in dHb (Fig. 1B). With increases in blood pressure alone there were increases in blood flow, MR signal intensity and oxyHb and decreases in dHb where the magnitude of these changes was dependent on the change in blood pressure. When both forepaw stimulation and increases in blood pressure were produced, the changes observed with forepaw stimulation alone were enhanced. The BOLD changes produced with the combination of forepaw stimulation and changes in blood pressure appeared to be additive when examining the responses to each paradigm separately. Such a relationship was less evident for the dHb and oxyHb changes.

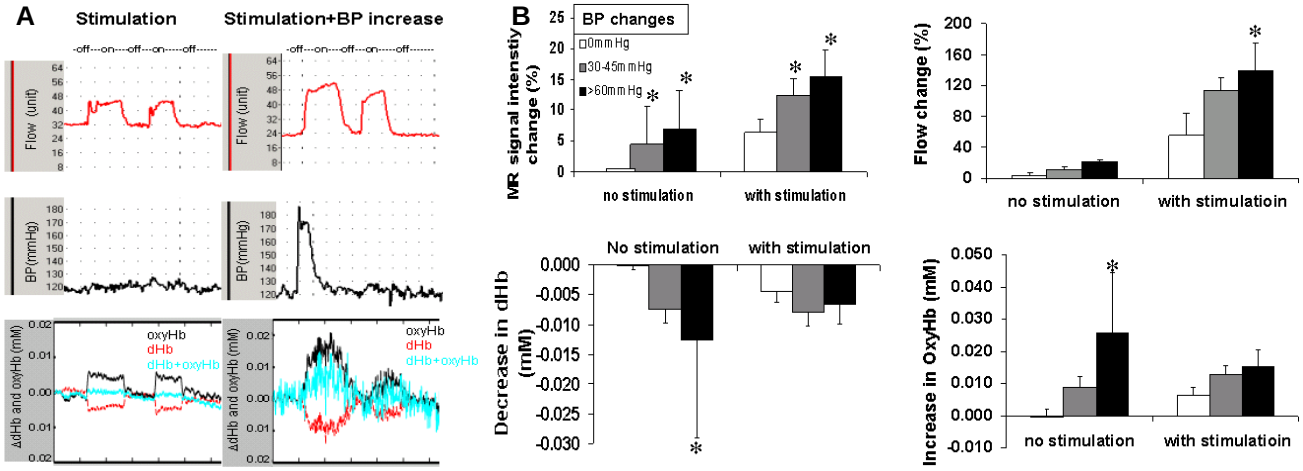

Fig. 1. Effect of changes in blood pressure (BP) on the changes in MR signal intensity, blood flow, dHb and oxyHb with or without electrical stimulation of the forepaw. A.Examples of these changes in response to i) forepaw stimulation and ii) a BP increase of 35 mm Hg during stimulation. B. Quantitative changes (mean ± SD) in MR signal intensity, flow, dHb and oxyHb in each of the change in blood pressure ranges examined - 0, 30-45, and >60mmHg. *P<0.05 vs. BP changes of 0 mmHg.

Conclusions

The response to either an increase in blood pressure (> 30 mm Hg) or electrical forepaw stimulation results in decreases in dHb and increases in flow, oxyHb and BOLD MR intensity. The changes produced by neuronal activation are enhanced by increases in blood pressure. The BOLD MR intensity changes produced by blood pressure and stimulation appear to be additive. *(Supported by Canadian Institutes of Health Research).*

References

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