Regional variations in BOLD Response during Transient Hemodilution in Rat.

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[Introduction]

BOLD-fMRI relies on the regional alternations in deoxyhemoglobin (dHb), based on the tight coupling between neural activity and hemodynamic response. Although it has a prominent role to explore cognitive neuroscience and pharmacological action, the precise physiological sources of the BOLD signal remain mostly unclear. Since the BOLD signal is dependent on many factors including; microvascular environment and physiological conditions, there are many variations in the BOLD signal reflecting both resting and activated conditions. Consequently, BOLD responses are hard to compare among different anesthetics, physiological conditions and brain regions. We propose a new method for the quantitative calibration of BOLD signal and dHb level. Specifically, if all Hb were washed out of vessels in the localized brain region without any systemic physiological changes, the MR signal would be independent of the distribution of dHb. We report initial results using this hemodilution model for calibration of the BOLD signal under a wide range of conditions and show that the temporal dynamics of the BOLD response can vary significantly across brain regions.

[Methods]

A thin polyethylene catheter was inserted into the left internal carotid artery under isoflurane anesthesia in rats. This catheter was used for repeated injection of saline at the rate of 0.005-0.08ml/second for two seconds. Systemic arterial blood pressure was continuously monitored thorough the experiments. MRI studies were performed on a 9.4T/20cm magnet (Varian) with 70mm volume transmit/15mm surface receive coil. A single 1mm slice was acquired using single–shot GE-EPI using TR=0.5s, TE=25ms, NEX=1, matrix 64x64 and FOV 3x3cm^2. Video microscopy was performed in the same model. A 2-mm burr hole was trephined and the dura was opened on the left somatosensory cortex. A simple white light was used illumination.

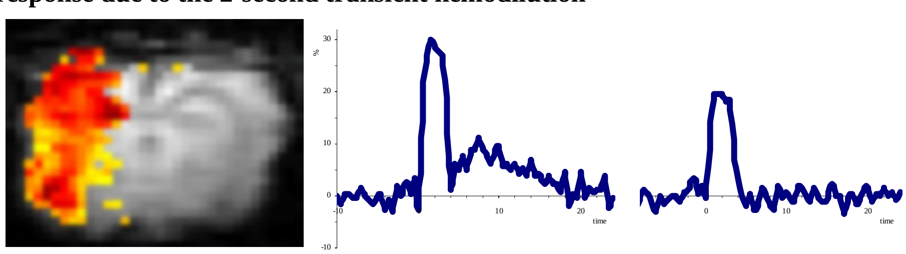
[Results]

BOLD responses were detected in the left middle cerebral artery (MCA) area. The BOLD response was correlated with the infusion rate up to 0.05ml/sec after which the BOLD response reached a plateau. At the high infusion rate, a rapid sharp response was followed by secondary slower response in the cortex, while only one sharp response was observed in the basal ganglia (Fig1). Microscopic observation revealed that when the rate exceeds 0.05ml/sec, the redness on the pial vessels and cortex transiently became pale in the order of arteriole, avascular area, venule, large veins (Fig2). Systemic arterial blood pressure and end-tidal CO2 level did not change through the 2-4seconds injection of saline. As a result, it is considered that all of the blood contents wash out of the microvasculature completely in the normal physiological condition at the infusion rate of 0.05ml/sec without any systemic physiological changes.

[Discussion]

Since the cross-hemispheric circulation is well developed in rats, CBF remains normal even after the ligation of the unilateral carotid artery. When saline is injected through the carotid artery at the low rate, feeding blood from the contralateral circulation and saline mix and flow into the MCA area. At the higher flow rate, the perfusion pressure of saline overcomes the blood pressure allowing undiluted saline to flow into the MCA area and displace blood. In another words, there is no dHb remaining in the MCA area. Since this hemodilution model can apply for wide ranges of anesthetics, and physiological conditions, it would guide development of the quantitative evaluation for the BOLD signal. We also found that the timecourse of the BOLD response varied across tissue type. For example, cortical pial arteries feed blood to the cortex, while thin perforators provide blood to basal ganglia. Such difference in microvasculature can remarkably alter BOLD response as shown in the timecourses of Figure 1. These differences in vascular response may have a significant impact on understanding BOLD activation in cortical and sub cortical structures. This model will be useful to evaluate regional metabolic and hemodynamic status under a wide variety of conditions.

Fig 1; BOLD response due to the 2-second transient hemodilution



Cortex Basal Ganglia

Fig 2; Video Microscopy at left somatosensory cortex during the injection of saline from the left carotid artery