Dynamic fMRI Acquisition of BOLD, rCBV, CBF, and Hypercapnic Reactivity for rCMRO2 Calculation during Rat Forelimb Stimulation

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ABSTRACT Accurate dynamic measurements of the relative cerebral metabolic rate of oxygen ($rCMRO_2$) are highly useful for understanding various pathological conditions (e.g., stroke) and assessing the integrity of neuronal responses. Using fMRI, we calculated the temporal changes of $rCMRO_2$ in the rat somatosensory (SS) cortex during electrical forelimb stimulation. The $rCMRO_2$ time courses were determined from the dynamic acquisition of blood oxygenation level dependence (BOLD), functional changes of cerebral blood volume (fCBV) and cerebral blood flow (fCBF), and the response to CO_2 (5%) exposure. The elimination of partial volume errors and other related measurement uncertainties greatly enhanced the precision of the $rCMRO_2$ calculation revealing low biological variability. Apparent ipsistimulus fCBV responses (e.g., left SS response to left forelimb stimulus) were not accompanied by concomitant increase of $rCMRO_2$. We demonstrated that the unbiased acquisition of local hemodynamic parameters is necessary for understanding the details of fMRI activities during the rat forelimb stimulation.

MATERIALS AND METHODS Using two healthy normal rats, fMRI activations of BOLD, fCBV, and fCBF responses were acquired using a horizontal bore 9.4T Bruker/Magnex system, equipped with a home-built surface coil and a labeling coil. The BOLD acquisitions were performed using Gradient Echo Planar Imaging (GEPI: TR/TE = 3700/15 ms) sequence with the alternating arterial spin labeling (ASL) on/off while the fCBV response was acquired with GEPI (TR/TE = 3700/12.84 ms). For all the measurements, MR images of three 1 mm slices (inter-slice separation=1 mm) were acquired using FOV = 2.5x2.5 cm^2 and 80x80 matrix zero filled to 128x128. A unilateral electrical stimulation paradigm, consisting of 3 periods of 37 sec 'stimulation on' separated by 185 sec 'stimulation off,' was alternated between the left and right forepaw and was repeated ~3 times. During the BOLD fMRI acquisition, ASL (labeling duration =3.0sec, post labeling delay=0.5sec) was used for the simultaneous acquisition of the fCBF. Following the BOLD and fCBF acquisitions, MION was intravenously administered (36mg (FeO_2)/kg), and the stimulation paradigm was repeated for the fCBV fMRI. Functional activation maps were generated using a voxel by voxel t-test between the on and off stimulus periods. In addition, the fMRI reactivity to the CO_2 (5%) exposure and the impulse response function (stimulus duration=2.5 sec) were acquired prior to and following the MION administration.

RESULTS AND DISCUSSION The dynamic $rCMRO_2$ (Figure 1: left and middle panel) of each SS cortex was calculated from the acquired fCBF, fCBV, and BOLD time course responses using the previously reported relation.[1] The Grubb's constant (γ) (i.e., $1+\Delta F(t)/F_o=(1+\Delta V(t)/V_o)^{\gamma}$) was calculated from each SS cortex with the 5% CO_2 challenge and was measured to be 2.58+/-0.69. As discussed by Mandeville et. al,[1] systemic errors were considerably reduced by avoiding partial volume and registration uncertainties. The small error bars of dynamic $rCMRO_2$ (Figure1: left panel) indicate low biological variability of metabolic demand during the electrical forelimb stimulation. For the ipsistimulus responses,[2] approximately 30% of the contrastimulus fCBV response magnitude was observed, during which little BOLD and slow CBF increase were detected. Despite the apparent ipsistimulus fCBV increase during the stimulus duration of 37 sec (Figure1: middle panel), the ipsistimulus fCBV IRF time course (stimulus duration=2.5 sec) did not reveal any significant temporal fCBV increase (Figure1: right panel), probably due to the delayed nature of the ipsistimulus fCBV response as reported previously.[2] The ipsistimulus $rCMRO_2$ did not appear to respond to the stimulation, showing that the metabolic demand of such responses is low and may be intrinsically different from the contrastimulus responses.

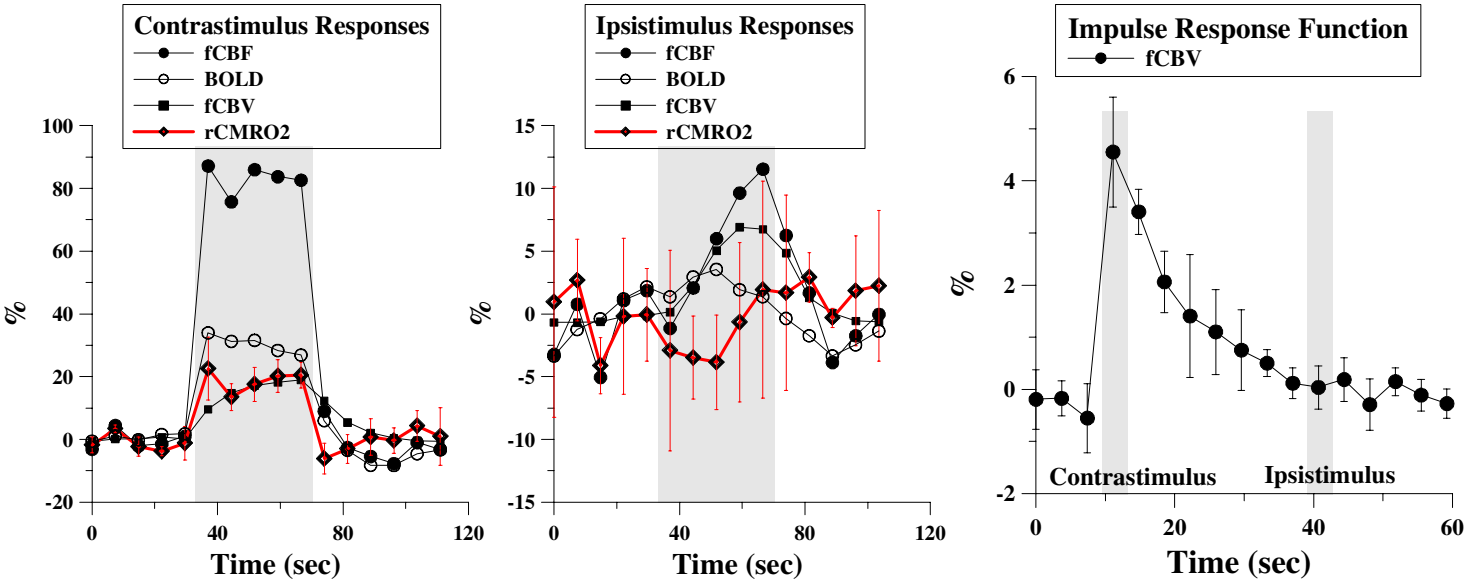

Figure 1. Percent change of CBF, BOLD, fCBV, and $rCMRO_2$ (mean+/-std) during the contrastimulus (left) and ipsistimulus responses (middle). Impulse response function of fCBV response was acquired using stimuli of 2.5sec (right). (n=2 rats: 3 somatosensory cortices).

REFERENCES

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