Relationship between changes in cerebral arterial blood volume and flow as measured by MOTIVE with ASL during neural activation

T. Kim[1], K. Hendrich[1], K. Masamoto[1], S-G. Kim[1]
[1]Neurobiology, University of Pittsburgh, Pittsburgh, PA, United States

Introduction

Since cerebral blood flow (CBF) is known to be tightly regulated by arterial vessels, an increase in CBF can be due to either blood velocity increases or vasodilation. Therefore, it is important to determine the relationship between CBF and cerebral arterial blood volume (CBVa) in order to understand the underlying mechanism of CBF regulation. Recent hypercapnic studies showed that elevated CBF is mainly due to an increase in CBVa in rats (using ^{19}F NMR with perflurocarbon injection) and in humans (using PET) (1,2). The relationship between CBF and CBVa may not be the same for hypercapnia and neural activation, but this could not be evaluated due to a lack of sensitivity and relatively poor spatial resolution in previously existing methods. We developed a high-sensitivity technique to simultaneously measure CBF and CBVa, dubbed the *mo*dulation of *ti*ssue and *ve*ssel (MOTIVE) method. Using MOTIVE with arterial spin labeling (ASL), we measured neural activity-induced CBVa and CBF changes in the rat somatosensory cortex.

Methods

Fourteen male Sprague-Dawley rats weighing 350-450 g were studied with 15 s forepaw electrical stimulation (1.3-1.6 mA, 6 Hz) under 1.3-1.4% isoflurane anesthesia. Rectal temperature, blood pressure and blood gases were maintained within normal physiological ranges; no significant blood pressure changes were observed during stimulation. Two actively detunable RF coils were used: a butterfly-shaped surface coil was positioned in the neck region for arterial spin labeling, while a surface coil was positioned on top of the rat head both for tissue saturation via magnetic transfer (MT) effects and for image acquisition. A single 2-mm thick coronal slice was selected. All images were acquired on a 9.4 T / 31 cm Varian NMR system using the single-shot spin-echo planar imaging technique with matrix size of 64 (readout) × 32 (phase-encoding), FOV = 3.0 × 1.5 cm^2, TR = 2.5 s, and TE = 30 ms or 40 ms.

In each animal, CBVa and CBF were simultaneously measured during both baseline and stimulation periods by the MOTIVE method with ASL (3). MT levels were randomly varied in each fMRI study: target values of S_{sat}/S_0 (where S_{sat} and S_0 are the equilibrium signal in the presence and absence of MT saturation, respectively) were 1, 0.7, and 0.44. ASL data ($\Delta S_{sat} = S_{sat} - S_{sat}^{labeled}$) were acquired at each MT level. CBVa and CBF were determined from the slope and intercept of the linear fit of normalized ASL ($\Delta S_{sat}/S_0$) vs. control (S_{sat}/S_0) values for results at the three MT levels. Since steady state was not achieved during the relatively short spin preparation period, CBF values were corrected by multiplication with [1-exp(-TR/T_{1app})], where T_{1app} (apparent T_1) = 1.9 s. It should be noted that the CBF measurement is not contaminated by arterial blood contributions. Functional maps of CBF and CBVa were obtained by cross-correlation analysis. Baseline and stimulation results were quantified within a 9-pixel region of interest (ROI) in the somatosensory cortex, where assignment was based on both stereotaxic coordinates and fMRI results.

Results and Discussion

In all animals, baseline (pre-stimulus) CBF and CBVa maps were obtained, as well as maps reflecting stimulation-induced changes. Activation maps overlaid on baseline maps of one representative animal are shown in Figure 1. In baseline maps, CBVa is highest near the cortical surface where there are large vessel contributions, and higher in gray matter than in white matter. Activation areas of both CBVa and CBF changes are localized to the contralateral somatosensory cortex. Similar observations were detected in all animals.

The average baseline values of CBVa and CBF in the somatosensory ROI were 0.9 ± 0.24 ml / 100 g and 151 ± 22 ml/ 100 g/ min, respectively (n = 14). During forepaw stimulation, CBVa and CBF values increased to 1.32 ± 0.31 ml / 100 g and 203 ± 35 ml / 100 g / min, respectively. For each animal, the increase in CBF (ΔCBF) was highly correlated with the increase in CBVa (ΔCBVa) (R=0.87):

ΔCBVa (ml/100g) = 0.0054 (min^{-1}) × ΔCBF (ml/100g/min) + 0.13.

Our data demonstrates that the increase in CBF during neural stimulation is caused mainly by an increase in arterial blood volume (i.e. arterial vessel dilation) rather than by an increase in blood velocity. This observation agrees reasonably well with previous direct measurements of arterial vessel diameter and CBF during stimulation and hypercapnia in α-chloralose anesthetized rats, although those diameter measurements were performed only in surface vessels (2, 4).

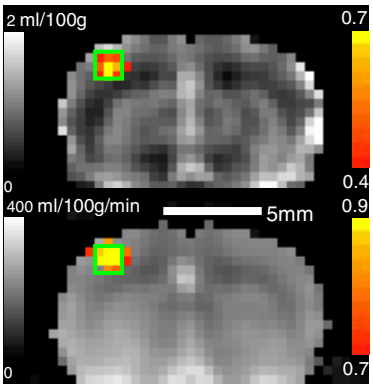

Figure 1. Activation maps (color) overlaid on baseline maps of CBVa (above) and CBF (below). The maps were calculated after application of a 2D Gaussian filter. Gray scale bars (left side) show baseline units and color scale bars (right side) show correlation coefficients for activated pixels. The green box shows ROI selected for this animal. Left side of image is the contralateral hemisphere

References: 1. Ito et al., JCBFM 25:852-857 (2005). 2. Lee et al., MRM 45: 791-800 (2001). 3. Kim and Kim, MRM 53: 333-342 (2005). 4. Ngai et al., JCBFM 15:124-127 (1995)

Acknowledgement: This study was supported by NIH (NS44589, RR17239) and CMU (EB001977, EB003375) grants