Comparison of CBF and $CMRO_2$ Measurements using MRI and PET in large Nonhuman Primates (Baboons)

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Introduction Obtaining quantitative CBF and $CMRO_2$ using noninvasive imaging methods has long been of great interests. When comparing the measurements made in normal subjects by PET and MRI, congruent values of stimulus evoked CBF changed were often shown, while contradictory results were reported for baseline CBF and stimulus-induced $CMRO_2$ [1-3]. Difference in experimental designs, inter-subjects variability, and fundamental differences of the techniques are possible contributing factors. The purposes of this study were to cross validate quantitative (1) CBF at rest and during global and regional activations using pseudo-continuous arterial spin labeling MRI and $^{1}H_2{}^{15}O$-PET, and (2) stimulus-evoked $CMRO_2$ using calibrated fMRI and $^{15}O_2$-PET on large nonhuman primates (baboons) when experimental differences were minimized. This study paves the groundwork for multimodalities CBF and $CMRO_2$ comparisons in diseases, such as stroke.

Methods Eight MRI studies (N = 8) and two PET studies (N = 2) were performed on six normal female baboons (Papio hamadryas Anubis, 12 to 19 kg, 15 ± 3 kg). All experimental preparations are identical for MRI and PET studies. Briefly, animals were anesthetized under 0.8~1.0% isoflurane with vecuronium (0.1mg/kg) and mechanical ventilated. Physiological parameters were carefully maintained within normal ranges. Hypercapnia (5% CO_2 in air) was introduced via a pre-mix tank. Simultaneous binocular visual and unilateral vibrotactile stimulations on the right hand were applied (detailed in [4]). An fMRI stimulation paradigm is consisted of 70 seconds OFF-ON for three repeats and end with a rest period. Separated rest and activation scans were acquired with PET (each for ~10 min). Data were analyzed with custom codes in MATLAB. Region-of-interets (ROIs) of the visual cortex and the primary somatosensory cortex were determined on T1-weighted images.

MRI scans were perfomed on a Siemens 3T TIM TRIO with standard huamn head coil. CBF images were acquired using single-shot gradient-echo EPI with TR/TE = 3500/16 ms, labeling duration = 2.1 s, post-labeling delay=700 ms, 12 slices, matrix = 64×64, FOV = 12.8×12.8 cm (2x2x4mm resolution). Each fMRI scan took ~ 8 min. Hypercapnic challenge included 3minutes baseline and 3 minutes 5% CO2 in air inhalation. T1-weighted MRI was also acquired for image registration.

PET scans were performed on an ECAT HR+ (Siemens/CTI, Knoxville, TN, USA) scanner with an axial FOV of 15.2 cm, in-plane resolution of 4.1 mm full width at half maximum (FWHM) and reconstructed in-plane spacing of 2.4 mm. The data were acquired in 2-dimensional (2D) frame mode to minimize the contribution of scattered photon events. Two radiotracers, i.e. ^{15}O-O_2 (740 MBq in 150 mL) and $H_2{}^{15}O$ (555 MBq in 5 mL), were alternately used with three different conditions (rest, hypercapnia, and visual and vibrotactile stimulation). A novel beta-probe system was used to acquire arterial input function for quantification.

Results and Discussion This study provided direct comparisons of (1) CBF at rest and during global and regional modulations and (2) stimulus-evoked regional $CMRO_2$ in the same subjects. **Figure 1** shows CBF maps at rest and during hypercapnic challenges using PET. There were differences in basal MRI CBF and PET CBF ($P<0.05$), but the stimuli-induced percent CBF and $CMRO_2$ changes between the two methods were similar ($P>0.05$). At rest, the global CBF were 70 ± 5 and 50.1 mL/100g/min as measured with MRI and PET respectively.

Figure 2 shows the ASL-fMRI activation maps from one representative animal. Stimulus-induced global and regional CBF changes were summarized in **Table 1**. Hypercapnia and simultaneous vibrotactile and visual stimuli induced comparable percent CBF changes measured with PET and MRI. Our preliminary findings of $CMRO_2$ changes in response to stimuli were ~5% by calibrated MRI and ~8% by PET.

Basal CBF was likely overestimated using ASL-MRI, which is in accord with a few earlier human studies [2, 3]. This difference might due to residual labeled spins in the vascular, single arterial transient time was used, etc. Similar percent CBF changes during global (hypercapnia) and regional stimuli further support this argument.

Future studies will investigate CBF and $CMRO_2$ measurements in stroke where CBF is compromised and to develop models to better determine CBF and $CMRO_2$ under perturbed conditions.

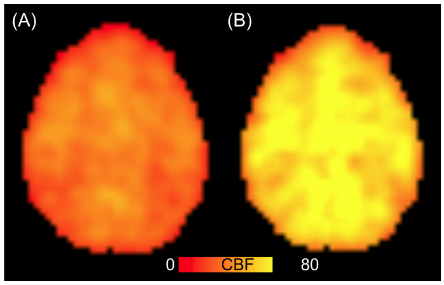

Fig 1. CBF maps from one representative animal acquired with PET during (A) rest and (B) hypercapnia. (color bar shows quantitative CBF in mL/110g/min)

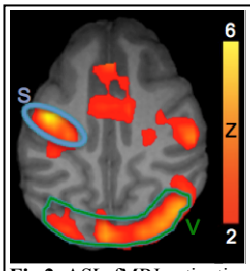

Fig 2. ASL-fMRI activation map from one subject. S and V represent the typical ROI used for somatosensory (S1) and visual (V1) cortex.

Table 1. Percent signal changes detected by MRI and PET. (HC: hypercapnia, V1: visual cortex ROI, S1: primary somatosensory cortex ROI.)

	MRI	PET
% CBF (HC)	48 ± 16	42
% CBF (S1)	21.1 ± 3.4	20
% CBF (V1)	19.9 ± 2.9	21.1

References: [1] Chen et al., Int J Biomed Imaging (2008). [2] Ye et al., Magn Reson Med (2000) [3] Kimura et al., J Magn Reson Imaging (2005) [4] Wey et al., NeuroImage (2010)