Cerebral blood flow and BOLD MRI during Isometric Exercise-Induced Increase in Blood Pressure

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INTRODUCTION Autoregulation is tightly controlled in the brain. Over a wide range of mean arterial blood pressure (MAP), cerebral blood flow (CBF) changes ~10% by vasoconstriction and vasodilation. CBF drops precipitously only when MAP drops below a critical threshold (e.g., in occlusive diseases), and similarly, CBF increases only when MAP increases above a critical threshold. The majority of studies employed PET measurements of CBF and most studies investigated changes in CBF immediately after (but not during) exercise. Moreover, how tissue oxygenation is affected by transient increases in MAP is unknown. Isometric exercise (such as handgrip) in which resistance involves muscle contraction in a static position can acutely increase MAP. This is done non-invasively without pharmacologic manipulation, avoiding potential drug side effects. Moreover, it can be used in a MRI environment. The goal of this study was to investigate the effect of increased MAP on CBF and oxygenation. Increased MAP was achieved by isometric exercise which consisted of bilateral handgrip. Combined BOLD and CBF was measured using the pseudo-continuous arterial spin labeling (pcASL) techniques.

METHODS Experiments were performed on four healthy human subjects (2 male, 2 female, 20-30 years old). Isometric exercise consisted of bilateral handgrip whereby subjects were instructed to squeeze a stress ball (diameter 7 cm) with sustained maximum force for duration of 1 minute. The exercise paradigm consisted of 1 min rest and 1 min handgrip, and repeated three times, followed by 1 min of rest. Mean Arterial Pressure (MAP), heart rate (HR), respiratory rate (RR), end tidal CO_2 ($EtCO_2$), and arterial oxygen saturation (SaO_2) were monitored during fMRI. Combined BOLD and CBF MRI data were acquired using pseudo-continuous ASL (pcASL) echo-planar imaging with a Siemens 3T TIM TRIO, TR=3.5s, TE=16ms, matrix = 64×64, FOV = 128×128mm, labeling duration=2.1s, and a post-labeling delay=700ms, 12 contiguous slices with 2mm slice thickness (2×2×2 mm resolution, 7 mins each trial). Absolute CBF, cross correlation analysis and % change maps were calculated. CBF, BOLD % changes and physiological parameters were statistically analyzed with paired t-test and significance was noted with $p < 0.05$.

RESULTS Vital signs during rest and exercise conditions are displayed in **Table 1**. During exercise, MAP increased 21 % (p=0.0001) and HR increased 15% (p=0.0005) compared to rest. RR, $EtCO_2$, and SaO_2 were unchanged. Basal CBF was 37 ± 4 ml/100g/min. Isometric exercise evoked bilateral activation of the motor cortex in BOLD and CBF fMRI maps, as expected. Moreover, there was a 15 ± 5 % global increase in CBF or 6.5 ± 2 % increase if the motor and supplementary motor area were excluded, demonstrating there is a global CBF increase in isometric exercise associated with increased MAP (**Figure 1**). By contrast, there was no significant global change in the BOLD signal except in the motor cortices (**Figure 2**). The average BOLD % change excluding the motor cortices and supplementary motor area was 0.05 ± 1 %, not statistically different from baseline.

DISCUSSION Isometric exercise increased global CBF albeit small (6.5%). Involuntary breath-holding during isometric exercise resulting in elevation of $PaCO_2$ and vasodilation could contribute to the increase in CBF. However, the absence of significant changes in $EtCO_2$ and RR ruled out this possibility.

A possible explanation is that CBF increases passively with increasing MAP. However, cerebral autoregulation should have been able to maintain CBF relatively constant across a range of MAP from 50-140 mm Hg.[1]

Another possible explanation is that this global CBF increase reflects an increase in brain activities, independent of MAP.[2] The absence of change in BOLD signal as observed herein supports the notion, because increased oxygen consumption could abolish BOLD signal increase brought about by the small CBF increase. Isometric exercise increases in MAP and HR by means of central command and activation of the sympathetic nervous system, and thus it is not surprising that there is an increase in brain activities. Measurement of oxygen consumption could directly validate this hypothesis.

CONCLUSION The current study demonstrates an interesting application of BOLD and CBF fMRI to investigate changes in CBF and oxygen metabolism associated with isometric exercise in the MRI environment. This paradigm may offer a simple and non-invasive way to study CBF autoregulation in normal and neurological diseases.

REFERENCES [1]Edwards, MR et al. *Med & Sci Sports Exerc* 34: 1207-11, 2002. [2]Ogoh, S. *Med & Sci Sports Exerc* 40: 2046-54, 2008.

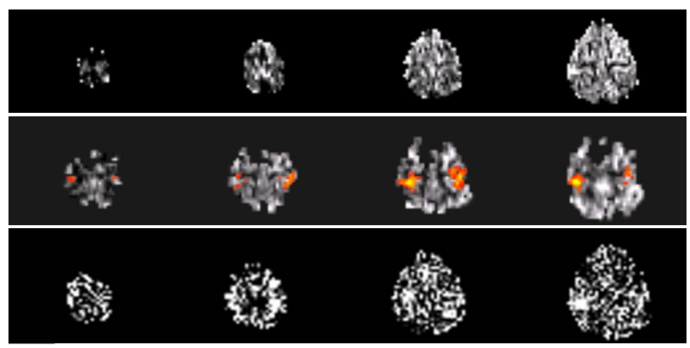

Figure 1. Basal CBF, threshold CBF activation map, and % difference between rest and exercise without threshold. Gray scale bars: 0-80 ml/100g/min, color bar: 1.96-6 Z score, and 0-50% change.

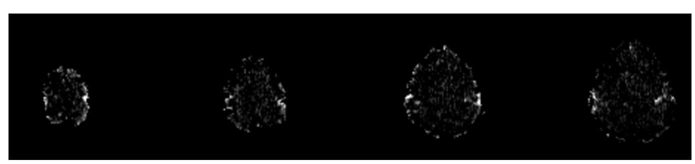

Figure 2. BOLD % difference between rest and exercise without threshold. Gray scale bars: 0-3% change.

Table 1. Physiological parameters.

	MAP (mm Hg)	HR (bpm)	RR (rpm)	$EtCO_2$ (mm Hg)	SaO_2 (%)
Rest	81±5*	61±16#	15±3	30±2	97.7±1.0
Exercise	98±11*	71±21#	16±3	29±2	97.8±0.6

* p=0.0001, # p=0.0005.