Caffeine does not affect regional vascular reactivity to CO2

Y. Chen[1,2], and T. B. Parrish[1,2]

[1]Biomedical Engineering, Northwestern University, Chicago, IL, United States, [2]Radiology, Northwestern University, Chicago, IL, United States

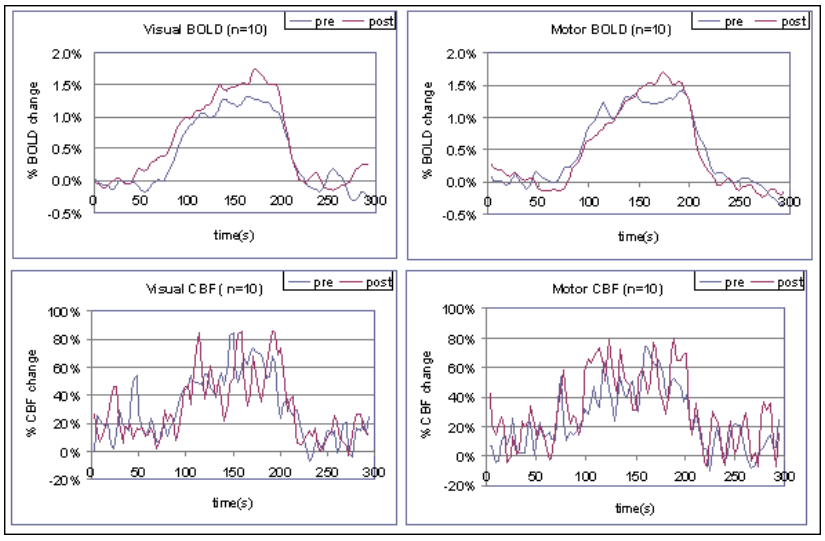
Introduction

Caffeine is a widely used methylxanthine found primarily in coffee and tea [1]. It is an adenosine antagonist and decreases cerebral blood flow through vasoconstriction. Hypercapnic challenge is commonly used in the clinical setting as a diagnostic tool for cerebrovascular diseases [2]. It is also gaining popularity rapidly in fMRI for calibrating BOLD studies. Previous work using ultrasound has shown that there are no differences in vasoreactivity in the middle cerebral arteries; however, detailed regional analysis has not been done to date. Since caffeine has already been shown to alter the BOLD response [3,4], it is important to understand its local effect on CO_2 reactivity. In this study, we use a combination of arterial spin labeling and BOLD to investigate caffeine's effects on CO_2 reactivity.

Methods

Ten healthy subjects were imaged on a 3T scanner (Siemens TIM Trio, Erlangen, Germany) using the posterior half of a twelve-channel head coil and an additional carotid coil placed at the top of the head to improve the signal from the motor cortex. Subjects were instructed to abstain from caffeine for at least 12 hours before the study. Blood samples were collected before each study and at 10min intervals after caffeine administration to monitor plasma concentrations of caffeine. Each experiment consisted of a pre-caffeine and a post-caffeine session. For both sessions, simultaneous ASL and BOLD images were acquired using PICORE Q2TIPS [5] with gradient echo EPI readout. Imaging parameters used were: $TI_1/TI_2/TI_{1S}$ = 700ms/1400ms/1200ms, 20cm tag, TR/TE=3s/23ms. Six oblique slices (5mm thick, 2.5mm gap, inplane resolution = 3.45mm x 3.45mm) were positioned to cover both visual and motor areas. Hypercapnia data were acquired in two scans (1min room air-2min 5% CO_2-2min room air). These were repeated after a 10min intravenous injection of 2.5mg/kg body weight dose of caffeine. High resolution T_1-weighted images were also acquired using a 3D anatomic scan (MPRAGE sagittal orientation, 1mm isotropic resolution, TI=900ms, TR=2300ms, TE=2.91ms, 176 partitions). End-tidal CO_2 ($etCO_2$) and other vitals such as heart rate, blood pressure and SpO_2 were continuously monitored.

ASL and BOLD images were calculated using surround subtraction and averaging [6] in Matlab (The MathWorks, Inc., Natick, MA) after motion correction. These were then processed and aligned to the high resolution T_1 images in Brain Voyager (Brain Innovations, Maastricht, The Netherlands). ROIs in both motor and visual areas were selected based on active voxels on the ASL timeseries (R>0.23). Time courses from these ROIs were averaged across all subjects.



Results

The average $etCO_2$ increased from 32.0 ± 6.8 mmHg to 48.7 ± 4.8 mmHg before caffeine, and from 35.0 ± 4.7 mmHg to 48.3 ± 3.2 mmHg after caffeine. The figures on the left show the group averaged time courses for BOLD (top) and CBF (bottom), visual (left) and motor (right) cortices. There is no significant difference before and after caffeine administration in the overall amplitude changes or the rise and fall times of the time courses.

Discussion

This study demonstrates that caffeine does not alter vascular reactivity to CO_2. This supports the results reported by Blaha et al., which demonstrates no change in CO_2 reactivity after caffeine administration by measuring blood velocities in the middle cerebral arteries using transcranial Doppler ultrasound. The current work demonstrates that spatially specific regions in the brain have similar vasoreactivity subsequent to caffeine administration. This finding is important for clinical hypercapnic challenges as it shows that caffeine will not have to be considered as a confounding factor in such studies.

References

1. Fredholm BB et al. *Pharmacol Rev.* 51(1):83, 1999.
2. Blaha M et al. *J Clin Neurosci.* 14:464, 2007.
3. Mulderink TA et al. *Neuroimage* 15(1):37, 2002.
4. Laurienti PJ et al. *AJNR Am J Neuroradiol.* 24(8):1607 2003.
5. Luh et al. *Magn Reson Med.* 41(6):1246, 1999.
6. Wong EC et al., *NMR Biomed.* 10:237, 1997.