Caffeine's effects on neurovascular coupling

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 popular substance found in many foods and drinks, primarily coffee and tea. It belongs to the methylxanthine family, and acts as an antagonist to adenosine, which causes vasoconstriction and affects neural activity [1]. Caffeine's nonspecific binding to adenosine receptors that reduce resting blood flow while improving attention and cognitive function suggests that it may be able to reset the coupling between cerebral blood flow and neural activity. In this study, we investigate this effect of caffeine using the Davis model [2].

Methods

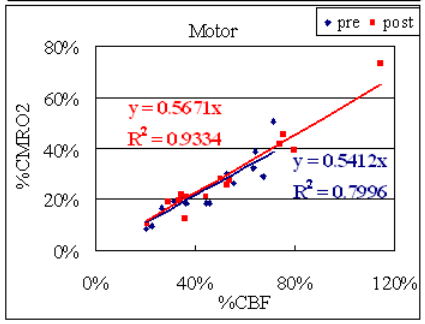
Seven healthy subjects were imaged on a 3T scanner (Siemens TIM Trio, Erlangen, Germany) using the posterior half of a twelve-channel head coil and an additional carotid coil placed at the top of the head to improve the signal from the motor cortex. Subjects were instructed to abstain from caffeine for 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 [3] 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. During two functional scans, subjects viewed a screen which alternated between a gray screen for baseline and a flashing checkerboard at either 4Hz or 8Hz as stimulus (90s baseline, 2 cycles of 45s on/45s off). A motor task involving auditory-cued finger tapping at 1Hz or 3Hz coincides with the visual epochs. Hypercapnia data were acquired in two additional scans (1min room air-2min 5% CO_2-2min room air). Both the functional and hypercapnic scans 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).

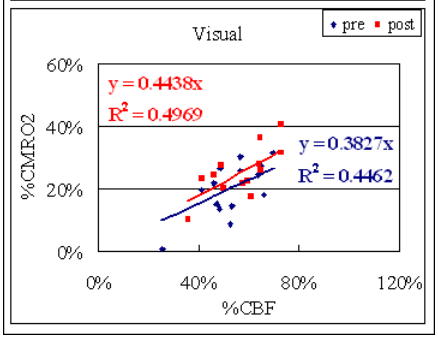
ASL and BOLD images were calculated using surround subtraction and averaging [4] in Matlab (The MathWorks, Inc., Natick, MA) after motion correction. These were then processed and aligned to the high resolution T_1 images in Brain Voyager (Brain Innovations, Maastricht, The Netherlands). ROIs in both motor and visual areas were selected based on active voxels on the ASL timeseries (R>0.23). M, the BOLD calibration factor, was calculated using the Davis model [2] from BOLD and CBF percent changes due to hypercapnia. This was then used to calculate $CMRO_2$ from the BOLD and CBF percent changes calculated from the functional runs.

Results

Caffeine decreased resting state CBF and BOLD signal by 28.4% and 1.9% respectively. The table on the right shows the M values calculated for both motor and visual before and after caffeine injection. These values are slightly lower than those reported in [5], likely due to the shorter echo time used in the current study. Caffeine appears to increase M, particularly in the visual cortex. The calculated $CMRO_2$ values are plotted against CBF percent changes in the two figures. The slope of the fitted line increases after caffeine for both motor and visual cortices, indicating a shift in neurovascular coupling.

	Pre-Caffeine	Post-Caffeine
Motor	3.8% ± 0.7%	3.9% ± 0.8%
visual	3.4% ± 1.0%	3.8% ± 1.3%





Discussion

The current study demonstrates that caffeine indeed alters coupling between CBF and $CMRO_2$ by increasing the $CMRO_2$:CBF ratio, which implies an increase in oxygen extraction fraction (OEF).This result is counterintuitive because caffeine decreases baseline CBF, which would theoretically decrease the oxygen supply to neurons. Another possible explanation could be that caffeine affects anaerobic metabolism of glucose to sustain the increased neural activity [1]. This hypothesis, however, is beyond the scope of the current study and would require further verification using methods such as PET.

References

1. Fredholm BB et al. *Pharmacol Rev.* 51(1) 83, 1999.
2. Davis et al. *Proc Natl Acad Sci USA.* 95(4) 1834, 1998.
3. Luh et al. *Magn Reson Med.* 41(6) 1246, 1999.
4. Wong EC et al., *NMR Biomed.* 10:237, 1997.
5. Chiarelli PA. et al., *Magn Reson Med.* 57:538, 2007.