Activation induced BOLD and CBF responses vary with caffeine dose

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Introduction

Caffeine is a powerful vasoconstrictor of cerebral vessels and also acts as a neuro-excitatory agent. As a result, caffeine has been shown to improve the BOLD response in humans performing simple motor, visual or memory tasks [1-3]. Additionally, previous work has shown that the blood flow induced changes due to activation are independent of the baseline flow condition when altered by changes in CO2 [4]. The purpose of this work is twofold: 1) to explore the caffeine dose response; 2) to investigate activation induced blood flow changes in the presence of a vasoconstrictor. This work measures BOLD and CBF changes simultaneously during a visually cued task. The hypothesis is that BOLD changes will increase with caffeine dose and that the CBF induced changes resulting from activation will also increase due to the increased vascular tone.

Methods

Images were acquired using a receive-only eight channel head coil on a 3T MR scanner (Magnetom TIM Trio, Siemens, Erlangen, Germany). Subjects were scanned on different days with different doses of caffeine (1mg/kg or 2.5mg/kg) or saline after 24 hours of caffeine abstinence. A visually cued (8 Hz flashing checkerboard) motor task (self-paced finger tapping) was performed before and after caffeine administration. Caffeine was injected intravenously over a 10 minute period while the 3D anatomic scan (MPRAGE sagittal orientation, 1mm isotropic resolution, TI=900ms, TR=2300ms, TE=2.91ms, 176 partitions) was collected. For the functional perfusion data collection a Q2TIPS/PICORE [5] pulse sequence was used with the following parameters: TI1=700ms, TI2=1400ms, TE/TR/FA=23ms/2s/90°, tag thickness=10cm, slice thickness=5mm and 2.5mm gap, 6 transversal slices with an in-plane resolution of 3.45x3.45 mm. The slices were orientated along a transverse to coronal oblique plane that captured the motor and visual cortices in the same acquisition. The task had 80s (40 measurements) of baseline followed by active (40s) and rest (40s) blocks repeated 4 times for a total of 202 measurements, allowing for 2 dummy scans. Time courses were extracted and percent signal change relative to baseline were calculated for BOLD and CBF.

Perfusion images were calculated using Matlab (The MathWorks, Inc., Natick, MA) with the surround subtraction method [6] after motion correction in BrainVoyager (Brain Innovations, Maastricht, The Netherlands). BOLD data were generated similarly using a surround averaging scheme to remove any perfusion weighting [6]. The data were then imported back into Brain Voyager for further preprocessing by spatial (8mm) and temporal (8s) smoothing. A general linear model was used for the statistical analysis using Brain Voyager. All data were coregistered to the 3D anatomic data. Time course data were collected from regions of the left and right motor and visual cortices that were suprathreshold (t>3.00) based on the perfusion data. These regions of interest were then applied to the BOLD data to generate similar time courses. The ROIs were 3x3 functional voxels in-plane and 1.5 voxels in the slice direction.

Results & Discussion

There was a global decrease in perfusion of 10.9% and 39% due to the 1mg/kg and 2.5mg/kg of caffeine, respectively. A similar but smaller trend was seen in the resting raw BOLD data, 4.0% and 4.4%. Results for the motor and visual ROIs are presented in the tables below. The values represent percent signal change relative to the rest condition. An increase in the post caffeine BOLD and CBF represent changes in the physiologic status of the brain. The larger blood flow response to the same stimulus post-caffeine may be the source of the increase in the BOLD response. These data support the hypothesis that the blood flow response to activation is dependent on the vascular tone.

MOTOR	BOLD pre-caf	CBF pre-caf	BOLD post-caf	CBF post-caf
1mg/kg	0.6%	28.3%	0.8%	34.1%
2.5mg/kg	0.8%	33.1%	1.5%	66%

Visual	BOLD pre-caf	CBF pre-caf	BOLD post-caf	CBF post-caf
1mg/kg	0.6%	38.5%	0.9%	56.5%
2.5mg/kg	0.7%	31.1%	1.7%	70.8%

Conclusion

The vasoconstrictive nature of caffeine reduces blood flow to the brain but allows task performance to remain the same or improve. Thus, caffeine acts to alter the normal coupling of blood flow to neuronal activity. The data presented demonstrate this effect and the possibility that the coupling may vary anatomically or as a function of adenosine receptor concentration. Further study of the physiologic effects of caffeine on the brain is required to better understand the mechanisms of fMRI.

References

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