Modulation of the Functional Cerebral Blood Flow Response by Reductions in Baseline Blood Flow

J. Liau[1], J. E. Perthen[1], R. B. Baxton[1], and T. T. Liu[1]
[1]UCSD Center for fMRI, La Jolla, CA, United States

Introduction

The effect of changes in baseline CBF on the neurovascular coupling mechanism between neural activity and cerebral blood flow is still not completely understood. Here we consider two possibilities: 1) an additive model, where the absolute increase in CBF (ΔCBF) is independent of the baseline condition and 2) a proportional model, where the functional percent increase in CBF (Δ%CBF) is independent of baseline CBF. Previous studies addressing this question have led to differing conclusions. Studies with hypocapnia-induced vasoconstriction (decreased baseline CBF) report no change in ΔCBF [1], no change in Δ%CBF [2], and a reduction in both ΔCBF and Δ%CBF [3]. A study with the vasoconstrictor indomethacin found that both ΔCBF and Δ%CBF with activation were reduced with lowered baseline CBF [4]. In this study, we show that reductions in baseline CBF due to caffeine (a known vasoconstrictor) lead to increases in Δ%CBF but decreases in ΔCBF.

Methods

Nine subjects participated after giving informed consent. They refrained from ingesting caffeine for 12 hours before the study. Experiments consisted of two imaging sessions (pre-dose and post-dose). Between sessions, subjects ingested a 200 mg caffeine pill and waited outside for 30 minutes. Each session had: (a) a high-resolution anatomical scan, (b) a resting-state scan (3min off), and (c) a block design run (20s head, 20s on, 40s off, 4 cycles). Images were acquired on a 3T GE system with a head transmit coil and an 8 channel receive head coil. Functional runs used a PICORE QUIPPSII ASL sequence with dual echo spiral readout (TE1/TE2=9.1/30ms; TI1/TI2=600/1500 ms; TR=2s) while subjects viewed a full-field radial 8-Hz flickering checkerboard. Three oblique axial 8-mm slices were prescribed about the calcarine sulcus. The anatomical scans were used to align the post-dose to the pre-dose data. The running difference of the control and tag images from the first echo of the block design run produced a CBF time series, and data from the resting-state scan was used to calibrate the block design data to absolute CBF values using the method described in [5]. A functional region of interest (ROI) was defined by correlation with a reference function ($p < 0.05$). Within the ROI, the block design data was averaged over cycles and voxels to produce the absolute CBF block response per subject. Subtraction of the baseline from the absolute CBF response produced the CBF response per subject and normalization by the baseline produced the Δ%CBF response per subject. To assess whether caffeine-induced reductions in baseline changed the functional CBF response across subjects, paired two-tailed t-tests were done between the pre-dose and post-dose data for the Δ%CBF and ΔCBF response amplitudes and the absolute CBF levels during activity and rest.

Results

The figure shows the pre-dose (blue) and post-dose (red) (a) Δ%CBF, (b) ΔCBF, and (c) absolute CBF block responses. Vertical bars show the standard error. The caffeine dose significantly increased the Δ%CBF amplitude ($p=0.046$, 60.7% increase), but significantly reduced the ΔCBF amplitude ($p=0.0088$, 42.3% decrease) and the absolute CBF levels during both activation ($p=0.00030$, 53.6% decrease) and rest ($p = 0.00008$, 62.5% decrease). It is also interesting to note that the post-dose absolute CBF level during activation was not significantly different from the pre-dose resting absolute CBF level ($p = 0.29$).

Discussion

The decrease in the amplitude of the ΔCBF response with reductions in baseline CBF is in agreement with those of [2,3,4] but differs from that of [1] which found no change in ΔCBF. Our findings of an increase in Δ%CBF are consistent with those of [1] but differ from those of [2,3,4]. On the whole, the findings of a decreased ΔCBF response with reductions in baseline CBF suggest that the coupling between neural activity and CBF is not driven by a need to deliver a fixed amount of incremental oxygen (which would imply constant ΔCBF) independent of the baseline CBF level. Instead, the results are more consistent with a feedforward model in which neural activity leads to the release of the same amount of vasodilatory agent regardless of the baseline level of CBF. The observed increase in Δ%CBF suggests a biomechanical interpretation in which the smooth muscle relaxation due to the vasodilatory agent results in a relatively greater percent increase in vessel radius when the initial baseline radius is smaller.

References [1] Ramsay et al, J Physiol 471:521-34;1993. [2] Shimosegawa et al, JCBFM 15:111-4;1995.[3] Kemna et al, JCBFM 21:664-70;2001. [4] St Lawrence et al, MRM 50:99-106;2003. [5] Floyd et al, JMRI 18:649,2003.