Concurrent ASL and BOLD FMRI of Working Memory in Typically Developing Population

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Target audience: Developmental neuroscientist and neuroimaging researchers

Introduction:

Developmental BOLD fMRI studies on executive functions, such as working memory, behavioral inhibition or cognitive control, reported either stable or age-related increases in BOLD signal in typically developing (TD) populations[1]. However, due to the lack of assays of baseline function and absolute quantification of task-induced effect size (both may vary with age), it is hard to interpret developmental BOLD fMRI findings. Arterial spin labeling (ASL) is a noninvasive MRI technique that can provide absolute quantification of cerebral blood flow (CBF) both at rest and during task activation. In the current study, a concurrent ASL/BOLD fMRI paradigm of working memory tasks was applied to examine the relationship between CBF and BOLD signal changes across age groups in a cohort of 57 healthy children and adolescents.

Method:

Fifty-seven TD children and adolescents participated in this study, including 27 children aged 7 to 12 (13 males) and 30 teenagers aged 13 to 17 (16 males). All images were acquired on a 3T Siemens TIM Trio scanner using a 12-channel head coil. A block-design was performed during fMRI scans with 5 cycles of interleaved 34s 0-back and 64s 2-back working memory (WM) tasks with the mean performance accuracy of 89±0.25% across the 57 participants. At the beginning of the fMRI scan, a 15s brief instruction was shown on the screen. A pseudo-continuous ASL (pCASL) sequence with dual-echo EPI readout was used to acquire ASL and BOLD data simultaneously. Twenty 5mm axial slices were acquired to cover the whole brain with imaging parameters: FOV=220mm, matrix size=64×64, TE1/2=10/25ms, TR=3.5s. The tagging plane was positioned 90mm inferior to the center of the imaging slab with a labeling duration of 1500ms and labeling delay of 1000ms. The subtraction of the tagging and control images from the first echo yielded perfusion-weighed time series, and the average of the tagging and control images from the second echo yielded BOLD time series. A 4min resting pCASL EPI scan was acquired to measure the CBF at baseline. CBF calculation followed a standard model taking into account age and gender dependent blood T1 changes[2].

All fMRI data were processed using SMP8 including motion correction, normalization and smoothing. Statistical group analysis of 2-back relative to 0-back WM was performed to acquire the activation map of BOLD and ASL fMRI for the 2 age groups respectively. The mean CBF and BOLD time series were extracted from the common activation ROIs. The average resting CBF and activation-induced CBF and BOLD changes were calculated. Unpaired t-test was used for the comparison of mean resting CBF, CBF changes and BOLD response between the 2 age groups. Regression of BOLD and CBF signals with age was also performed.

Results:

Reliable brain activations associated with 2-back relative to 0-back WM were obtained in bilateral prefrontal, parietal cortex and ACC in BOLD and ASL data in both age groups, as shown in Fig. 1a. BOLD data provided stronger task-induced brain activation than ASL. The percentage BOLD signal change between 2 and 0-back from each group is shown in Fig. 1b. Compared to the children, adolescents showed a trend of greater BOLD response ($p=0.30$) and regression analysis showed a significant increase of BOLD signal change with age ($r=0.26$, $p=0.047$). No difference was found between the percentages of CBF change between the 2 age groups. Figure 1c shows the mean resting CBF and absolute task-induced CBF change within the activation ROI for each age group. The resting CBF was significantly increased in the children compared to the teenager group ($p<0.01$). A similar trend was also observed in the task-induced absolute CBF change but failed to reach significance. Besides greater resting CBF in children, greater absolute CBF was also observed during both the control task (0-back WM) and activation task (2-back WM) compared to the teenager group (0back:$p=0.064$, 2back:$p=0.056$).

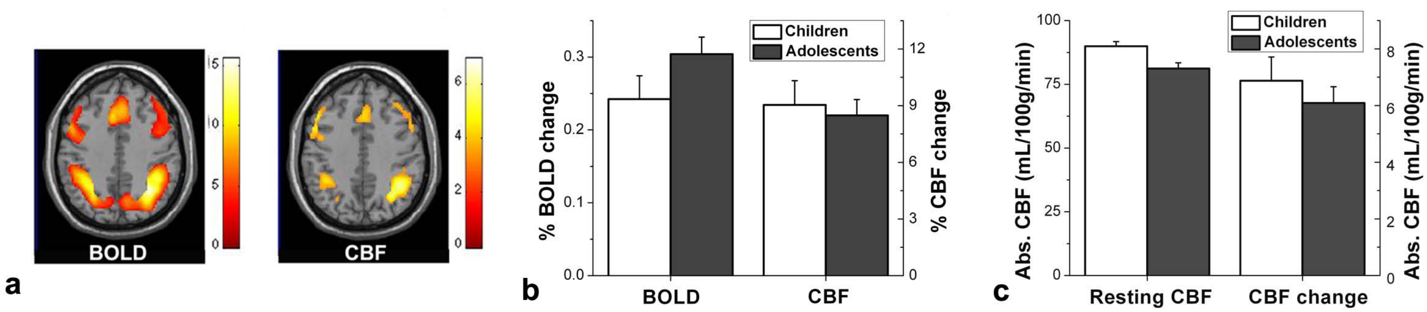

Fig. 1a) Group activation t-maps of BOLD and ASL fMRI of 2-back vs. 0-back WM task in the whole group; **b)** relative BOLD and CBF signal changes and **c)** absolute baseline CBF and CBF increases in the child (7-12yr) and adolescent (13-17yr) groups respectively.

Discussion:

Using concurrent ASL/BOLD fMRI, our study revealed differences in baseline CBF and task-induced CBF responses between 2 groups of children and adolescents. Children showed greater CBF at rest and during WM tasks compared to adolescents. A trend of greater absolute CBF change was also observed in children when performing 2-back WM relative 0-back condition. However, when the baseline difference is taken into account, there is no difference in the task-induced CBF response in terms of a percentage change between children and adolescents. Our results are consistent with a recent concurrent ASL/BOLD fMRI study using an auditory stimulation task[3]. Combined with the previous finding that baseline $CMRO_2$ decreases with age during brain development[4], our findings of greater BOLD response with reduced absolute CBF change in adolescents indicate that $CMRO_2$ change induced by WM tasks may decline with age, which may be translated into more efficient use of oxygen of the brain with development.

References: 1. Klingberg et al., J Cogn Neurosci 2002;14(1):1-10. 2. Jain V et al., Radiology. 2012;263(2):527-36. 3. Moses P et al., Hum Brain Mapp. 2013. 4. Jog M et al., ISMRM2013;no. 2953.