Arterial Spin Labeling in Children: BOLD and CBF Hemodynamic Response to Visual Stimulation

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Introduction

Arterial spin labeling (ASL) presents a means for measuring cerebral blood flow (CBF) in a noninvasive manner that is well suited for the study of hemodynamic response to activation in the healthy developing brain. Previous studies of CBF using radionucleotide tracing methods to measure resting CBF in patients have found elevated CBF in childhood followed by a decline during adolescence to adult levels [1-3]. Since resting CBF influences the CBF response during activation and CBF contributes to the blood oxygen level dependent (BOLD) signal, assessment of potential age-related differences in CBF and BOLD responses in children is critical for interpretation of developmental FMRI. Although developmental studies have begun to use ASL to examine functional BOLD and CBF in sedated infants and preschoolers [4] and resting state perfusion in infants and children [5], ASL has not yet been applied to investigate BOLD and CBF in a functional paradigm with normal school-age to adolescent children, the age range most commonly targeted in developmental FMRI studies. We used pulsed ASL to measure BOLD and CBF responses during visual stimulation in two groups of healthy, non-anesthetized children (8 year olds and 12 year olds) and adults to compare FMRI response dynamics.

Methods

Participants in three age groups were studied: 8 year olds (n=7, 4 males), 12 year olds (n=8, 4 males) and adults (19-25 years old, n=10, 4 males). None of the subjects had a history of neurological disorders, none were anesthetized, and all were low caffeine users with no caffeine intake on the day of the scan.

Image acquisition: Scanning was performed on a 3T GE Signa whole body system, with a body transmit coil and an 8 channel receive only head coil. A PICORE QUIPSS II [6] sequence was used with a dual gradient echo spiral readout. Imaging parameters were: TR=2s, TI1=600ms, TI2=1500ms, θ=90°, FOV=24×24 cm^2, matrix size=64×64, TE1=9.1ms, TE2=30ms, with four 7mm slices positioned through the primary visual cortex at an oblique angle parallel to the calcarine sulcus. The tagging band was 100mm thick, positioned 10mm from the proximal edge of the first slice. For each subject, four functional runs were acquired while subjects viewed a colored radial checkerboard flashing at 8 Hz that was presented in a block design. The block design began with 40s of rest followed by 4 cycles of 20s of stimulation and 40s of rest. Cardiac pulse and respiratory effort were recorded.

Image processing: Datasets were co-registered for motion correction. CBF time series were formed from the running subtraction of the ASL data derived from echo 1, and BOLD time series from the running average of echo 2. Cardiac and respiratory confounds were removed from the data [7]. For each subject, BOLD and CBF time series were averaged over runs. Runs were included if the number of voxels that correlated with the stimulus waveform (correlation coefficient r >0.4 on the CBF time series) exceeded 20. For 2/15 children and 3/10 adults one or two runs were excluded. In the averaged data, activated voxels with a correlation ≥0.5 for the CBF data and ≥0.6 for the BOLD data were identified for further analysis. The average % signal change of activated voxels during the peak response (four time points acquired 14-20s after stimulus onset) and the post-stimulus period (four time points acquired 14-20s after stimulus cessation) was calculated for each subject, and compared between the three groups using an unpaired t-test.

Results

Mean BOLD and ASL responses are shown in Fig. 1. There are no significant differences in the peak BOLD or CBF amplitudes between the three groups. The post-stimulus period was lower in the adults compared to either of the child groups, for BOLD ($p<0.05$) and CBF ($p<0.007$) responses.

Discussion

This study demonstrates the use of pulsed ASL for quantitative assessment of BOLD and CBF in children. The magnitude of change in the BOLD signal and CBF during stimulation is similar between children and adults. The enhanced undershoot in the BOLD data for the adults may reflect a slower return to baseline for cerebral blood volume [8] in adults.

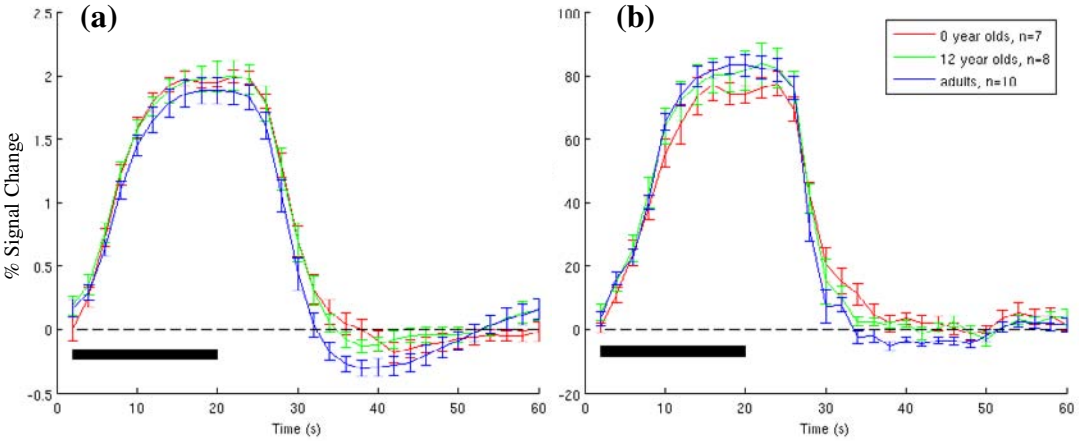

Figure 1. (a) BOLD and (b) CBF mean responses to visual stimulation. Error bars show +/- 1 standard error. The solid line indicates the period of stimulus presentation.

References

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