CASL Perfusion MRI in Normal Infant Brain Development

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Introduction

Imaging changes in regional brain function with development may provide new insights into brain organization. MRI is an entirely noninvasive modality that does not require exposure to ionizing radiation, and is therefore well suited to longitudinal studies in children. With adequate training, BOLD fMRI with cognitive activation can be successfully carried out in young children of preschool age who can comply with task instruction. However, while the first years of life are accompanied by dramatic changes in sensorimotor and cognitive skills, infants and toddlers probably cannot comply with task activation studies, and have typically been studied while sedated. A limited amount of existing knowledge about changes in regional brain function has been derived from cross sectional studies of development with FDG-PET imaging [1, 2].

Perfusion MRI with arterial spin labeling (ASL) allows quantification of regional brain function at rest, as manifested in regional cerebral blood flow (CBF) values, and can be obtained without subject cooperation beyond keeping still. Changes in CBF can be correlated with demographic or behavioral variables either longitudinally or cross-sectionally to draw inferences about brain-behavior relationships during development.

The Santa Fe Institute Consortium (SFIC) is a privately-funded research initiative to explore brain-behavior relationships during discrete stages of development. One arm of this study concerns infant development. As part of this study, normal infants recruited to participate undergo MRI scanning during natural sleep, including both structural imaging and ASL perfusion MRI. Here we report initial results from 19 infants recruited into the SFIC study at Rutgers University and imaged 6 or 12 months of age.

Materials and Methods

Parental consent to participate in a broad range of serial cognitive, electrophysiological, and MRI testing was obtained for all participants. MRI scanning was carried out at 1.5T (GE Signa 5.X) using a product adult head coil. Infants were fed and allowed to fall asleep. Foam padding restricted head movement and provided sound attenuation. Standard T1- and T2-weighted MRI was performed. Continuous arterial labeled perfusion MRI was performed using a 3D fast spin echo (FSE) sequence with an interleaved stack of variable density spirals acquisition. Continuous labeling was performed using the amplitude modulated control approach [4]. For hardware compatibility, the labeling was performed for 60 ms followed by a 40 ms gap. Labeling was performed for a total duration of 1.2 s and a 1s post-labeling delay [3] was employed. Background suppression [5,6] was achieved with adiabatic inversion pulses. Images were acquired with a 3.8 mm cubic resolution. Several 1.5 minute acquisitions were sequentially performed followed by a reference acquisition without suppression for blood flow quantification.

Raw MRI data were reconstructed using customized software and CBF values were derived from a single compartment model [3]. CBF maps showing spuriously low values (<20 ml/100g/min for whole brain) suggested ineffective labeling and were discarded. CBF maps were then converted to relative CBF (rCBF) by adjusting global CBF relative to a fixed value of 50 ml/100g/min. Manually assisted normalization of CBF maps to a standard anatomical space was carried out using T1-weighted images acquired concurrently and using SPM2 software. Average CBF maps for the 6-month and 12-month group were generated from the spatially normalized rCBF maps, along with a difference map. An ROI analysis also compared CBF in sensorimotor (Brodmann's areas 4-6), visual (areas 17-19) auditory (areas 40-42) and dorsolateral frontal (areas 8-9, 44-46) regions based on the Wake Forest Pickatlas utility [7]. The relative regional CBF change was calculated through dividing the difference between the regional CBF value and the whole brain CBF value by the whole brain CBF value. This relative regional CBF change was then averaged in the 6-month and 12-month old subgroups.

Results and discussions

Acceptable CBF data was obtained from 8 infants aged 6.9 ± 0.2 months and 8 infants aged 12.7 ± 0.2 months. Group maps of rCBF are shown in Fig 1. An increase in rCBF is evident in dorsolateral prefrontal, insular and cingulate cortex. Figure 2 shows results from the extracted ROI. A significant increase in the frontal ROI is observed (p=0.04), along with a significant decrease in the sensorimotor ROI (p=0.02). The increase in frontal activity and decrease in motor activity are consistent with prior observations using FDG-PET [1, 2]. These findings suggest that ASL perfusion MRI should be useful in characterizing brain development even in infants studied during natural sleep without sedation.

Reference

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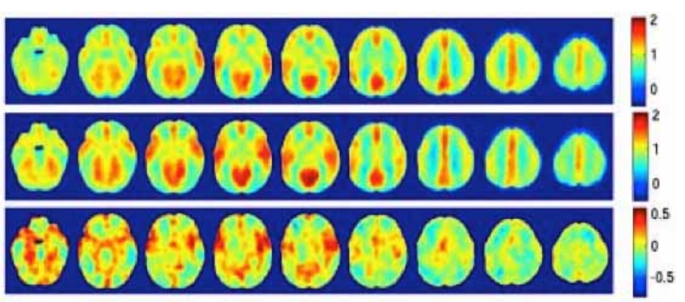

Fig 1. Relative CBF maps (normalized to 50 ml/100g/min) from 6 month old (n=8, TOP) and 12 month old (n=8, MIDDDLE) infants, along with a difference image showing increased CBF in frontal regions with development (BOTTOM).

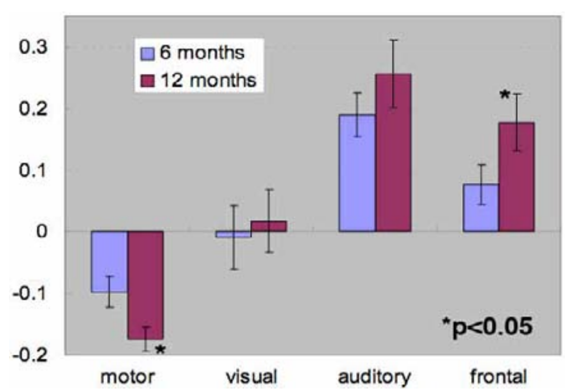

Fig 2. ROI analysis showing changes in relative CBF within sensorimotor, visual, auditory, and frontal regions.