Resting State CBF with PASL in Developing Brains

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Introduction

Resting state fMRI is becoming more popular in studying the development of functional brain connectivity. Since the development of brain circuits are coupled with changes in neurovascular coupling [1], studying the characteristics of cerebral blood flow (CBF) in developing brain can be a complementary way to understand the functional connectivity of the developing brain. The change of regional CBF throughout childhood has been measured with PET or SPECT [2]. Arterial spin labeling (ASL), as a noninvasive MR technique, is particularly attractive for studying cerebral perfusion in children [3], even newborns [4]. Although the period from birth to adolescence is most important in brain development, the pediatric CBF data is still sparse due to a lack of consensus and the limited availability of CBF techniques.

Materials and Methods

All MRI scans were approved by the local IRB, and informed content was obtained. During the ASL scans, all subjects were instructed to stay awake. We have collected ASL data for 28 healthy subjects: 6-8 year-old (N=5, 7.3±0.5 years), 9-11 year-old (N=5, 10.3±0.5 years), 12-14 year-old (N=6, 12.6±0.6 years), 15-17 year-old (N=7, 15.7±0.6 years), and 18-20 year-old (N=5, 19.0±0.4 years). All scans were performed on a GE Signa 3T HDx system with an 8-channel head coil. A Pulsed ASL (PASL) perfusion sequence was implemented using a proximal inversion with control for off-resonance effects (PICORE) quantitative imaging of perfusion using a single subtraction (QUIPSS II) sequence [6]. A single-shot gradient-echo EPI sequence was used for image acquisition. The time to QUIPSS saturation is TI1 = 600 ms and inversion time of the first slice is TI2 = 1300ms. Other acquisition parameters included: FOV 24 cm, 64 x 64 matrix, TE/TR =26/2300ms, flip angle 90°, slice thickness 6 mm, inter-slice spacing 0.5 mm. Each ASL scan with 151 acquisitions and 5 dummies required 5 min 59 sec. A separate M0 scan using gradient-echo EPI with TR of 15s was acquired in order to quantify CBF. The PASL data was preprocessed for head motion correction and spatial smoothing with an 8-mm Gaussian kernel via SPM8. Any volumes with large motion (translation larger than 2mm and/or rotation larger than 1.5 between consecutive volumes) were removed. Perfusion-weighted images were calculated by pair-wise subtraction of the control and labeled images, and CBF maps were then calculated. Average CBF map was obtained by averaging across the imaging time series. The static CBF map of each subject was divided by the global CBF of that subject, so that the CBF map was converted to relative CBF map. For comparison, all CBF maps were normalized to the same template via SPM8. We also used ROI seed-based analysis to analyze the CBF time series extracted from the original PASL signals with reduced BOLD contamination [7].

Results and Discussions

The average values of global CBF in different age groups are shown in Fig.1. The global CBF rises in the early childhood, and then falls in the late childhood. This trend is similar to that shown in [2]. The average relative CBF maps for different age groups are shown in Fig.2. As a comparison, we also calculated the relative CBF maps acquired using similar method in newborns (N=10, 0.5±0.1 months). For newborns, CBF is higher near the basal ganglia, temporal lobe, and posterior cingulate cortex (PCC). For the other age groups (from 6 to 20 y.o.), the CBF in PCC, MPFC, thalamus, and insula, are higher than the global CBF of whole brain. In groups 6-8 y.o., relCBF values in the posterior regions with relCBF >1 are greater than those in the anterior regions. In groups 9-11 y.o. and 12-14 y.o., relCBF around insula and MPFC become stronger gradually. Then the pattern of relCBF remains similar for groups 15-17 y.o. and 18-20 y.o.. A voxel-wise one-sided one-sample t-test against 1 was performed on the relative CBF maps for each age group. Fig 3 shows the regions with CBF significantly higher than global CBF (P=0.001), while Fig 4 shows the mean values of relative CBF in the ROIs within PCC, MPFC, thalamus, and insula. For groups 12-14 y.o. and 15-17 y.o., the regions with relCBF>1 (P=0.001) are larger than other groups.

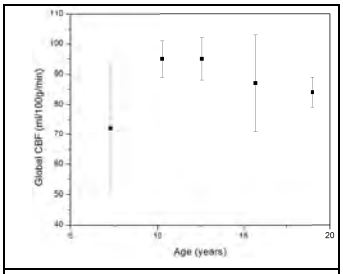

Fig 1. The global CBF in differing age groups.

We selected a seed ROI in the anterior region of insula on the right side. After extraction with reduced BOLD contamination [7], the time course of each voxel in the brain was correlated with the average time course with the reference ROIs. Then the correlation coefficient (CC) map for each subject was normalized to the same template. In each age group, a voxel-wise one-sided one-sample t-test against CC=0.5 was performed on the individual CC maps. Fig 5 shows the regions with CC>0.5 significantly (P=0.05). The groups 12-14 y.o. and 15-17 y.o. show more extended regions correlated to the chosen ROI seed in insula.

To study the resting state network, we need to do a more detailed analysis on the dynamic characteristics of CBF time series in differing brain regions, similar to those done with resting-state fMRI data. The resting-state CBF data should be complementary to the resting-state BOLD fMRI data in studying the functional connectivity of the developing brain. The current sample size for younger children is still small. As we continue collecting ASL data at differing ages through the development, we should be able to better study the changes in the characteristic of CBF, therefore better understand the development of functional brain connectivity.

References: [1] Harris JJ, et al, Develop Cogn Neuro 2011;1:199-216. [2] Chiron C, et al, J Nucl Med 1992; 33:696-703. [3] Biagi LB, et al, JMRI 2007;25:696-702. [4] Wintermark P, et al, ISMRM 2009; 1246. [5] Fair DA, et al, PNAS 2008;105:4028-4032. [6] Wong EC, et al, MRM 1998;39: 702-708. [7] Chuang KH, et al, NeuroImage 2008;40:1595-1605.

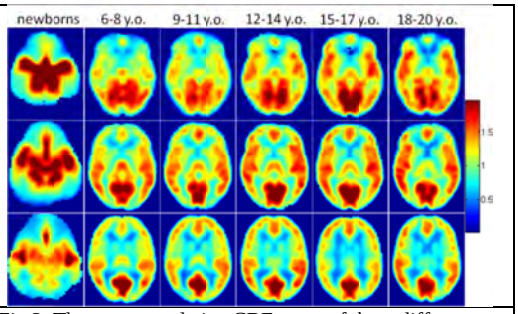

Fig 2. The average relative CBF maps of three different slices from inferior to superior (top row to bottom row) in different age groups. As a comparison, the average relative CBF maps for a group of ten newborns (N=10, 0.5±0.1 months) is shown on the 1st column.

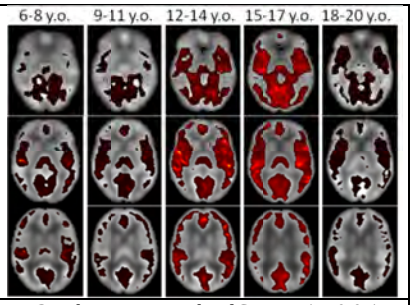

Fig 3. The regions with relCBF>1 (P=0.01) overlayed on average relCBF maps.

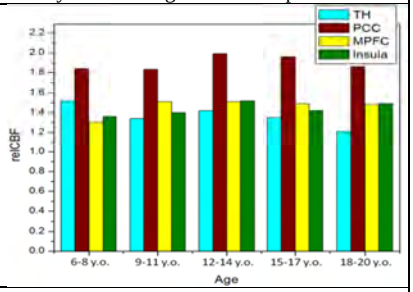

Fig 4. The relCBF values of differing brain regions in each age group.

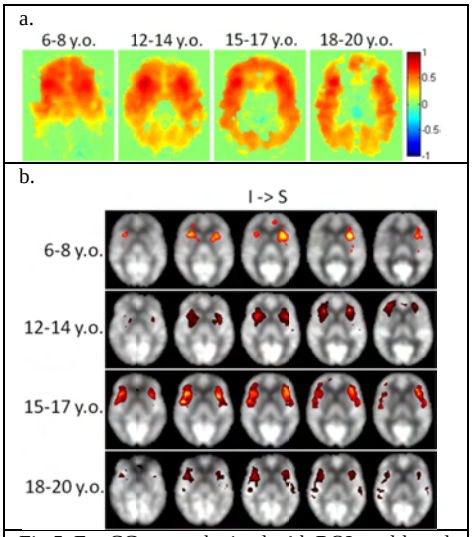

Fig 5. For CC maps obtained with ROI seed-based analysis (seed ROI selected in left insula), (a) the average CC maps; (b) the regions with CC>0.5 for differing age groups.