Perfusion Imaging of Normal Brain Development from Childhood to Young Adulthood

H. Rao[1], S. Wang[2], J. Giannetta[3], K. M. Cecil[4], J. VanMeter[5], T. A. Zeffiro[6], H. Hurt[3], J. A. Detre[1], and J. Wang[2]

[1]Dept of Neurology, University of Pennsylvania, Philadelphia, PA, United States, [2]Dept of Radiology, University of Pennsylvania, Philadelphia, PA, United States, [3]Dept of Pediatrics, the Children's Hospital of Philadelphia, Philadelphia, PA, United States, [4]Dept of Radiology, Cincinnati Children's Hospital, Cincinnati, OH, United States, [5]Dept of Neurology, Georgetown University Medical Center, Washington DC, United States, [6]Neural system group, Massachusetts General Hospital, Boston, MA, United States

Introduction Considerable progress has been made in understanding anatomical changes associated with brain development using structural MRI analyses. Two major neurodevelopmental trends have been revealed, including a continuous increase in the volume of white matter with age that has been attributed to myelination and improved connectivity between brain regions, and an inverted U-shaped function for age-related variations in grey matter, likely the result of the "pruning" of excitatory synaptic connections (1). Further, there appears to be a sequential maturation from lower-order sensorimotor to higher-order association cortex (2). Compared to these neuroanatomical findings, relatively little is known regarding the spatial and temporal patterns of functional brain development. Arterial spin labeling (ASL) perfusion MRI offers an ideal tool for studying development of brain function because it is noninvasive and provides absolute quantification of cerebral blood flow (CBF) – a surrogate index of brain metabolism and neuronal activity (3). In the present study, we examined the normal development of brain perfusion from childhood to young adulthood using a continuous ASL (CASL) technique at 3.0T.

Methods Written informed consent was obtained from all adult participants and parents/guardians of children, from whom written informed assent was also obtained. The data set consisted of 90 subjects recruited and scanned at four institutes, including University of Pennsylvania, Children's Hospital of Philadelphia, Georgetown University Medical Center, and Cincinnati Children's Hospital Medical Center. All data were acquired using the same amplitude-modulated continuous ASL perfusion MRI sequence (4) on Siemens 3T Trio scanners using product Tx/Rx head coils. Imaging parameters included: FOV = 22 cm, matrix size = 64x64, 16 axial slices with a thickness of 6 mm and an inter-slice gap of 1.5 mm, TR = 4 sec, TE = 17 msec, labeling duration = 2 sec, post-labeling delay = 1.2 sec, 80 pairs of control and tag images. These subjects were divided into 3 age groups: 31 children (15 female, age 5-10 years, mean age = 7.7 years), 33 adolescents (19 female, age 11-16 years, mean age = 13.3 years), and 26 young adults (11 female, age 18-30 years, mean age = 23.7 years). Perfusion image processing and analysis were carried out with Voxbo and SPM2. For each subject, one quantitative CBF image was generated based on a single-compartment model, normalized to a customized template by applying the parameters from normalization of the raw EPI images, and then averaged within each age group. Quantitative analyses on global and regional CBF values, as well as voxel-wise general linear modeling were conducted on these individual CBF images.

Results The global CBF decreased monotonically with age ($R = -0.64$, $p < 0.001$). The mean global CBF decreased from 81.2±15.2 (SD) ml/100g/min in the child group, to 64.4±11.3 ml/100g/min in the adolescent group, and to 43.5±5.8 ml/100g/min in the young adult group. Figure 1 shows the mean CBF maps for each group, which clearly demonstrate the overall decrease of global CBF, as well as the growing fraction of white matter and declining fraction of grey matter during brain development. After adjusting the global CBF differences, both voxel-wise and region of interest analyses (using automated anatomical label toolbox in SPM2) revealed significant relative regional CBF increases with age in cingulate cortex, angular gyrus, hippocampus (all $p < 0.001$), and frontal cortex ($p = 0.02$, Fig. 2), which may reflect the late maturation of cortical regions associated with integration, cognitive control, executive and memory functions (2).

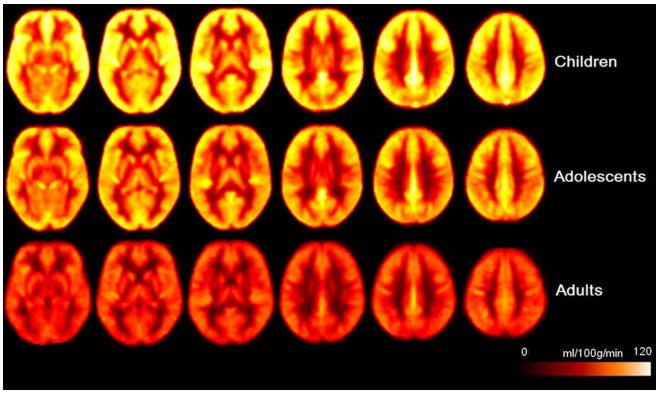

Fig1. Mean CBF images for the child group (age 5-10 years, top), adolescent group (age 11-16 years, middle) and young adult group (age 18-30 years, bottom).

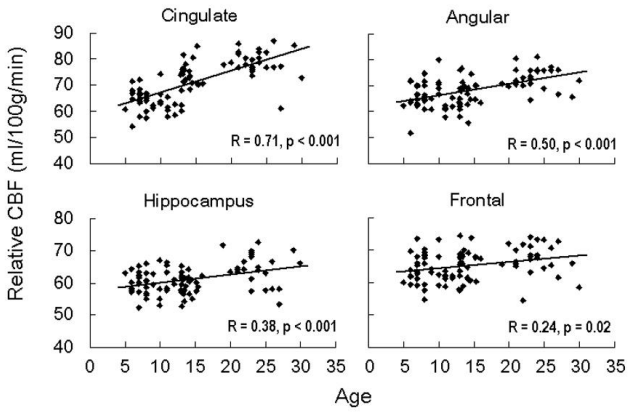

Fig2. Age related regional CBF changes in cingulate, angular, hippocampus, and frontal cortex. After adjusting the global CBF differences, all regions show significant positive correlations between age and relative CBF (all $p < 0.05$).

Discussion and Conclusions Our developmental CBF data are in excellent agreement with nuclear medicine and anatomical MRI studies on brain development. Although the test-retest repeatability of ASL perfusion MRI across the participating sites was not established, the excellent concordance of current CBF data with the literature strongly supports the feasibility and potential of ASL perfusion MRI for longitudinal neurodevelopmental studies of the growing human brain.

References

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