Age-dependent diffusion and perfusion normal values in gray matter brain structures in children

Nils Daniel Forkert[1], Zhaoying Han[1], Matthew Daniel Li[1], Roland Bammer[1], and Kristen Yeom[1]
[1]*Department of Radiology, Stanford University, Stanford, CA, United States*

Purpose: Image-based extraction of biomarkers from diffusion- and perfusion-weighted MR imaging have shown high clinical utility in various neurological diseases. Recognizing pathological changes based on these biomarkers requires knowledge about the distribution of the normal range in different brain regions in healthy subjects. Although distribution of diffusion and perfusion metrics is well-documented for normal adults, this information cannot be directly applied to children who undergo significant brain structural and functional development. A few studies have analyzed cerebral blood flow (CBF) and diffusion metrics of normal children within limited age ranges[1,2]. However, no comprehensive data across all age spectrums exist in pediatric subjects that reflect age-dependent diffusion and perfusion values measured in the same subjects and at the same time. The aim of this study was to investigate age-dependent diffusion and perfusion patterns in normal children from birth up to age 18.

Material and Methods: 108 normal children from ages 0 month to 18 years, who obtained MRI at 3T, were selected from our database. These children were confirmed to be cognitively normal based on a thorough clinical chart review. Among others, each dataset consisted of a diffusion-weighted MRI (DWI) dataset (two b-weightings: b=0s/mm² and b=1000s/mm², TR=10000ms, TE=86.1ms, 90° flip angle) as well as a 3D pseudo-continuous arterial spin labeling (pCASL, TR=4674ms, TE=10.5ms, TI=1525ms, 111° flip angle) dataset containing information about the regional cerebral blood flow (CBF). In the first step, each DWI dataset acquired with strong diffusion weighting was registered to the corresponding T2-weighted DWI dataset (b=0s/mm²) using a rigid-body registration and mutual information (MI) as the cost function for registration. The registered b=1000 DWI dataset and the b=0 DWI dataset were then employed to calculate the corresponding apparent diffusion coefficient (ADC) map for each subject. In the following step, the pCASL dataset was also registered to the corresponding b=0 DWI dataset using a rigid-body transformation and optimization of the MI metric. Finally, the 152-MNI brain atlas was registered to each b=0 DWI dataset using a concatenated affine and non-linear spline transformation, which were both determined by using the MI metric within a multi-resolution registration framework. The resulting non-linear spatial deformation field was then used to warp the Harvard-Oxford subcortical brain regions – as defined in the MNI atlas space – to each b=0 DWI dataset by applying a nearest-neighbor interpolation. After registration of all datasets, the median ADC and CBF values were determined for each patient within the following gray matter brain structures: cerebral cortex, hippocampus, thalamus, caudate, putamen, and pallidum.

Results: The age-dependent distribution of normal ADC (blue) and CBF values (orange) for the selected gray matter brain structures in the 108 healthy pediatric subjects are displayed in fig. 1. The ADC values decrease with increasing age in all brain structures analyzed. The normal ADC values were approximately 10% higher in cerebral cortex and hippocampus compared to the deep gray matter regions. In comparison, the CBF values increase with age in all brain structures except for the pallidum, which was constant across age. The degree of CBF increase over age was similar in the caudate, thalamus and putamen. In comparison to these deep gray nuclei, a smaller degree of CBF increase was seen in the hippocampus and a larger degree of CBF increase in cerebral cortex.

Discussion and Conclusion: Our results show age-dependent diffusion and perfusion parameters and patterns of parametric change in children. These findings are a key information when applying diffusion and perfusion metrics to evaluate various neuropathological conditions of childhood, especially in the early childhood years. A more detailed statistical analysis will be performed to obtain more reliable conclusions from this database.

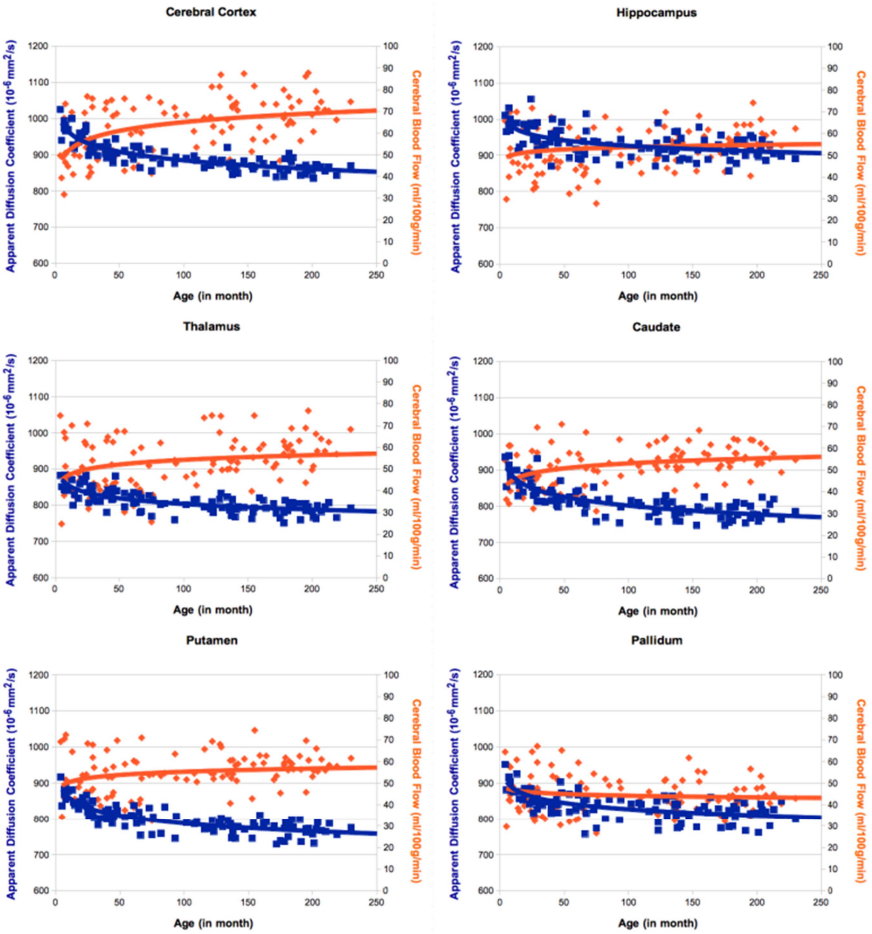

Fig. 1: Age-dependent ADC (blue) and CBF (orange) normal value and corresponding fits of logarithmic function

References:
1. Duncan et al. Regional Cerebral Blood Flow in Children From 3 to 5 Months of Age. Am J Neuroradiol. 2013
2. Engelbrecht et al. Diffusion-weighted MR imaging in the brain in children. Radiology. 2002; 222(2):410-8.

Acknowledgements: NIH (2R01 EB002711, 5R01 EB008706, 5R01 EB011654), the Center of Advanced MR Technology at Stanford (P41 RR009784), Lucas Foundation.