Diffusion Changes During Human Brain Maturation

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Purpose
The purpose of this study was to develop non-invasive quantitative methods to monitor the diffusion changes in maturing human brain.

Introduction
During human brain maturation various anatomical changes occur. The water content decreases, number of cells and number of neuronal connections change, the myelination continues (1). It would be important to quantify these changes so that developmentally delayed infants can be diagnosed early.

Since MR has a very good tissue contrast, it has been used extensively to monitor myelination changes in developing brain (2-5). Also, recently MR diffusion tensor imaging is used in newborns to assess white matter, quantitatively (6).

Diffusion of water in human brain is sensitive to the water content and tissue microstructure. So by monitoring the diffusion changes in the developing human brain microscopic information can be obtained using macroscopic imaging means.

In this preliminary work, we report age dependency of diffusion changes in normal patients.

Methods
15 patients less than 11 years old and 24 adults (21 to 69 years old) were imaged using a clinical whole body MR scanner (1.5 T GE Signa Echospeed). The clinical images were read normal. In addition to the standard clinical MR sequences, as part of the clinical protocol a diffusion-weighted echo planar multislice imaging sequence was used. Matrix of 128 by 128, FOV of 24 cm and slice thickness of 5mm were used. The diffusion-weighted images were collected in 3 orthogonal directions in addition to an image without diffusion weighting gradients. In some of the patients diffusion was measured in 4 more non-collinear directions in addition to the 3 orthogonal directions.

Diffusion maps were calculated from the diffusion-weighted images. Using the tensor components an orientationally invariant diffusion constant $D_\text{iso} = \text{Trace}/3 = (D_{xx} + D_{yy} + D_{zz})/3$ was calculated for each pixel. A C program was then used to calculate diffusion histograms (bin-width=0.02x10^{-2} cm^2/s) from the entire brain. The histograms were fitted to a double compartment model which allowed partial voluming between compartments. This model recognizes the brain tissue compartment and the high diffusion compartment consisting of CSF and non-brain tissue. For the brain tissue compartment, peak location (mean of the brain tissue compartment) and its distribution width ($\sigma$) were determined from the fitted data. The peak location was interpreted to be mean diffusion constant for the entire brain ($BD_\text{nu}$). We also measured the $D_\text{iso}$ values of the periventricular white matter and centrum semiovale by placing regions of interest (ROI) on the diffusion maps.

Results
Figure summarizes our mean diffusion constant measurements for the entire brain ($BD_\text{nu}$). The mean diffusion constant of the brain is high at birth and decreases quite rapidly in the first year of life. The rate of decrease slows down after this age. At the age of 11, the mean diffusion constant is still above (6%) adult normal value which is 0.75 x 10^{-2} cm^2/s.

The double exponential fit to the data gave:
$BD_\text{nu} = 0.18 \exp(-0.13 \text{age}) + 0.26 \exp(-2.6 \text{age}) + 0.75$
where age is in years and $BD_\text{nu}$ in $10^{-2}$ cm^2/s.

The region of interest measurements from different regions such as centrum semiovale and periventricular white matter also show similar age dependency (data not shown).

Discussion
Our results showed that the mean diffusion constant in human brain changes quite rapidly as the brain matures. The data can be fitted by a double exponential model suggesting at least 2 distinct processes are at work. First process which seems to be responsible in the first year is much faster that the second process which becomes dominant after age 1 and continues to early teens. In the adult population, the mean diffusion constant is fairly constant between age (21-69).

References