Impacts of Prematurity on Neonatal Deep Gray Matter Using Diffusion Basis Spectrum Imaging

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Background

MRI has been used to understand the impact of prematurity on brain development in the last 30 years. Diffusion tensor imaging (DTI) allows the characterization of brain microstructure. However, most studies have focused primarily on major fiber bundles. Yet, evidence showed very preterm infants at term equivalent age had risk of having reduced deep gray matter volumes compared to term controls (Boardman et al., 2006). Diffusion basis spectrum imaging (DBSI) model allows for a more comprehensive understanding of microstructural development in the brain by decomposing diffusion signals into fiber fraction, hindered diffusivity (extracellular), restricted diffusivity (intracellular) and water fraction. It has been applied on neonatal white matter injury (Isaacs et al., 2021) but not yet on neonatal deep gray matter.

Objective

Our goal is to characterize deep gray matter integrity in preterm infants by using DBSI to gain a deeper understanding of the complex processes that occur in the developing brain following prematurity. More specifically to: 1) Detect intracellular and extracellular fraction in preterm deep gray matter; 2) Assess potential differences with term controls.

Design/Methods

Two groups of infants were scanned on a 3T GE MRI scanner. Preterms born at 32.00 ± 1.49 weeks, scanned at 34.14 ± 1.19 weeks (G_1, $n = 15$) and at 40.18 ± 0.90 weeks (G_2, $n = 11$); Five term control infants scanned at 39.51 ± 1.38 weeks (G_3). Data was acquired with resolution $2 \times 2 \times 2mm^3$, 2 b0 and an array of 25 b values ($0 < b \leq 800s/mm^2$).

Data was processed by denoising, TOPUP distortion correction. The diffusion volumes were registered to the T2-weighted map (first b0 to T2w, then diffusion volumes to b0) nonlinearly. DTI metrics were then obtained by DIPY-DTI and fraction maps were extracted by the DBSI package (Garyfallidis et al., 2014; Wang et al., 2011). Also, templates for both 34 weeks and 40 weeks were built using DTI-TK. Regions of interest (ROI) were placed on the caudate nucleus, lentiform nucleus and thalamus using the color-coded FA template maps generated from DTI-TK (Zhang et al., 2006). ROIs were transformed back to original data space to mask interested metrics values combined with DTI and DBSI derivatives maps.

Statistics: comparisons (G1 vs G2, G2 vs G3) were done in each ROI by using masked metrics from DBSI and DTI. Mann-whiteney test ($p < 0.05$) was used for the statistics.

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Results

Preterm at term vs Term controls:
The caudate nucleus was the only structure to retain differences in preterms at term equivalent age with higher axial diffusivity (2.87% higher, $p = 0.01$) compared to term controls.

Preterm at 34 weeks vs Preterm at term equivalent age:
Diffusivity values (AD, RD, MD) extracted from DTI showed significant decrease (more than 11%) in all three ROIs with most significant changes in the caudate nucleus. DBSI model showed that water fraction in all three regions were dramatically decreasing (-82.78% ($p = 0.01$), -66.65% ($p = 0.004$) and -72.69% ($p = 0.003$) in caudate, lentiform and thalamus respectively). In the lentiform nucleus, extracellular diffusion fraction decreased significantly ($+219.4\%$, $p = 0.003$) and intracellular diffusion fraction decreased ($-15,73\%$, $p = 0.004$) significantly. This probably reveals that the lentiform nucleus experienced cell enlargement more than volume increase.

Conclusion

Our data revealed an increased vulnerability of the microstructural maturation of the caudate nucleus in a rather healthy preterm born at 32 weeks of gestational age. This resonates with data in preterm children born under 32 weeks of gestation found to have smaller caudate and putamen volumes when scanned at term equivalent age (Loh et al., 2017). These changes may have a profound impact as when persisting at age 7, a strong correlation was found with IQ Abernethy et al. (2004).

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Figures

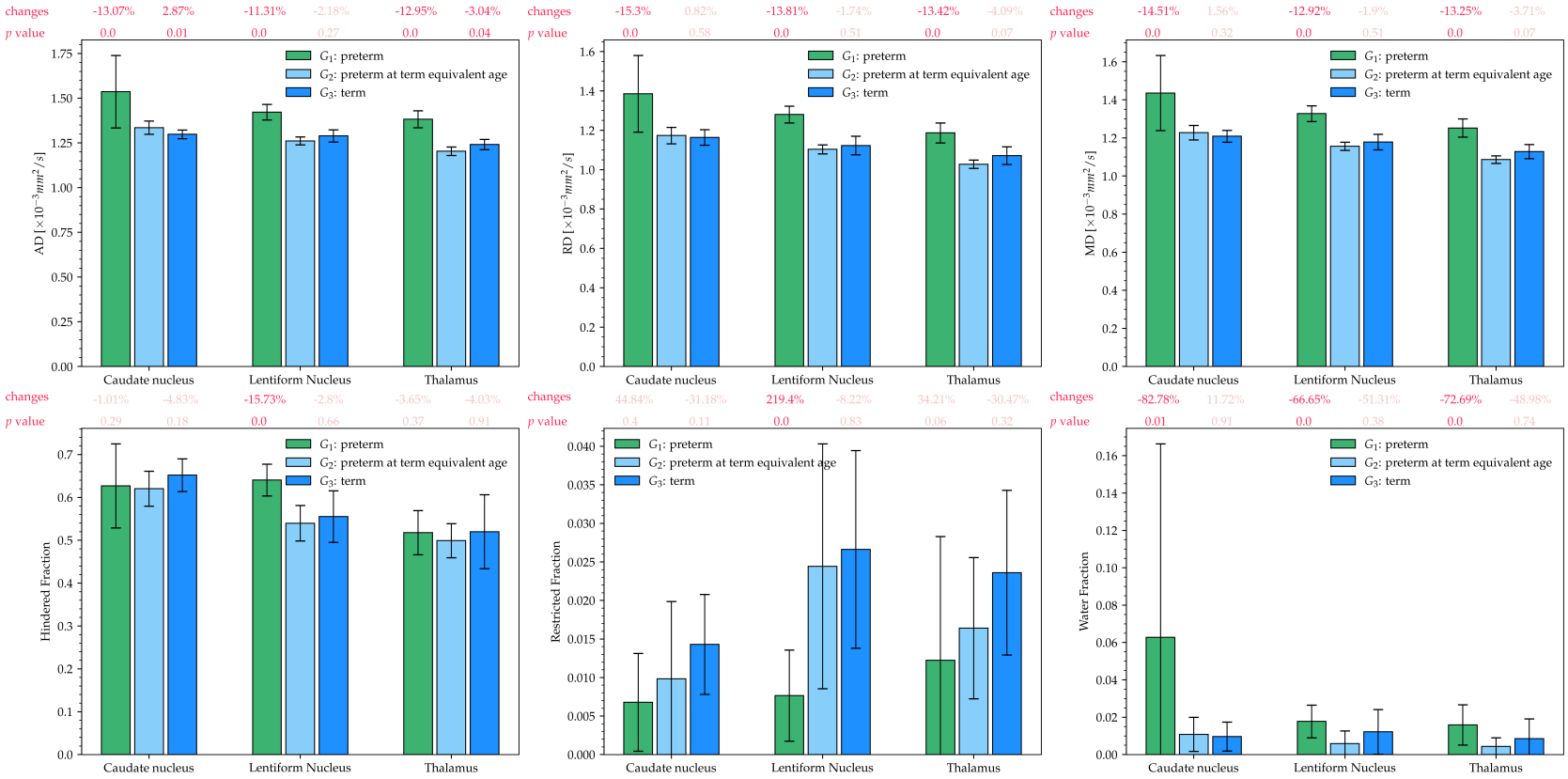

Figure 1: Bar plot of diffusion metric of two groups of preterm infant and term control. First row: DTI metrics; Second row: DBSI metrics. Group 1 (G_1): 15 preterm infants born at 32.00 ± 1.49 weeks, scanned at 34.14 ± 1.19 weeks; Group 2 (G_2): 11 preterm infants born at 32.30 ± 1.40 weeks, scanned at 40.18 ± 0.90 weeks; Group 3 (G_3): 5 term control infants (born at 39.11 ± 1.09 weeks, scanned at 39.51 ± 1.38 weeks). For the p values and changes, values were aligned as: G_2 vs G_1 G_3 vs G_2. Mann-Whitney tests with test strength $p < 0.05$ were used for statistics (red color for $p < 0.05$, pink color for $p \geq 0.05$). Abbreviation: DBSI=Diffusion basis spectrum imaging, DTI = Diffusion tensor imaging, AD=Axial diffusivity, RD=Radial diffusivity, MD=mean diffusivity.