Evaluation of neonatal brain white matter development by using diffusion basis spectrum imaging

Version: Final, Jan. 04, 2023

Erjun Zhang[1,2], Benjamin De Leener[1,2,4], Gregory A. Lodygensky[2,3]

[1]Institute of Biomedical Engineering, Polytechnique Montreal, Montreal, QC, Canada
[2]CHU Sainte-Justine Research Centre, Montreal, QC, Canada
[3]Department of Pharmacology and Physiology, University of Montreal, Montreal, QC, Canada
[4]Department of Computer Engineering and Software Engineering, Polytechnique Montreal, Montreal, QC, Canada

Background

Preterm infants are a major paediatric public health problem in decades (Ment and Vohr, 2008). The evaluation of preterm brain white matter is much needed. Diffusion tensor imaging (DTI) allows mapping and characterizing cerebral microarchitecture by detecting signal attenuation caused by water molecular movement. However, DTI only shows the overall effects of voxels, thus details in voxel are neglected. Recently, a new model DBSI was developed by decomposing the voxel diffusion weighted signal into the combination of fiber bundles, intracellular components, extracellular components as well as water components. To our knowledge, it has not been applied on preterm infants to do the white matter development analysis.

Objective

The purpose of this study was to characterize main white matter micro-architecture development in preterm by using DBSI. In more details: 1) Apply DBSI model on neonatal brain MRI; 2) Detect fiber fraction, intra-cellular and extra-cellular component fraction development in preterm neonatal brains; 3) Detect fiber fraction, intra-cellular and extra-cellular component fraction differences between term infant brains and preterm (at term-equivalent age) brains.

Methods

Three groups of infants were scanned by using *GE Discovery™ MR750* scanner. 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, term control): 5 term control infants (born at 39.11 ± 1.09 weeks, scanned at 39.51 ± 1.38 weeks). Diffusion-weighted MRI data was acquired with resolution $2 \times 2 \times 2mm^3$, TR/TE of $8s/120ms$ and 2 b_0 and 25 non-collinear diffusion volumes ($0 < b \leq 800s/mm^2$).

Data was preprocessed following these steps: denoising (Coupe et al., 2008), fsl-TOPUP (Andersson et al., 2003), registration. Then, DBSI package (Chiang et al., 2014; Wang et al., 2011) was used to process the brains. Optic radiation (OR), posterior limb of the internal capsule (PLIC), corpus callosum (CC), external capsule (EC) and anterior limb of the internal capsule (ALIC) were located on color-coded FA maps using small manual regions of interest (ROI).

To explore the white matter development of infants, comparisons (G_1 vs G_2, G_2 vs G_3) were done in each ROI by using each metrics from DTI and DBSI. Mann-whitney test with test strength < 0.05 was used for the statistics.

Results

Group 2 vs Group 3: DTI metric and DBSI fractions showed no significant changes in all ROIs (EC, ALIC, PLIC, OR, CC).

Group 1 vs Group 2: 1. In EC, PLIC, and CC, DBSI results showed drastic changes: significant fiber fraction increase (16.79%, 7.74% and 19.77%), significant extra-cellular (hindered) diffusion fraction decrease (-15.83%, -28.22% and -54.76%) and significant intra-cellular (restricted) diffusion fraction increase (487.22%, 154.90% and 87.64%).

Conference Pediatric Academic Societies (PAS 2023), Washington, USA.

DTI results showed moderate changes: significant RD decrease (-13.49%, -16.76% and -21.15%), significant MD decrease (-12.51%, -10.25% and -12.81%) and significant FA increase (17.16%, 23.34% and 35.63%), which is symilar with previously publication (Kersbergen et al., 2014). 2. In ALIC, significant changes were found in DBSI results (324.23% increased intra-cullular diffusion fraction), as well as in dti metrics (9.44% decreased AD, 10.69% decreased RD, 10.17% decreased MD). 3. Optic radiation (OR) show early maturation already at Group 1 infants, with no major changes in either DTI metrics and DBSI results.

Conclusion

Infants, from 34 weeks to 40 week age, experienced significant brain development (fiber fraction increase (mature), cell component increase, extra-cellular space decrease) in external capsule, posterior limb of the internal capsule and corpus callosum as well as early maturation in optic radiation. 32 weeks preterm infants managed to reach the same level of maturation in major white matter bundles comparing as term control infants. DBSI metrics, especially hindered fraction and restricted fraction, have the potential to show the development of neonatal brains.

References

Jesper L R Andersson, Stefan Skare, and John Ashburner. How to correct susceptibility distortions in spin-echo echo-planar images: application to diffusion tensor imaging. *Neuroimage*, 20(2):870–888, October 2003.

Chia-Wen Chiang, Yong Wang, Peng Sun, Tsen-Hsuan Lin, Kathryn Trinkaus, Anne H Cross, and Sheng-Kwei Song. Quantifying white matter tract diffusion parameters in the presence of increased extra-fiber cellularity and vasogenic edema. *Neuroimage*, 101:310–319, November 2014.

P Coupe, P Yger, S Prima, P Hellier, C Kervrann, and C Barillot. An optimized blockwise nonlocal means denoising filter for 3-D magnetic resonance images. *IEEE Trans. Med. Imaging*, 27(4):425–441, April 2008.

Karina J Kersbergen, Alexander Leemans, Floris Groenendaal, Niek E van der Aa, Max A Viergever, Linda S de Vries, and Manon J N L Benders. Microstructural brain development between 30 and 40 weeks corrected age in a longitudinal cohort of extremely preterm infants. *Neuroimage*, 103:214–224, December 2014.

Laura R Ment and Betty R Vohr. Preterm birth and the developing brain. *Lancet Neurol.*, 7(5):378–379, May 2008.

Yong Wang, Qing Wang, Justin P Haldar, Fang-Cheng Yeh, Mingqiang Xie, Peng Sun, Tsang-Wei Tu, Kathryn Trinkaus, Robyn S Klein, Anne H Cross, and Sheng-Kwei Song. Quantification of increased cellularity during inflammatory demyelination. *Brain*, 134(Pt 12):3590–3601, December 2011.

Figures

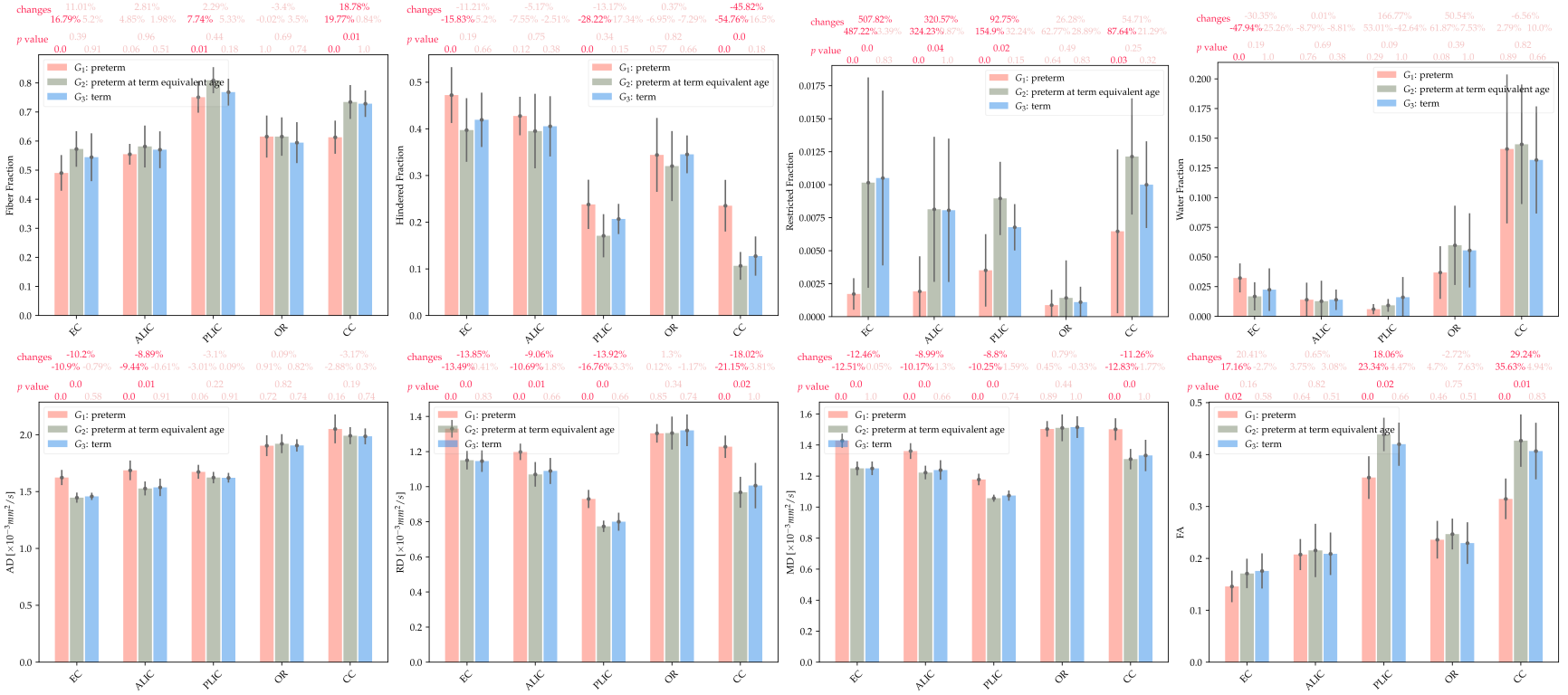

Figure 1: Results of DBSI fractions (first row) and DTI metrics (second row) of three infant groups. Group 1 (G_1): 15 preterm infants born at 32.00 ± 1.49 weeks, scanned at 34.14 ± 1.19 weeks; Group 2 (G_2): 11 preterm infants born at 32.30 ± 1.40 weeks, scanned at 40.18 ± 0.90 weeks; Group 3 (G_3): 5 term control infants (born at 39.11 ± 1.09 weeks, scanned at 39.51 ± 1.38 weeks). Abbreviation: Optic radiation=OR, posterior limb of the internal capsule=PLIC, corpus callosum=CC, external capsule=EC and anterior limb of the internal capsule=ALIC. For the p values and *changes*, values were aligned as $\begin{matrix} G_3 \textbf{ vs } G_1 \\ G_2 \textbf{ vs } G_1, \ G_3 \textbf{ vs } G_2 \end{matrix}$. Mann-whitney test with test strength < 0.05 were used for statistics (red color for $p < 0.05$, pink color for $p \geq 0.05$).

Reviewer Comments

Reviewer 1

Promising technical advancement for neonatal imaging. Surprised with no diff in pre-term v term, raises doubts on clinical utility.

Reviewer 2

New information. Not sure how relevant in clinical setting.

Reviewer 3

Despite some evidence, still need more clear information about what is inmportant for performing DBSI.

Reviewer 4

Solid abstract. Could be stronger if authors make a more clear case of how this would be clinically relevant.

Reviewer 5

N/A

Reviewer 6

Very interesting data., but the figure is almost impossible to interpret.