Probabilistic Neighbourhood Tractography in the Preterm Neonatal Brain

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Introduction:

Preterm birth is a leading cause of cognitive impairment in childhood and is associated with alterations in brain development. Diffusion MRI (dMRI) and tractography may provide insights into the cerebral changes that accompany preterm birth by supplying biomarkers of white matter microstructure in tract or fasciculi-of-interest (FOI).[1] This pilot work describes the first application of an automatic single seed point tractography-based segmentation method, probabilistic neighborhood tractography (PNT),[2,3] to study the developing brain.

Methods:

Twelve preterm infants born at a mean postmenstrual age (PMA) of 28 ± 2 weeks underwent a high resolution axial dMRI protocol at term equivalent age (mean PMA 40 ± 2 weeks) without sedation, with informed parental consent. The dMRI protocol was acquired using a MAGNETOM Verio 3 T clinical scanner (Siemens AG, Germany), and consisted of 11 T2- and 64 diffusion-weighted ($b = 750$ s/mm^2) single-shot spin-echo EPI volumes acquired with 2 mm isotropic voxels (256 × 256 mm field-of-view, 50 contiguous interleaved slices with 2 mm thickness). Eight FOI were identified using PNT from the dMRI data (http://www.tractor-mri.org.uk).[3] Tracts assessed were the genu and splenium of corpus callosum, cingulum cingulate gyri (CCG), corticospinal tract (CST), and inferior longitudinal (ILF) fasciculi. Using a neighborhood of seed voxels, the seed point that produced the best matching tract to the reference (MNI standard space) was determined using tract shape models determined from a group of normal volunteers aged 25–65 years. To reduce false positives and reduce noise-related fall-off in connection probability with distance from the seed point, pruning of streamlines that did not resemble the median path of the best match tract was employed.[3] Then, all best match tracts were visually assessed by an experienced rater and any subject with aberrant or truncated pathways that were not anatomically plausible representations of the FOI were excluded from further analysis. For anatomically acceptable tracts, the resulting tractography masks were applied to each subject's mean diffusivity ($\langle D \rangle$), fractional anisotropy (FA), axial (λ_{Ax}) and radial (λ_{Rad}) diffusivity volumes to provide tract-averaged measures of these biomarkers for the eight FOI. A model-based goodness-of-fit measure (R) was also calculated for each tract in each subject.[2,4] This measure of topological similarity generally has a negative value, and the more negative it is, the less good is the fit between the reference and best matching tract.

Results:

Figure 1 shows the tract segmentation across all 12 subjects for genu and splenium, indicating the close spatial correspondence of the segmented pathways for these two tracts. Visual assessment of the individual segmented tracts indicated that PNT provided anatomically acceptable representations of the FOI for the vast majority of pathways (92% over all subjects and tracts), with a minimum of 75% for right CCG. Values of $\langle D \rangle$ ranged from 1139 ± 70 for right CST to 1707 ± 209 μm^2/s for left ILF, while FA ranged from 0.19 ± 0.02 in left ILF to 0.31 ± 0.03 in splenium. Values of λ_{Ax} varied from 1512 ± 76 for right CST to 2061 ± 161 μm^2/s for splenium, while λ_{Rad} ranged from 952 ± 87 for right

CST to 1532 ± 200 μm^2/s for left ILF. Finally median (± IQR/2) values of *R* ranged from -3.68 ± 0.79 for genu to -47.26 ± 7.45 for left CST and are generally lower, i.e. showing less topological similarity to the reference tract, than those seen in the adult brain.[4]

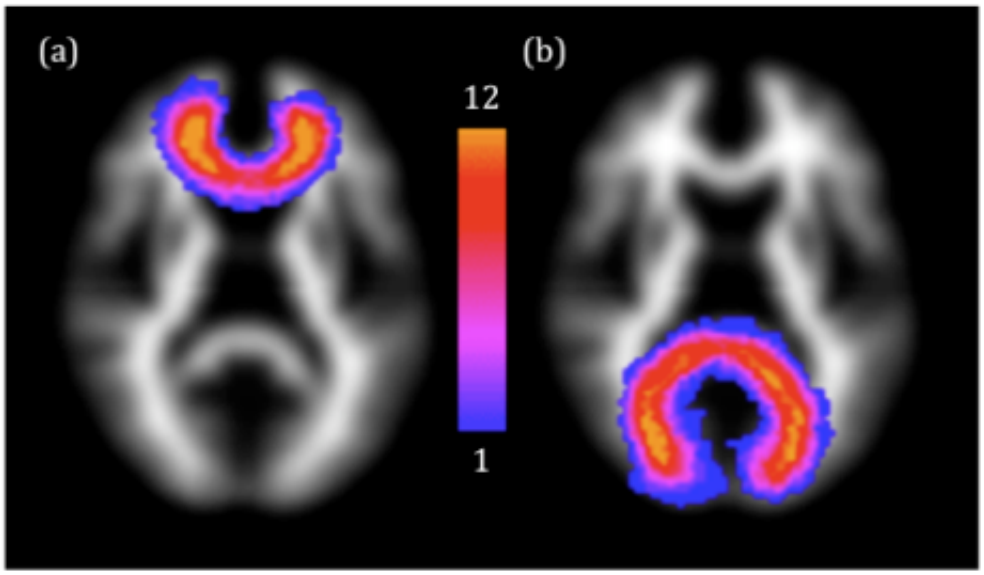

Figure 1. Group maps of (a) genu and (b) splenium generated by transforming the best match tract from each subject into MNI standard space and overlaying them as maximum intensity projections on an MNI white matter volume.

	Acceptable Tracts (%)	⟨D⟩ (μm²/s)	FA	λ_{Ax} (μm²/s)	λ_{Rad} (μm²/s)	*R*
Genu	100	1521 ± 80	0.27 ± 0.05	1973 ± 74	1296 ± 105	-3.68 ± 0.79
Splenium	100	1543 ± 128	0.31 ± 0.03	2061 ± 161	1284 ± 117	-22.18 ± 4.77
Left CCG	92	1466 ± 236	0.21 ± 0.03	1779 ± 257	1310 ± 227	-11.49 ± 6.21
Right CCG	75	1359 ± 56	0.20 ± 0.02	1643 ± 74	1216 ± 50	-25.54 ± 11.29
Left CST	92	1187 ± 73	0.29 ± 0.03	1562 ± 85	999 ± 75	-47.26 ± 7.45
Right CST	92	1139 ± 70	0.30 ± 0.05	1512 ± 76	952 ± 87	-30.85 ± 6.34
Left ILF	83	1707 ± 209	0.19 ± 0.02	2058 ± 229	1532 ± 200	-11.90 ± 2.37
Right ILF	103	1559 ± 273	0.22 ± 0.03	1924 ± 290	1376 ± 267	-21.00 ± 5.29

Table 1: Mean (± SD) values for tract-averaged ⟨D⟩, FA, λ_{Ax} and λ_{Rad} for the eight fasciculi-of-interest. Also shown are median (± IQR/2) values for the absolute goodness-of-fit of the best match tract to the reference (*R*) and the number of tracts that were considered anatomically plausible representations of each fasciculus.

Conclusions:

We have shown that quantitative measurements of dMRI biomarkers can be made in a number of FOI in preterm brain from dMRI data using single seed point PNT. These values demonstrate the increased diffusivities and reduced FA indicative of white matter development at neonatal stage compared with the adult brain.

Lifespan Development:

Normal Brain Development: Fetus to Adolescence

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