Mapping the preterm newborn brain: a diffusion tensor study of the cerebellum's early neural connections

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Target audience Researchers and clinicians using neonatal magnetic resonance imaging to investigate early brain development.

Purpose Despite the small size of the cerebellum, the white matter pathways connecting it to the cerebrum are some of the largest in the brain, with increasing evidence that they subserve important motor and cognitive functions. Investigating the early development of these cerebello-cerebral pathways is critical for our understanding of their structure-function relationships. This knowledge, combined with longitudinal analyses, may aid in the identification of early *in vivo* biomarkers suitable for assessing the developmental trajectory of cerebellar white matter pathways. Diffusion tensor imaging (DTI) and white matter tractography of preterm newborns is a unique non-invasive way of investigating early cerebellar development at a time when axonal connections are still being formed. Tractography applications in the neonatal cerebellum, however, are scarce, and existing work has been limited by small sample sizes. Moreover, methodological issues associated with traditional deterministic approaches and single fibre models have led to an inability to resolve the contralateral cerebral projections of these tracts in the neonate brain. The goal of the current study was to use DTI and a probabilistic tractography method to reconstruct the corticopontocerebellar (CPC) and dentatothalamic (DTT) tracts in a large neonate dataset.

Methods ***Participants*** Three groups of participants were examined in this study: very preterm infants born <30 weeks' gestational age (GA) (n=40), moderate and late preterm infants born 32–36 weeks' GA (n=40), and healthy term-born infants born ≥37 weeks' GA (n=40). All participants were scanned at approximately term-equivalent age (TEA 38.43–44.14 weeks' GA). ***MRI acquisition*** Participants were scanned on a 3T Siemens Magnetom Trio Tim scanner (syngo MR B17) during natural sleep, at the Royal Children's Hospital, Melbourne, Australia. Structural images were acquired using a T_2 RESTORE sequence with the following parameters: 1 mm thick axial slices, flip angle = 120°, TR = 8910 ms, TE = 152 ms, FOV = 192×192 mm, matrix = 192×192, in-plane resolution 1×1 mm^2. Diffusion-weighted data were acquired with an echo planar imaging (EPI) sequence with the following parameters: TR = 20400 ms, TE = 120 ms, FOV = 173×173 mm, matrix size= 144×144, voxel size= 1.2 mm^3, 45 non-collinear diffusion-weighted gradient directions with b values ranging from 100 to 1200 s/mm^2, 3 non diffusion-weighted images b= 0 s/mm^2. ***Pre-processing*** An image pre-processing pipeline was developed and optimised for the neonate brain using ExploreDTI version 4.8.2[1] and involved correction for motion and eddy current induced distortions, and correction for EPI-induced geometrical distortions.[2] The diffusion tensor was estimated using DTIFIT from the FMRIB Software Library (FSL),[3] employing the weighted linear least squares tensor model. ***Probabilistic tractography*** FSL's BEDPOSTX and PROBTRACKX were used to fit a multi-fibre model and perform probabilistic tractography of the CPC (Fig. 1) and DTT tracts (Fig. 2). A two region-of-interest (ROI) approach was used based on methods previously described in the adult literature.[4,5]

Results

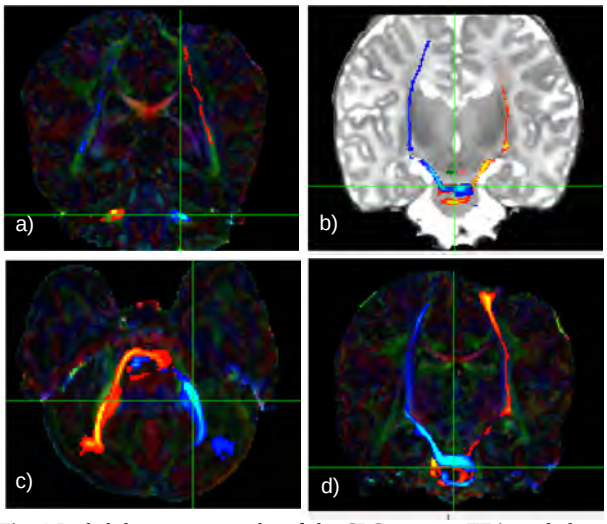

Fig. 1 Probabilistic tractography of the CPC tracts at TEA, including their contralateral cerebral projections. The cerebellum receives input from the contralateral cerebral hemisphere through the CPC tract via the middle cerebellar peduncles (crosshair in *a)* & *c)*). *a)* & *d*) Coronal plane, directionally encoded colour fractional anisotropy (FA) map, *b*) Coronal plane, T_2, *c*) Axial plane, directionally encoded colour FA map. Red = right CPC tract; blue= left CPC tract.

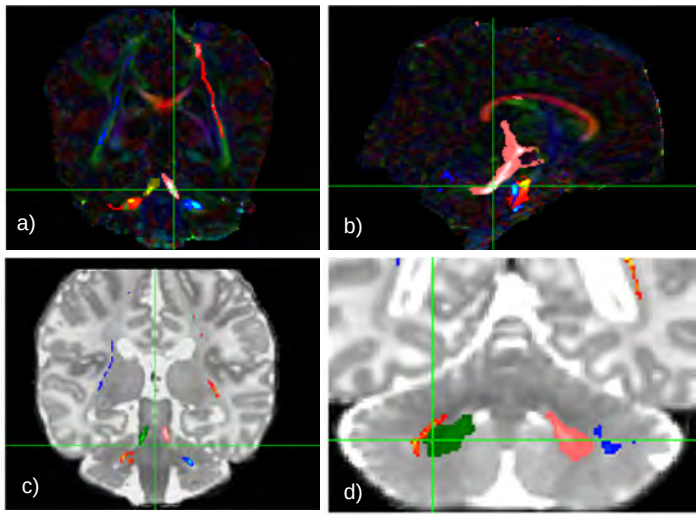

Fig. 2 Probabilistic tractography of the DTT tracts at TEA in relation to the CPC tracts. The DTT tract originates within the deep cerebellar nuclei (crosshair in *d)*) and send output via the superior cerebellar peduncles (crosshair in *a)* & *b*)) through to the thalamus and cerebral cortex. The DTT tract was consistently reconstructed up to the level of the decussation of the superior cerebellar peduncle. *a*) Coronal plane, directionally encoded colour FA map, *b*) Sagittal plane, directionally encoded colour FA map, *c*) & *d)* Coronal plane, T_2. Green = right DTT tract; pink= left DTT tract.

Discussion & Conclusion The probabilistic tractography approach used in the current study enabled the reconstruction of the full extent of the CPC tract, with clear delineation of the left and right tracts and their contralateral cerebral projections, which to date has not been reported in the neonate brain. The DTT tract was consistently reconstructed to the level of the decussation of the superior cerebellar peduncle. Cerebellar white matter tractography in the preterm brain as described here will facilitate further research into the microstructural organisation of these tracts during this critical period of brain development.

References

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