Using probabilistic tractography to detect decreases in thalamo-cortical connectivity following preterm birth

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Background

Thalamo-cortical connections are established during the third trimester of human development1 and almost all cortical regions receive some form of thalamic input2. Due to the timing of key developmental processes, disruption of the thalamo-cortical system is thought to represent a major component of preterm brain injury3,4 and may be a neural substrate for the later cognitive deficits prevalent in this population5,6. Tractography is an in vivo technique for inferring connective pathways through the brain based on diffusion MRI. Here, a novel pipeline for describing thalamo-cortical connectivity in neonates is proposed and used to test the hypothesis that thalamo-cortical connectivity is significantly diminished in preterm infants at term-equivalent age in comparison to term-born controls.

Methods

47 preterm infants (median gestational age at birth = 28⁻¹³ weeks; range: 23⁻¹⁴ – 34⁻⁶) underwent 3-Tesla 32-direction DTI acquisition at term-equivalent age. Additionally T2-weighted (FSE) anatomical pseudo-volumes were acquired. 18 healthy term-born infants (median gestational age at birth = 39⁻¹² weeks; range: 36⁻¹⁰ – 41⁻⁸), recruited as part of ongoing studies, were included as controls. Cortical segmentation was performed on individual T2-weighted images using age-specific tissue probability priors6 and cortical masks were parcellated using Fast Poisson Disk Sampling7 to produce a set of around 500 randomly distributed cortical labels per hemisphere with similar volume and even spacing. Using a modified probabilistic tractography algorithm8, mean anisotropy along the length of each tract connecting a manually-defined thalamic mask and each cortical label was calculated. A per-voxel estimate of mean anisotropy was derived from the distribution of values obtained by repeating cortical parcellation and tractography a total of 25 times. This provided average thalamo-cortical connectivity maps that were aligned to regions with significantly lower connectivity to the thalamus in preterm infants.

Results

Figure 1 shows cortical regions with significantly lower connectivity to the thalamus, as measured by mean anisotropy calculated along the length of connective tracts, in preterm infants at term-equivalent age compared to term-born controls (FDR-corrected for multiple comparison, p < 0.001). This bilateral pattern includes the lateral frontal cortex, medial supplementary motor areas, the superior temporal gyrus and the medial occipital lobe.

Conclusion

Using a novel processing pipeline, we have shown that thalamo-cortical connectivity is significantly diminished in preterm infants compared to term-born controls. This study represents the first time that thalamo-cortical connectivity has been comprehensively mapped in a neonatal population, and the tractographic framework described represents a novel method for analysing system connectivity that can be readily applied to other populations and to investigate other neural systems.

References