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

Gareth Ball[1], James P Boardman[1,2], Paul Aljabar[3], Anand Pandit[1], Tomoki Arichi[1,4], Nazakat Merchant[1,4], Daniel Rueckert[3], A David Edwards[1,4], and Serena J Counsell[1]
[1]Centre for the Developing Brain, Imaging Sciences Department, MRC Clinical Sciences Centre, Hammersmith Hospital, Imperial College London, London, United Kingdom, [2]Simpson Centre for Reproductive Health, Royal Infirmary of Edinburgh, Edinburgh, United Kingdom, [3]Biomedical Image Analysis Group, Department of Computing, Imperial College London, London, United Kingdom, [4]Division of Neonatology, Imperial College London Healthcare NHS Trust, London, United Kingdom

Background

Thalamo-cortical connections are established during the third trimester of human development[1] and almost all cortical regions receive some form of thalamic input[2]. Due to the timing of key developmental processes, disruption of the thalamo-cortical system is thought to represent a major component of preterm brain injury[1,3] and may be a neural substrate for the later cognitive deficits prevalent in this population[4,5]. 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^{+3} weeks; range: 23^{+4} – 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^{+2} weeks; range: 36^{+0} – 41^{+6}), recruited as part of ongoing studies, were included as controls. Cortical segmentation was performed on individual T2-weighted images using age-specific tissue probability priors[6] and cortical masks were parcellated using Fast Poisson Disk Sampling[7] to produce a set of around 500 randomly distributed cortical labels per hemisphere with similar volume and even spacing. Using a modified probabilistic tractography algorithm[8], 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 a population-based anatomical template using nonlinear registration (IRTK; www.doc.ic.ac.uk/~dr/software/) and smoothed with a Gaussian kernel (FHWM = 8 mm) before cross-subject analysis of mean anisotropy was performed using FSL's Randomise (v2.5; www.fmrib.ox.ac.uk/fsl/).

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.

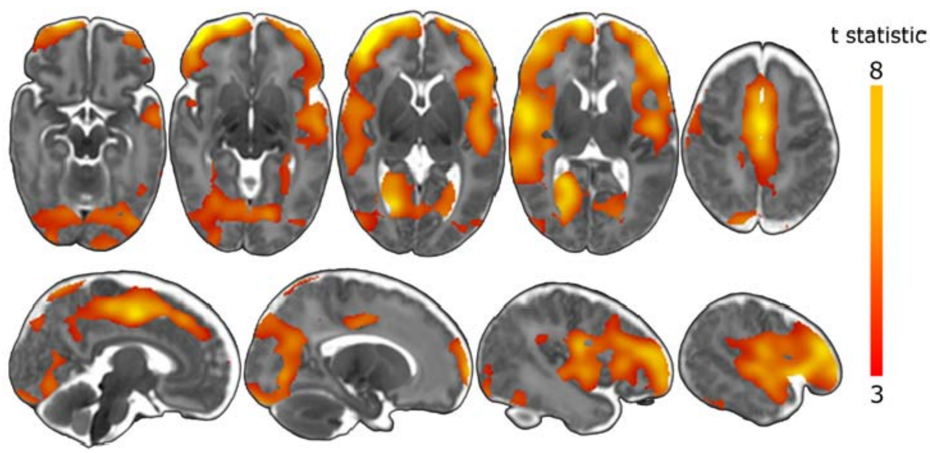

Figure 1. Cortical regions with significantly lower connectivity to the thalamus in preterm infants.

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

1. Kostovic and Judas. *Acta Paediatr.* **99**, 1119-1127 (2010).
2. Molnar et al. *Cereb Cortex* **13**, 661-669 (2003).
3. Volpe *Lancet Neurol.* **8**, 110-124 (2009).
4. Inder et al. *Pediatrics* **115**, 286-294 (2005).
5. Boardman et al. *Neuroimage* **52**, 409-414 (2010).
6. Kuklisova-Murgasova et al. *Neuroimage* **54**, 2750-2763 (2011).
7. Bridson. In *ACM SIGGRAPH*. ACM Press, **22** (2007)
8. Robinson et al. *Neuroimage* **50**, 910-919 (2010).