Exploring the development of the human structural connectome in preterm neonates

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Introduction:

Using diffusion tractography, long-distance connections in the brain can be traced non-invasively and used to construct complex networks at a millimetre-range resoution[1]. Little is known about the evolution of structural connectivity during the preterm period but due to the timing of key developmental processes it is likely that disruption of the connective pathways of the brain will impact negatively on the outcome of prematurely born infants[2,3]. The aim of this study is to map the developing human connectome during the early neonatal period. To achieve this we use an atlas-free approach to comprehensively map whole-brain, structural connectivity in eight preterm neonates at two timepoints: during the early preterm period and at term-equivalent age.

Methods:

Research Ethics Committee approval was granted for this study. MRI was acquired at two timepoints in 8 infants born preterm. Median gestational age (GA) at birth was 26^{+4} weeks (range: 25^{+2}–30^{+3}), median age at the first scan was 30^{+6}w (28^{+1}–30^{+0}) and at the second scan was 41^{+2} (39^{+3}–43^{+0}). 32-direction DTI was acquired with *b* value = 750 s/mm^2 alongside high resolution T2-weighted (FSE) images using a 3 Tesla Philips system. Cortical segmentation and parcellation was performed as described previously[4]. Briefly, cortical voxels were segmented from individual T2-weighted images using age-appropriate anatomical priors and cortical hemispheres were parcellated into around 250 randomly-distributed labels of similar volume. Probabilistic tractography[5,6] was performed between every cortical label in order to construct a dense connectivity matrix. After symmetrising and binarising, nodal degree was calculated, normalised by the total number of nodes and mapped back onto the corresponding cortical label. Random parcellation and whole-brain tractography was repeated 100 times, each time producing a map of nodal degree. These maps were averaged to produce a voxelwise map of structural connectivity for each infant at each timepoint. Connectivity maps were aligned to a population-based template using nonlinear registration before paired analysis of degree was performed with FSL's Randomise (v2.9; www.fmrib.ox.ac.uk/fsl/).

Results:

Figure 1 shows whole-brain maps of average, normalised node degree for a single infant (GA = 25^{+3}w) at the first (A, top row; age at scan = 29w) and second scan (A, bottom row; age at scan = 41^{+6}w). Degree of connectivity varied across the cortex at both timepoints, with higher degree – indicating greater cortico-cortical connectivity – in anterior frontal, medial and parietal regions, and lower degree in occipital and temporal cortex.

Paired comparison of node degree in 8 preterm infants showed a significant increase ($p<0.05$, FWE-corrected after TFCE) in connectivity across the cortex between first and second scans (Figure 1, panel B).

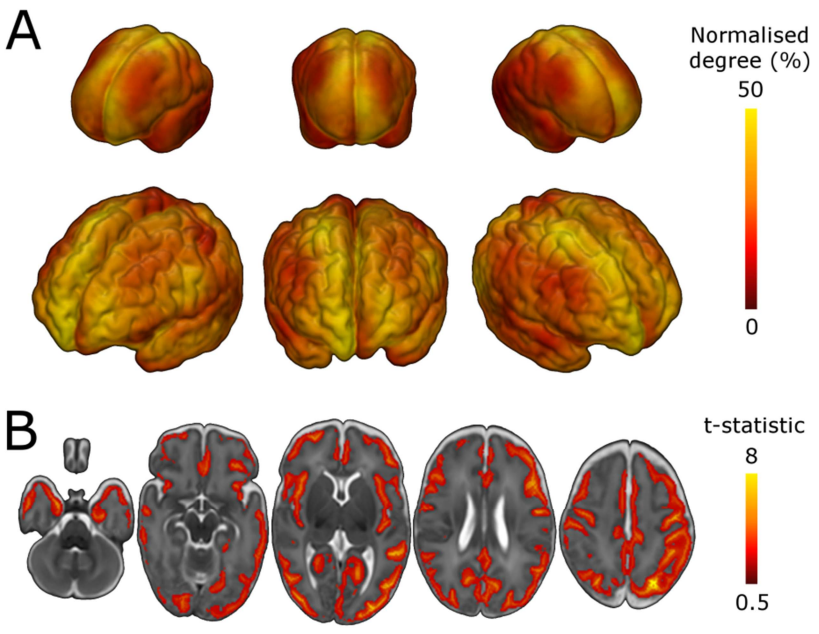

Figure 1: Mapping structural connectivity in the preterm brain

Conclusions:

This study represents the first time whole-brain structural connectivity has been comprehensively mapped during the early neonatal period in the preterm brain. By extending the framework to incorporate more complex network features this method can provide insights into human brain development.

References

1. Sporns et al. *PLoS Comput.Biol.* **1**, 42 (2005).
2. Kostovic and Jovanov-Milosevic. *Semin.Fetal.Neonatal Med.* **11**, 415–422 (2006).
3. Volpe. *Lancet Neurol.* **8**, 110–124 (2009).
4. Ball et al. *Cortex.* in press (2012).
5. Behrens et al. *Neuroimage.* **34**, 144–155 (2007).
6. Robinson et al. *Neuroimage.* **50** 910–919 (2010).