The effect of preterm birth on cortico-cortical connectivity: the preterm connectome

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Target audience: Researchers and clinicians with an interest in structural connectivity alterations following preterm birth

Purpose: Preterm birth is associated with a high prevalence of adverse neurodevelopmental outcome. Non-invasive techniques which can probe the neural correlates underpinning these deficits are required. This can be achieved by measuring the structural network of connections within the preterm infant's brain using diffusion MRI and tractography.

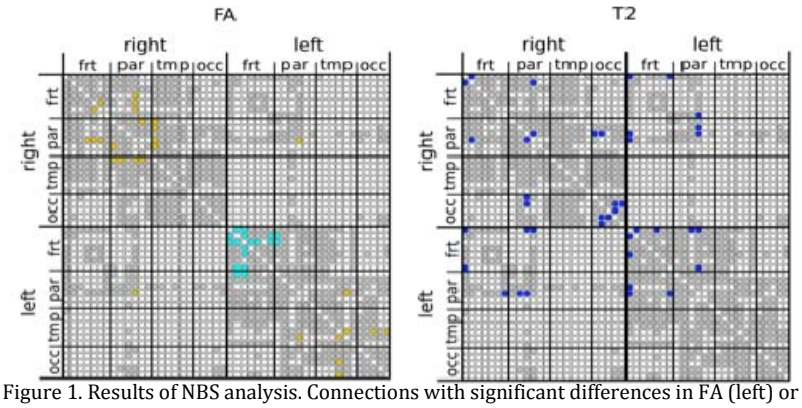

Figure 1. Results of NBS analysis. Connections with significant differences in FA (left) or T2 (right) are highlighted.

Methods: Diffusion MRI and T2 relaxometry were performed on 18 preterm (born at less than 32 weeks gestational age) and 9 term infants at term equivalent age. FA maps and fibre orientation probability distribution functions[1] were calculated after careful preprocessing. Probabilistic whole-brain tractography was performed with FSL. T2 maps were co-registered with diffusion images via the track-density image. FA and T2 values were sampled at every streamline step. Streamlines were transformed to JHU neonatal space[2] using transformation obtained from the symmetric diffeomorphic registration of the native FA map to the JHU neonatal FA template. Twenty-four cortical regions per hemisphere were extracted from the JHU neonatal template and used as target regions. Connections containing less than 50 streamlines in any term born neonate were excluded from further analysis. FA and T2 within every connection were calculated. Connections of altered FA or T2 were identified using the network based statistic[3].

Results: A total of 433 connections were assessed. FA was significantly reduced in 23, and T2 significantly increased in 20 connections in preterm infants, following correction for multiple comparison (Figure 1). Only a single connection showed FA as well as T2 alterations. Cortical networks associated with affected connections mainly involved left frontal and motor cortical areas, with no striking pattern in the right hemisphere (Figure 2).

Discussion: Changes in FA indicate ongoing organization and premyelination, while changes in T2 indicate ongoing changes in brain water content and premyelination. The cortical regions identified as connected to pathways of altered FA or T2 are associated with higher cognitive function, working memory, language production, verbal comprehension, executive function and motor function. Deficits in these functions are often observed in children and adults born preterm. Previous reports, which investigate cortical thickness in children and adolescents born preterm, also identified reduced cortical thickness in similar areas.

Conclusion: This study demonstrates that alterations in the structural connectome can be identified in infants at term equivalent age, and that incorporation of non-diffusion measures such as T2 in the connectome framework provides complementary information for the assessment of brain development.

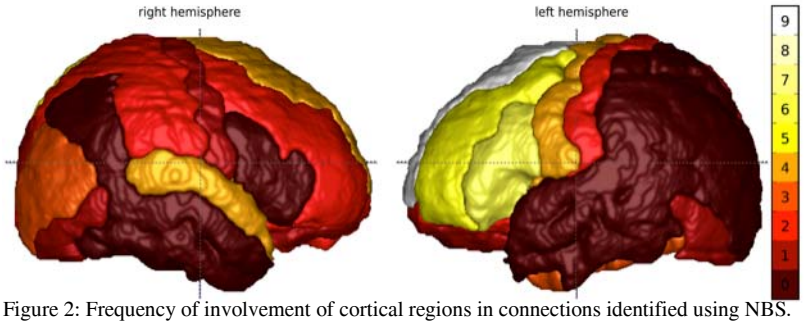

Figure 2: Frequency of involvement of cortical regions in connections identified using NBS.

References: 1. Behrens TE, Berg HJ, Jbabdi S, Rushworth MF, and Woolrich MW. Probabilistic diffusion tractography with multiple fibre orientations: What can we gain? *Neuroimage.* 2007;34(1):144-55. **2.** Oishi K, Mori S, Donohue PK, et al. Multi-contrast human neonatal brain atlas: application to normal neonate development analysis. *Neuroimage.* 2011;56(1):8-20. **3.** Zalesky A, Fornito A, and Bullmore ET. Network-based statistic: identifying differences in brain networks. *Neuroimage.* 2010;53(4):1197-207.