Minimum Spanning Trees reveal the development of functional connectivity in the preterm brain

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Introduction

The developing brain displays a rich pattern of structural connectivity by 30 weeks gestation that is significantly altered by preterm birth[1]. Functional networks develop rapidly during this period, reaching a state similar to that in adults by term-equivalent age[2]. However, it is not clear when properties such as interhemispheric connectivity or modular organisation emerge during this period. Minimum spanning trees (MST) have recently been introduced as a density-independent method for network comparison, capturing important topological properties of complex genetic, transport and neuronal networks[3]. A subset of the MST – the infinite percolation cluster (IPC) - has been shown to isolate the most central paths in transport networks[4] and may provide a method to identify to the most important links for efficient information flow across networks. We hypothesise that the MST and IPC can characterise functional network development during the time leading up to normal birth.

Methods

122 preterm infants (median age at birth = 30^{+2} weeks^{+days}) were scanned once between 30 and 48 weeks postmenstrual age. 3T T2-weighted MRI (TR: 8670msec; TE: 160msec; voxel size: 0.86×0.86×1mm) and resting-state functional MRI (TR: 1500msec; TE: 45msec; voxel size: 2.5×2.5×4mm; 256 volumes) were acquired. Cortical masks, segmented from each T2 image, were parcellated into 200 regions of roughly equal size, symmetrically across both hemispheres. After motion correction and ICA-based denoising[5], mean fMRI timeseries were extracted from each region and sparse partial correlation matrices estimated using graphical lasso[6]. The MST and IPC were then extracted from each network[4,7].

Results

Across the whole network, edge strength increased with age ($r=0.53$, $p<0.01$) and connectivity was stronger between nodes in the same hemisphere ($t=23.8$, $p< 0.01$). Within the MST, connectivity increased with age but inter- and intrahemispheric edge strengths were balanced ($t=1.5$, $p=0.12$). MST leaf fraction (the fraction of isolated nodes) decreased with age ($r=0.46$, $p<0.01$). Connectivity in the MST and IPC was strongest between regions within the same cerebral lobe, regardless of hemisphere (Figure 1). When compared to a Euclidean MST constructed by minimising the wiring distance between all nodes, edge strength and centrality were significantly higher in the empirical MST ($t=22.1$, $p<0.01$; $t=63$, $p<0.01$). Edge centrality within the IPC was significantly higher than both the remaining MST edges, and the rest of the network ($t=35.5$, $p<0.01$; $t=175.3$, $p<0.01$). Local connectivity dominated the IPC, with highly central, interhemispheric IPC edges also prominent between frontal and parietal cortex, and basal ganglia. The number of interhemispheric edges in the IPC did not increase with age ($r=0.1$, $p=0.27$).

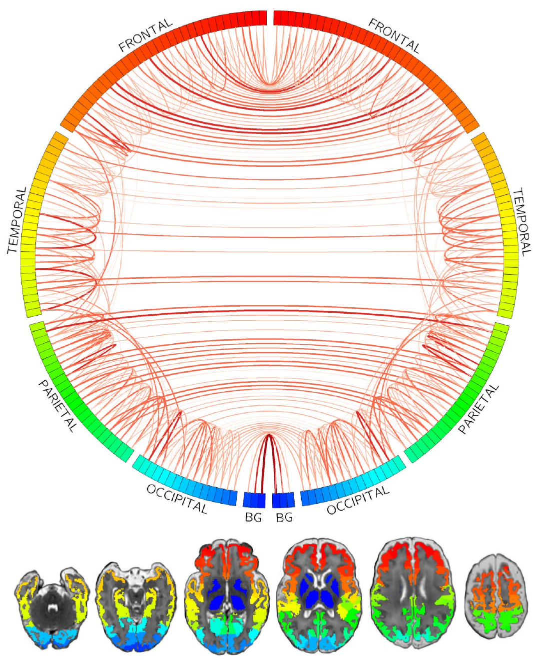

Figure 1: The functional core in the developing preterm brain. Edges are shown that form part of the IPC in at least 10% of subjects. Edges are weighted by centrality. Regions of interest are ordered according to their position in the brain as illustrated (bottom row)

Conclusions

Our analysis reveals a functional core of highly-central edges present in the neonatal brain that allows for more efficient information transfer than one based solely on minimising Euclidean connection length. The IPC core reveals locally-dominant functional connectivity with strong interhemispheric connectivity between homologous cortical regions present from an early gestational age.

References

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