Altered structural connectivity in preterm children: Network-based statistical analysis

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Target audience: Basic research scientists, Neuroscientists, Clinicians, Pediatricians.

Purpose

The impact of prematurity on structural connectivity is not yet understood. The aims of this study were to compare network measures of structural connectivity between very preterm (VP) and full-term children, and to determine if network measures were correlated with gestational age in the VP group.

Methods

Participants and scanning: Twenty five full-term [37 to 42 weeks' gestational age (GA) and ≥2500 g birthweight,12 male and 13 female, mean age: 7.54±0.21 years] and 107 VP 7 year-olds (GA <30 weeks and/or birthweight <1250 g, 46 male and 61 female; mean age 7.54 ± 0.25 years) underwent T_1 weighted (TR = 1900ms, TE = 2.27ms, flip angle = 9°, FOV = 210 x 210mm, matrix= 256 x 256, 0.85mm sagittal slices,), and single-shot echo-planar diffusion weighted imaging (TR = 7600 ms; TE = 110 ms; flip angle = 90°, FOV = 240 × 240 mm; matrix = 104 × 104; 2.3 mm axial slices; 45 diffusion directions with b = 3000 s/mm^2; 6 baseline images with b = 0 s/mm^2) on a 3T Siemens magneto Trio scanner.

Network measures: White matter fiber network analysis based on graph theory metrics was utilized to investigate full-term and VP brains. For tractography, cerebral white matter and cerebral cortex labels from FreeSurfer parcellations of T1 weighted images were used as the seed and termination masks, respectively. A connectivity matrix was constructed by performing probabilistic constrained spherical deconvolution crossing fiber model based tractography using mrtrix[1] and normalizing streamline counts using streamline length and average size of end regions[2]. Connectivity matrices were thresholded to produce a density of 30%. Graph metrics were computed using the python networkx package (http://networkx.github.io). Normalized characteristic path lengths and clustering coefficients (λ and γ) scores were computed using randomized graphs preserving degree distribution, generated using 5000 double-edge swaps, and 10 repeats.

Statistical analyses: Two-sample *t*-tests were performed to compare network measures between groups, controlling for intra-cranial volume (ICV) and gender. These network properties were also regressed against GA in the VP group, controlling for ICV and gender.

Results

There were no significant differences in age and gender between the groups. The ICV of VP subjects was significantly smaller than full-term subjects (p=0.0001). Network characteristics were different between the full-term and VP groups, where VP children trended toward increased γ (p=0.120), increased λ (p=0.056), and decreased global efficiency (p=0.113); and had significantly increased local efficiency (p=0.026). There were no robust differences between groups for small-worldness (p=0.206) (Figure 1). As GA increased, λ (p=0.05) and local efficiency (p=0.021) decreased, while global efficiency increased (p=0.036).

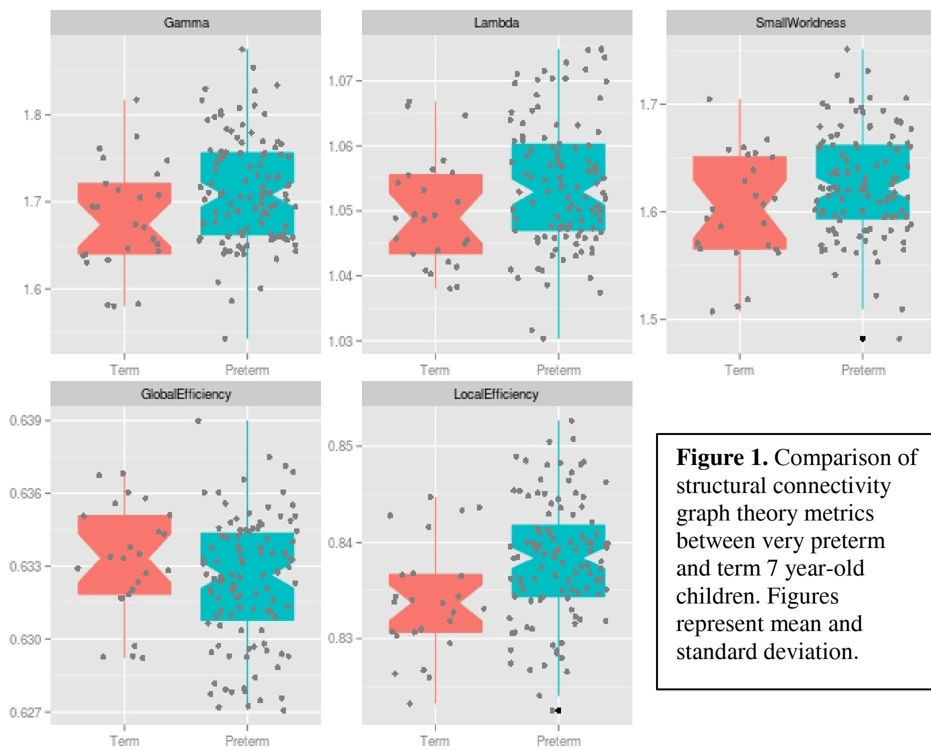

Figure 1. Comparison of structural connectivity graph theory metrics between very preterm and term 7 year-old children. Figures represent mean and standard deviation.

Discussion and Conclusion

Results indicated that the brains of VP children had altered network topography compared with full-term controls. Specifically, VP brains had higher local efficiency of information transfer than full-term brains. VP brains also trended towards reduced global efficiency, meaning connections between nodes of the network required more steps, and therefore higher cost. VP brains trended towards higher γ, meaning the minimum number of connections required to link nodes of the network was higher; as well as higher λ, reflecting better local efficiency of information transfer in a network. These findings are consistent with Hagmann et al. (2010) who showed that increasing integration and deceasing segregation of structural connectivity occurs during development, promoting increased global efficiency, and may be related to the white matter maturation[3]. Together our findings suggest that the VP brain has a less integrated and more segregated brain than full-term 7 year olds. This may contribute to the poor neurodevelopmental outcomes that are common in very VP children compared with controls.

References

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