Assessment of structural connectivity in congenital hemiplegia: The connectome in unilateral Cerebral Palsy

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Target audience: Researchers and clinicians with an interest in structural connectivity in children with cerebral palsy

Purpose: Cerebral Palsy (CP) is a group of non-progressive disorders with impaired motor function that is caused by a static brain lesion occurring early in development. Prediction of outcome from T1 or T2-weighted images is difficult. Diffusion MRI has been used to study white matter microstructure in pathways likely to be impacted by CP. The purpose of this study was to identify pathways with altered connectivity in children with unilateral CP from the network of connections.

Methods: 24 children with unilateral CP (12 left, 12 right) and 15 typically developing children, aged 5 – 16 years, were scanned at 3T. High-resolution structural MPRAGE and 64-direction HARDI data (b = 3000 s/mm^2) were acquired. Structural images were processed using FreeSurfer, parcellating the cortex into 34 cortical regions per hemisphere, as well as the thalamus, cerebellum and brain stem (below the level of the cerebellar peduncle). HARDI data were preprocessed to identify and reduce head motion, cardiac pulsation and image distortions. Fractional anisotropy (FA) and Mean Diffusivity (MD) were calculated using the tensor model. Fibre orientation distributions for tractography were estimated using constrained spherical deconvolution with MRtrix. One million streamlines were generated, seeding randomly over the entire brain volume. Structural and diffusion images were co-registered using rigid-body registration. Connections between each pair of regions were extracted from the whole brain tractogram, and median FA and MD within the connection were calculated. Connections containing fewer than 50 streamlines were excluded from further analysis. Connection with altered diffusion were identified from the connectome using the network based statistic[1] (NBS), employing a one-tailed t-test with 5000 permutations.

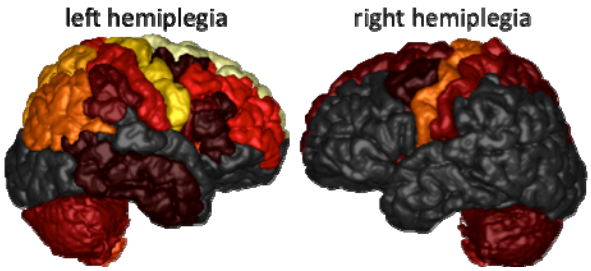

Figure 2: Frequency of identified cortical regions. Shown is only the lateral view of ipsi-lesional hemisphere for both groups.

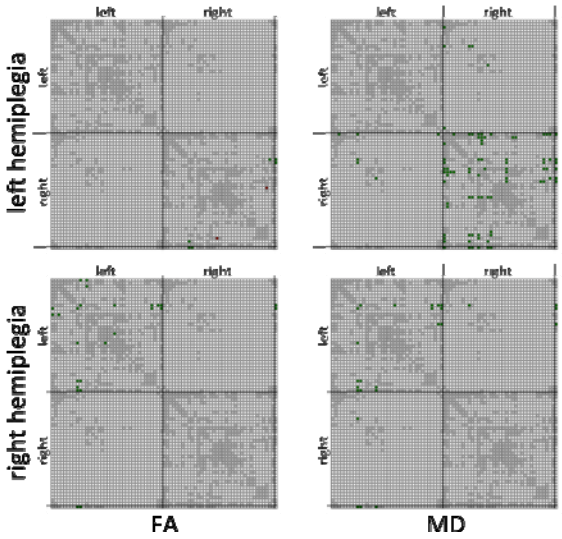

Figure 1: results of NBS analysis

Results: FA was significantly reduced in 4 pathways, and MD increased in 47 pathways for children with left hemiplegia. For children with right hemiplegia, FA was significantly decreased in 13 pathways, and MD increased in 13 pathways. For right hemiplegia, 9 pathways showed simultaneously increased FA and decreased MD, while for left hemiplegia only 3 pathways showed simultaneously increased FA and decreased MD. Results of the NBS analysis are shown in Figure 1. In both groups, only pathways in the ipsilesional hemisphere, as well as interhemispheric connections were identified. Sixteens pathways were significantly altered for both participant groups, including ipsilesional projection and association pathways, as well as the interhemispheric precentral pathway (Table 1). The frequency with which any region was identified with a pathway of altered diffusion is shown in Figure 2. We found a more widespread cortical involvement in children with left hemiplegia compared to children with right hemiplegia. Frontal and parietal regions were less frequently identified in children with right hemiplegia.

ipsilesional intrahemispheric		
precentral	-	brain stem
postcentral	-	brain stem
paracentral	-	brain stem
precentral	-	thalamus
postcentral	-	thalamus
paracentral	-	thalamus
precentral	-	cerebellum
postcentral	-	cerebellum
precentral	-	posterior cingulate
paracentral	-	posterior cingulate
superior frontal	-	paracentral
superior frontal	-	superior parietal
rostral middle frontal	-	superior parietal
interhemispheric		
precentral	-	precentral

Table 1: pathways identified consistently for left and right hemiplegia

Discussion: A number of pathways were identified consistently across both participant groups (Table 1); however, a number of pathways were identified only in children with left hemiplegia. Interestingly, FA and MD analysis revealed alterations in identical connections in children with right hemiplegia, while in children with left hemiplegia MD analysis showed significantly more connections than FA analysis. This finding indicates that, in our cohort, lesions in the right hemisphere (i.e. left hemiplegia) lead to different alterations in connectivity (i.e. more widespread involvement and alterations predominantly in MD) than lesions in the left hemisphere (i.e. right hemiplegia). Future research will investigate the influence of lesion type and severity of impairments on structural connectivity.

Conclusion: Pathways of altered diffusion in children with CP can be identified using connectome analysis, extending previous research employing diffusion MRI in CP which focused mainly on the cortico-spinal tract. Pathways identified using this approach can be subjected to more detailed analysis, including correlations with functional scores or the effects of interventions.

References: 1. Zalesky A, Fornito A, and Bullmore ET. Network-based statistic: identifying differences in brain networks. *Neuroimage.* 2010;53(4):1197-207.