The impact of extreme prematurity on motor tract development in adolescence

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Background: Extremely preterm (EPT) birth (<28 weeks of gestational age) and extreme low birth weight (<1000 g) are associated with higher rates of lifelong motor impairments than in term children, with educational and social implications. MRI techniques which assess the microstructural organisation of the motor tracts may explain the underlying neuropathology associated with the motor impairment in those born extremely preterm. The aims of this study were to 1) compare corticospinal tract volume and diffusion measures between the EPT and term adolescents, 2) identify perinatal factors associated with corticospinal tract measures in the EPT cohort and 3) determine relationships between corticospinal tract microstructural measures and motor impairment within the EPT cohort.

Method: 133 term controls and 189 EPT adolescents were scanned at 18 years of age with a Siemens Trio 3T MRI scanner using a 32 channel head coil. b1000 diffusion images (TR= 8800ms, TE= 110ms, FOV= 240 x 240mm, Matrix= 96 x 96, 2.5mm^3 isotropic voxels, b-value 1= 0s/mm^2, b-value 2= 1000s/mm^2, 25 gradient directions) and b3000 diffusion images (TR=8100ms, TE=110ms, FOV= 240 x 240mm, Matrix= 96 x 96, 2.5mm^3 isotropic voxels, b-value 1= 0s/mm^2, b-value 2= 3000s/mm^2, 45 gradient directions) were acquired. Probabilistic tractography using constrained spherical deconvolution was achieved by identifying three seed points within the posterior limb of the internal capsule, cerebellar peduncles and pontine nuclei. Tract volume, fractional anisotropy, mean, axial and radial diffusivity were computed for the corticospinal tracts within the left and right superior, middle and inferior regions. Tract measures were associated with perinatal factors and motor impairment. Motor impairment was defined as a diagnosis of cerebral palsy and/or a score below the 5th percentile for the Movement Assessment Battery for Children.

Results: Extremely preterm infants had decreased corticospinal tract volume in the left and right inferior regions, as well as increased axial, mean and radial diffusivity in the superior regions (Table 1). The presence of neonatal brain injury (cystic periventricular leukomalacia and/or stage III/IV intraventricular hemorrhage) was independently related to decreased fractional anisotropy and increased radial diffusivity in the extremely pre-term cohort. Motor impairment was related to a reduced tract volume in the right medial region (p=0.001).

Table 1: Left and right inferior corticospinal tract measures for extremely preterm and full term adolescents

	Left				Right			
	EPT, mean(SD)	FT, mean(SD)	Mean Difference (95% CI)	P value	EPT, mean(SD)	FT, mean(SD)	Mean Difference (95% CI)	P value
Inf TV	2.79 (0.70)	3.18 (0.97)	−0.38 (−0.57, −0.20)	<0.0005	2.75 (0.73)	3.20 (0.95)	−0.44 (−0.63, −0.26)	<0.0005
Sup AD	1.11 (0.08)	1.09 (0.05)	0.02 (0.01, 0.04)	0.003	1.11 (0.08)	1.09 (0.05)	0.02 (0.01, 0.04)	0.002
Sup RD	0.62 (0.07)	0.60 (0.06)	0.02 (0.00, 0.03)	0.02	0.61 (0.06)	0.59 (0.05)	0.02 (0.01, 0.03)	0.003
Sup MD	0.78 (0.08)	0.76 (0.05)	0.02 (0.00, 0.03)	0.03	0.77 (0.07)	0.75 (0.05)	0.02 (0.00, 0.03)	0.008

EPT= Extremely preterm, FT= Full term, Inf= Inferior, Sup= Superior, TV= Total volume (cc), FA= Fractional anisotropy, MD= Mean diffusivity (x10^{-3} mm^2/s), AD= Axial diffusivity (x10^{-3} mm^2/s), RD= Radial diffusivity (x10^{-3} mm^2/s), SD= Standard deviation, CI= Confidence interval

Conclusions: This study shows that diffusion measures in the corticospinal tract are altered in extreme preterm adolescents and may reflect delayed corticospinal tract development. Neonatal brain injury appears to have significant consequences for the corticospinal tract which persist into adolescence. Altered corticospinal tract development is associated with impaired motor outcomes in extreme prematurity.