

Integrity of callosal motor pathways correlates with motor-related function in term-equivalent neonates

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Introduction: Preterm birth carries an increased risk of impaired motor function. Early interventional neurorehabilitation therapies which target such impairment are now being developed. The development of non-invasive neuroimaging techniques, which can accurately assess injury to motor pathways and can be used to monitor brain reorganization over time, would be highly informative for such interventions. We have applied diffusion tractography to identify interhemispheric motor pathways in preterm and term-born neonates, scanned at term equivalent age and correlated summary measures of the integrity of these white matter pathways (*i.e.* fractional anisotropy [FA] and mean diffusivity [MD]) with motor function scores from a standard clinical assessment.

Methods: Four term born neonates (1 male) and nine very preterm infants (5 male, mean gestational age at birth: 31⁶ weeks; mean postmenstrual age at scan 42⁶ weeks) were scanned using a 3T scanner. Infants were scanned unsedated during natural sleep, using an MR compatible incubator with dedicated neonatal head coil. The imaging protocol included a diffusion imaging sequence ($b = 1000 \text{ s/mm}^2$, 30 directions, resolution 1.75x1.75 mm, 2 mm slice thickness). Data from one preterm infant were excluded due to extensive head motion artefacts. Data pre-processing included correction for head movement, susceptibility distortion correction, intensity inhomogeneity correction and rejection of outlier voxels caused by motion. FA maps were generated and non-linearly registered to the JHU neonatal atlas template [1]. Probabilistic whole brain tractography was performed using MRtrix in diffusion space. The generated streamlines were transformed to JHU space and terminated when attempting to cross the midline outside the corpus callosum. Bilateral masks of precentral and postcentral gyrus were extracted from the JHU neonatal atlas and used as tractography waypoint regions to extract homologous connections. Mean FA and MD were calculated after weighting each voxel according to the number of streamlines traversing it, both on the midsagittal plane and for the entire tract volume. Infants were assessed with the Dubowitz Neonatal Neurological Assessment [2] by a neonatologist. A motor-focussed subscore from the Dubowitz assessment was calculated by summing the scores for the following items of this assessment: Posture and Tone, Tone Patterns, and Reflexes. Clinical assessments were performed on the same day as MRI in all but two infants. Correlations between diffusion measures and clinical scores were assessed using Spearman's rho.

Results: Figure 1 shows the delineated interhemispheric precentral and postcentral connections for one representative neonate. Connections were successfully delineated in all infants. Results of the correlation analysis between summary diffusion metrics and motor scores are given in Table 1. Tract FA measures were positively correlated with motor scores, while tract MD measures correlated negatively with motor score (Figure 2). Interestingly, no significant correlations were found between motor scores and either midline FA or MD measures and motor score.

Discussion: Using diffusion tractography, interhemispheric connections can be delineated in a fully automated fashion in the neonate and preterm brain at term equivalent age, and can be used to study the integrity of associated white matter, either on the mid-sagittal slice or throughout the entire pathway. Importantly, connections are derived using

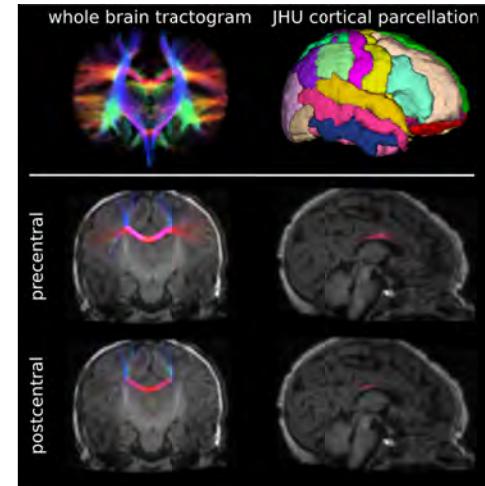


Figure 1: Whole brain tractography was used in conjunction with target ROIs obtained from the JHU cortical parcellation (top panel) to delineate interhemispheric pre- and post-central connections (bottom panel). Summary diffusion metrics were calculated for the entire tract volume (left) and for the midsagittal plane (right).

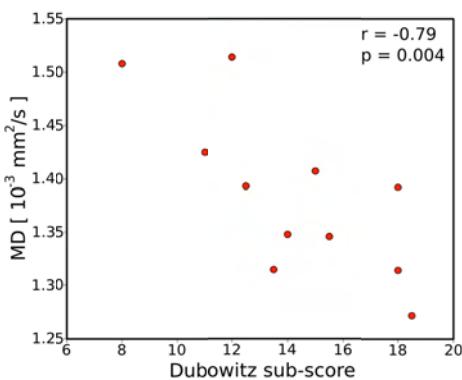


Figure 2: Scatterplot showing the correlation between precentral tract MD and motor score

anatomically defined cortical target regions rather than geometric partitions of the CC on the midline, thereby providing more accurate information. As expected, better motor function was associated with relatively higher FA and lower MD values, which are both believed to indicate increased white matter integrity. Interestingly, correlations with motor scores were only found for diffusion metrics computed across the entire tract, and not when only the midsagittal slice was evaluated. These findings highlight the importance of using tractography to identify tract-specific white matter. The approach presented here may be used to inform early interventions such as neurorehabilitation strategies in neonates.

References: [1] Oishi et al., 2011. Neuroimage 56: 8-20. [2] Dubowitz et al., 1998. J Pediatr 133(3): 406-416

	precentral	postcentral
tract FA	$r = 0.64 (p = 0.035)$	$r = 0.64 (p = 0.035)$
tract MD	$r = -0.79 (p = 0.004)$	$r = -0.68 (p = 0.023)$

Table 1: Correlations between diffusion measures and motor score