Corpus Callosum Development in the Preterm Infant: A DTI Study

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Introduction: Very preterm (PT) infants (<30 weeks' gestational age, or <1250 g at birth) are surviving in increasing numbers. The PT infant brain is vulnerable to damage, which often leads to adverse neurodevelopmental outcomes.1 PT birth has been shown to result in altered brain structure, with reduced cerebral tissue volumes. The most common cause of such alterations is white matter injury,2 therefore detailed examination of WM is warranted. Diffusion MRI provides insight into the structure of white matter tracts and connectivity. The Corpus Callosum (CC) is the largest white matter tract and is important for interhemispheric communication of sensory, motor and higher-order information. CC deficits have been previously implicated in delayed motor functioning3 and reduced IQ.4

Aims: To investigate the differences in CC development and inter-hemispheric connectivity between PT & full term (FT) infants using structural & diffusion MRI, and to determine perinatal causes and functional consequences of changes to the PT CC.

Methods: 114 PT and 24 healthy FT infants were scanned in a 1.5 T General Electric MRI scanner at term equivalent (38 - 42 weeks) without sedation. Whole brain structural 3-D T1 spoiled gradient recalled images were acquired (1.2mm coronal; flip angle 45°;TR 35ms; TE 9ms; FOV 21 x 15cm2; matrix 256 x 192). Diffusion images were acquired utilizing the line scan protocol (2 baselines, b=5, b=700s/mm2; 6 gradient directions, in-plane resolution 0.86mm, axial slices 4-6mm). T1 weighted scans were oriented along the AC-PC line, and the CC was traced on the mid-sagittal slice (Fig 1a). The mean of the six diffusion images was registered to the T1image, and the transformation matrix applied to the diffusivity/anisotropy images (Fig 1b). Probabilistic tractography was initiated from the CC region of interest (ROI) using the FSL diffusion toolbox. The mean diffusivity (MD), fractional anisotropy (FA), parallel (λ1), and perpendicular ((λ2+ λ3)/2) diffusivity measures were obtained within the CC ROI and the white matter fibre tracts. Inter-hemispheric connectivity (volume of the thresholded fibre tracts) was also calculated. To measure the regional diffusivity along the CC, a skeleton was made through the midline of the CC (Fig 1c), and 60 points with a radius of 5 voxels (excluding those outside CC ROI) were sampled along the skeleton. A range of perinatal variables were collected and the Bayley Scales of Infant Development (BSID-II) was administered at 2 years corrected age.

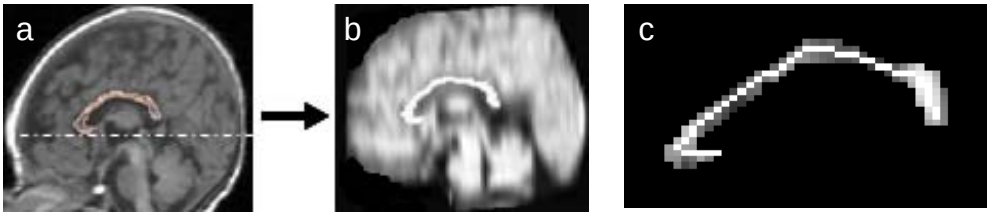

Figure 1: a) CC traced on mid-sagittal slice of T1. b) CC overlaid on mean diffusivity image registered to T1. c) CC skeleton overlaid on FA image (within the CC mask)

Results: Within the CC ROI, MD was significantly higher in PT CCs (p=0.025), indicating more water movement within the CC. Whereas, the FA was significantly lower in PT infants (p=0.01) (Fig 2a), indicating reduced integrity of WM fibers. The parallel diffusivity (λ1) was not significantly different between PT and FT infants (p=0.7), indicating no difference in axonal integrity. However, perpendicular diffusivity values were significantly larger in PT infants (p<0.02) which may be due to disruption or delay in myelination of PT CC fibers. The volume of tracts obtained from the CC ROI seed mask was reduced for PT infants (p=0.004), indicating fewer connections between the CC and other brain regions (Fig 2b). The MD & λ1 within tracts were significantly larger for PT infants (p<0.0005), but the FA and perpendicular diffusivity within tracts were not significantly lower (p>0.1).

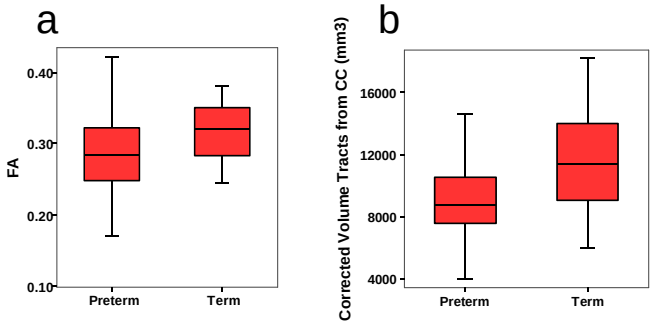

Figure 2: a) FA within the CC of PT and FT infants. b) Connectivity, measured as the volume of voxels into which 50 or more tracts entered from CC for PT and FT infants

For each infant, the values along the skeleton image differed significantly from one another for all diffusivity and anisotropy values (p<0.0005), indicating that the regions of the CC develop differently. Comparing FT and PT infants, the distribution of FA, sampled along the skeleton was significantly different (p=0.019). Remaining measures (MD, λ1, λ2&3) were not significantly different. T-tests comparing FA at each point along the Skeleton between FT and PT infants showed a significant difference in regions corresponding to the posterior part of the rostral body and anterior mid-body of the CC, which includes tracts terminating in the premotor, supplementary motor and motor regions of the cortex. The perinatal factors contributors to these reductions in white matter integrity within the PT CCs included brain injury (WMI and IVH), as well as patent ductus arteriosus and necrotizing enterocolitis. FA within the CC was significantly correlated to cognitive development at 2 years of age, even after correction for WMI (p=0.04). FA was also correlated with motor development at 2 years, after correction for WMI (p=0.02).

Conclusions: PT infants have altered CC structure and connectivity at term equivalent compared with FT infants, which may reflect delayed development. Previous studies have found that PT children and adolescents have smaller and thinner CCs.4 Other diffusion analyses have shown that the integrity of white matter fibres in the CC of PT infants is compromised.5 This study related abnormal CC development to brain injury, cognitive and motor development, implying that the current findings may have functional significance. We found the main region of difference between PT and FT infants CC fibres were those leading to motor areas. This may provide insight into the etiology of motor dysfunction common to PT children.

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