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. The therefore detailed examination of WM is warranted. Diffusion MRI provides insights 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 = 700ms/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.

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=0.002) 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 significantly larger for PT infants (p<0.0005), but the FA and perpendicular diffusivity within tracts were not significantly lower (p>0.1).

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. 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 insights into the etiology of motor dysfunction common to PT children.