

DTI of the Inter-hemispheric Connectivities in Neonates with Transposition of the Great Arteries Undergoing Cardiopulmonary Bypass Surgery.

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Introduction: The basic structure of the corpus callosum is completed by 18–20 weeks' gestation, but continues to increase in size over the third trimester [1]. It grows dramatically from anterior to posterior over the first 2 postnatal years [2] while preoligodendrocytes are thought to appear at the extremities e.g the genu (GCC) and splenium (SCC) [3]. Little is known on the characterization and the development of this structure around time of birth for full-term neonates with d-transposition of the great arteries (d-TGA). The aims of this study were to investigate post-surgical WM microstructural development in the inter-hemispheric brain connectivity in neonates with d-TGA following cardiopulmonary bypass surgery (CPB) and compare it to age matched healthy neonates.

Methods: Fifteen patients with d-TGA underwent both pre and post surgical DTI exams. Post-conceptional age ranged from 37 weeks to 41 weeks, with mean value of 39 weeks (± 1). Pre-surgical MRI (Pre) was carried out around 8 days (± 6) after birth. The post-surgical MRI (Post) was performed about 21 days (± 8) following the 1st exam. Ten healthy term neonates were recruited and served as control group (HC). The institutional ethical committee approved this study and informed consent was obtained from their parents. The DTI sequence was performed on 3T scanner using 35 gradient directions with a b-value of 700 s/mm². Two observers manually delineated the GCC and SCC on direction color encoded maps over at least 3 adjacent slices and measured the parallel diffusion (E_1), perpendicular diffusion (E_{23}), ADC, and FA. The between-groups statistical comparison (pre-surgery, post-surgery, healthy-controls) was carried out separately for each structure with a post-hoc repeated measures with multiple analysis of covariance using post-conceptional age at MRI as covariate.

Results: General linear model analysis revealed significant differences in E_{23} (GCC: $p = 0.01$; SCC: $p = 0.026$), ADC (GCC: $p = 0.002$; SCC: $p = 0.05$) and FA (GCC: $p = 0.006$; SCC: $p = 0.021$). Post-hoc follow up analysis between the HC and the pre-surgery group in the GCC (Fig 1) demonstrated significant lower E_{23} ($p = 0.013$), higher ADC ($p = 0.0012$) and lower FA ($p = 0.039$). In the SCC, the pre-surgical group had a significantly lower FA ($p=0.033$) compared to HC and all other indices were not significantly different. With regard of the post-surgical group, the GCC had a significantly lower E_{23} ($p = 0.013$), higher ADC ($p=0.012$) and lower FA ($p=0.039$) when compared to the HC (Figure 1). In the SCC we did not measure any significant difference between these 2 groups. Post-surgery vs pre-surgery analysis demonstrated abnormal increase in both E_{23} and ADC with a simultaneous decrease in FA in both the GCC and SCC despite the 20 days average time that separated the 2 exams.

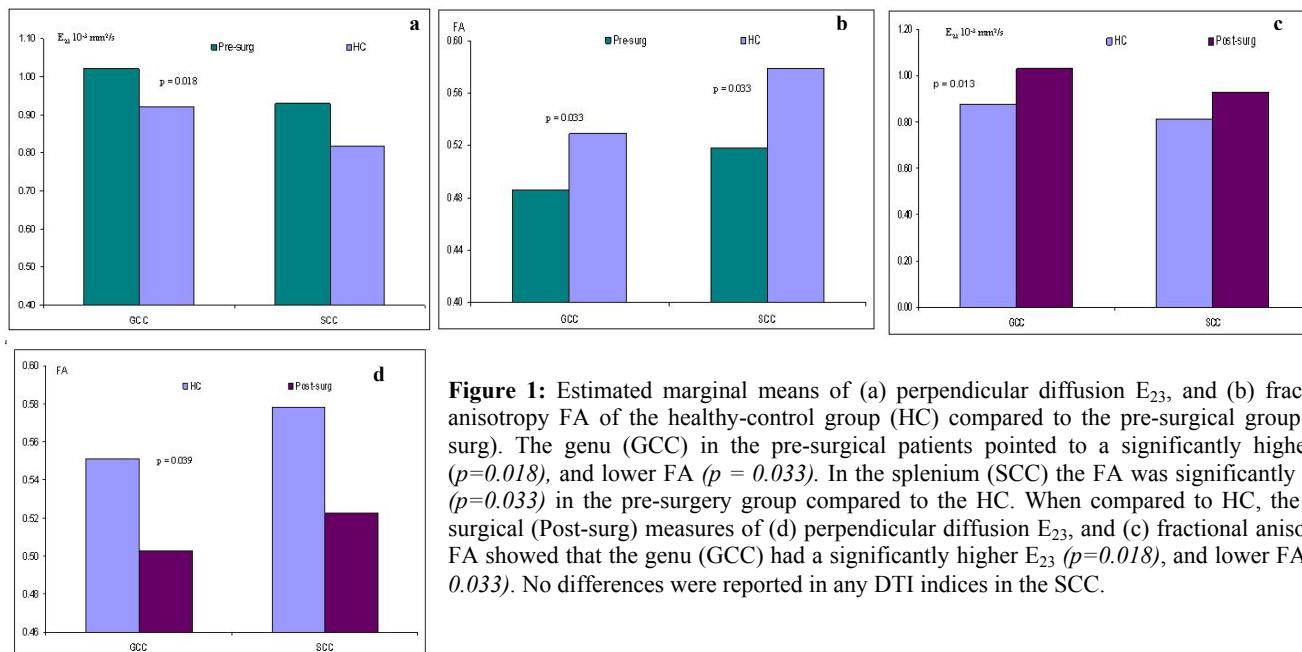


Figure 1: Estimated marginal means of (a) perpendicular diffusion E_{23} , and (b) fractional anisotropy FA of the healthy-control group (HC) compared to the pre-surgical group (pre-surg). The genu (GCC) in the pre-surgical patients pointed to a significantly higher E_{23} ($p=0.018$), and lower FA ($p = 0.033$). In the splenium (SCC) the FA was significantly lower ($p=0.033$) in the pre-surgery group compared to the HC. When compared to HC, the post-surgical (Post-surg) measures of (d) perpendicular diffusion E_{23} , and (c) fractional anisotropy FA showed that the genu (GCC) had a significantly higher E_{23} ($p=0.018$), and lower FA ($p = 0.033$). No differences were reported in any DTI indices in the SCC.

Discussion: We found disruption in the microstructural organization of the genu WM as reflected by higher E_{23} in patients with d-TGA compared to HC. Modifications of the intracellular or extracellular spaces, as well as the abnormalities contributed by astrocytic activation may influence the perpendicular component of water diffusivity. The disruption of myelin sheath has been found to increase perpendicular diffusion without affecting parallel diffusion [4,5]. Furthermore, we observed an increase in both ADC and E_{23} in GCC of d-TGA patients before and after surgery suggestive of delayed maturation of the anterior callosal WM in these patients compared to HC neonates. Together all these differences in the GCC rather than the SCC of neonates with d-TGA indicated that frontal WM microstructures were more immature than that of HC neonates and it is likely that this was an ongoing process that started at the fetal level and not affected by the surgical procedure.

References: [1] Malinger and Zakut, *Am J Roentgenol* (1993); [2] Richards et al., *Clin Genet.* (2004), [3] Huppi et al., *Pediatrics* (1998). [4] Beaulieu *NMR Biomed.* (2002) [5] Song SK *Neuroimage* (2005)