Microstructural Development of the Corticospinal Tract in Neonates with Transposition of the Great Arteries Investigated with DTI Before and After Cardiopulmonary Bypass Surgery.

Malek Makki[1], Rabia Liamlahi[2], Hitendu Dave[3], Klaudija Batinic[2], Walter Knirsch[2], Vera Bernet[4], Ianina Scheer[5], Cornelia Hagmann[6], and Bea Latal[7]

[1]MRI Research, University Children Hospital, Zurich, Switzerland, [2]Cardiology, University Children Hospital Zurich, [3]Congenital Cardiovascular Surgery, University Children Hospital Zurich, [4]Pediatric Intensive Care, University Children Hospital Zurich, [5]Diagnostic Imaging, University Children Hispital Zurich, [6]Neonatalogy, University Hospital Zurich, [7]Child Development, University Children Hospital Zurich

Introduction: Neonates with d-transposition of the great arteries (d-TGA) require cardiopulmonary bypass (CPB) surgery within the first weeks of life. Despite improving perioperative intensive care management with lowering overall mortality rate, morbidity remains high, in particular regarding the neurodevelopmental outcome in psychomotor and cognitive abilities during long term follow up [1,2]. There is a growing recognition of central nervous system impairments in surviving newborns with congenital heart disease (CHD) [3,4]. The aim of our study was to separately investigate the corticospinal tract (CST) of both hemispheres in neonates born at term with d-TGA before and after CPB surgery and compare it to age matched healthy controls. We hypothesized that the integrity of the white matter and intactness of the fibers will be abnormal in neonates with d-TGA. Furthermore, the development will be not be homogenous along the CST.

Methods: Fifteen term born neonates (GA 39 ± 1 weeks) with d-TGA had both pre and post surgical DTI scans on a 3.0 T scanner using 35 gradient directions with b-value = 700 [s/mm^2]. The whole brain was covered with 2.5 mm slice thickness and in plane resolution of 0.86 x 0.86 mm^2. The neonates were prepared in advance (feeding, wrapping, ear plugs muffin) and were scanned in natural sleep. In addition ten healthy term neonates (GA = 39 ± 1 weeks) were recruited and had same MRI exam. At time of MRI the age of the pre-surgical group was 8 days (±6), the HC was 26 days (±5), and the post surgical group was 29 days (±5). Four levels of the brain pyramidal WM tract were chosen: ***1)*** superior corona-radiata (CR), ***2)*** posterior-limb of the internal capsule (PLIC), ***3)*** cerebral peduncle (CP). and ***4)*** medullar CST (M-CST). The study was approved by the local ethics committee and written informed consent was obtained from parents.

Results: Between groups analysis (general linear model controlling for conceptional age at time of MRI was corrected for multiple comparisons test and significance was set to $p < 0.002$. The FA decreased bilaterally in both the CR (Figure 1) and M-CST of the post-surgical group (Figure 2) compared to both the HC and the pre-surgical group. This was mainly caused by an abnormal increase of E_{23} in these structure in the post-surgical group compared to pre-surgical group (left: $p = 0.012$; right: $p = 0.042$). In the CR there was a higher E_1 in the post compared to the pre surgical groups (left $p=0.013$; right $p=0.013$) and a higher right E_1 in the post-surgical group compared to HC ($p=0.045$). The CP of the post-surgery group had lower left E_1 ($p=0.01$) and lower left ADC ($p=0.026$) when compared to pre-surgical group.

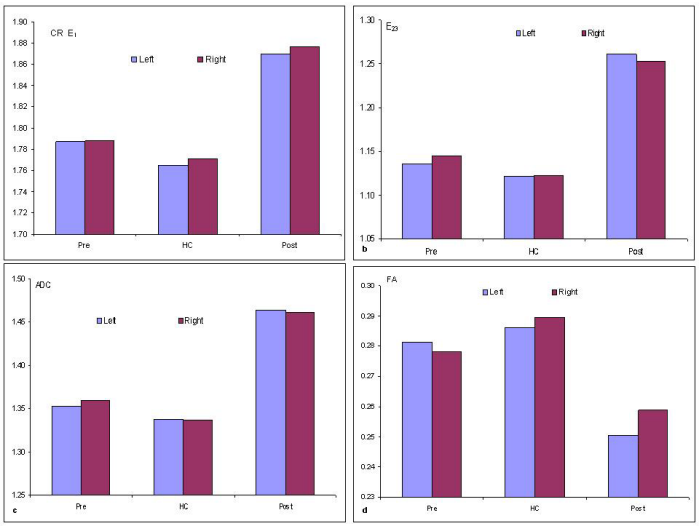

Figure 1: Estimated marginal means (corrected for age) of (a) parallel diffusion E_1, (b) perpendicular diffusion E_{23}, (c) ADC, and (c) FA assessed in the corana-radiata (CR). There were abnormal increases of E_{23} and ADC, and decrease of FA in the post-surgical group (Post) compared to the healthy control (HC) anfd pre-surgical group (Pre).

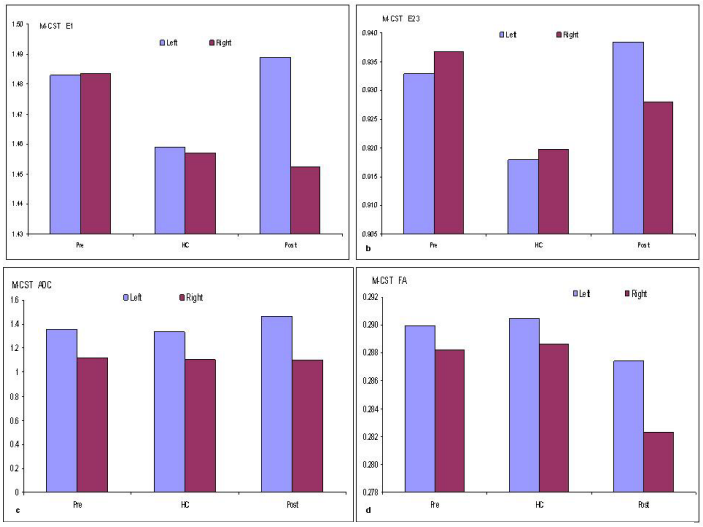

Figure 2: Estimated marginal means (corrected for age) of (a) parallel diffusion E_1, (b) perpendicular diffusion E_{23}, (c) ADC, and (c) FA assessed in the medullar cortico-spinal tract (MCST). There was an abnormal increase of E_{23} and decrease of FA in the post-surgical group (Post) compared to healthy controls (HC).

Conclusion: Our findings demonstrated that following CPB surgery there was abnormal bilateral pattern of DTI indices in the CR, and M-CST of the dTGA patients compared to healthy neonates. Higher E_{23}, lower E_1 and lower FA values may be explained by abnormal axonal pruning, axonal swelling, thinner myelin sheaths, fewer degree of white matter organization, smaller axonal diameter, more oligodendrocytes or a combination of these processes. These early brain abnormalities and structural changes observed with non-conventional MRI along the cortico-spinal pathway may contribute to adverse neuro-developmental outcomes at older ages**.** It remains unclear whether the detected growth delay which is likely to start in-utero occurs in the third trimester of gestation or earlier, is of cyanotic or genetic origin.

References: [1] Miller SP, et al. N Engl J Med. (2007); [2] Licht DJ, et al. J Thorac Cardiovasc Surg (2009); [3] Majnemer A, et al. J Pediatr (2006); [4] Mahle WT, et al. Circulation (2002).