Agenesis of Arcuate Fasciculus in children with global developmental delay of unknown etiology: A diffusion tensor imaging study.

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Introduction: The etiology of global developmental delay can not often be found even after comprehensive evaluation with genetic/metabolic testing and conventional MRI (1). Since higher cortical functions are affected in these children, we hypothesized that tractography of cortical association tracts using Diffusion Tensor Imaging (DTI) may be able to identify abnormalities in this population.

Materials and Methods: We performed DTI in twenty patients (age range: 18 – 83 months, mean age: 45 $\pm$ 16 months, 12 males, 8 females) with a history of global developmental delay and 10 typically developing children (age range: 26 – 99 months, mean age: 54$\pm$24 months, 5 males and 5 females). Diffusion weighted images were acquired in axial plane with diffusion sensitization gradients applied in 6 non-collinear directions, averaged 6 times, and a b_value = 1000 s/mm^2, voxel=0.93x0.93x3mm^3. The reference images (T2W, b~0 s/mm^2) were acquired with same imaging parameters. Twice refocusing pulses (2) and array spatial sensitivity encoding technique were added to reduce eddy-current and geometric distortion. DTI tractography using Fiber Assignment by Continuous Tracking (3) was performed to isolate the major cortical association tracts (arcuate fasciculus (AF), inferior longitudinal fasciculus (ILF), inferior fronto-occipital fasciculus (IFO), uncinate fasciculus (UF) and cingulate fasciculus (CF)) using DTI-Studio software.

Results: We found that in 9 out of 20 patients, the arcuate fasciculus (AF) was absent bilaterally. In another 2 patients, the arcuate fasciculus was absent on the left side. In contrast, the arcuate fasciculus was never absent in any of the typically developing children. In normal controls, we observed a significant asymmetry (paired t-test) in FA values of inferior longitudinal fasciculus (ILF) ($p<0.001$) of normal controls (Table 1), whereas this asymmetry was lost in patients with developmental delay (p = NS). There was no difference between patients and normal controls in the FA values of other tracts (IFO, UF, and CF; p=NS). The apparent diffusion coefficient (ADC) and number of fibers (NOF) showed no hemispheric asymmetry for any of the measured tracts in normal controls and in children with developmental delay (p=NS). The inter-observer variability in FA and ADC was less than 5% for all the tracts.

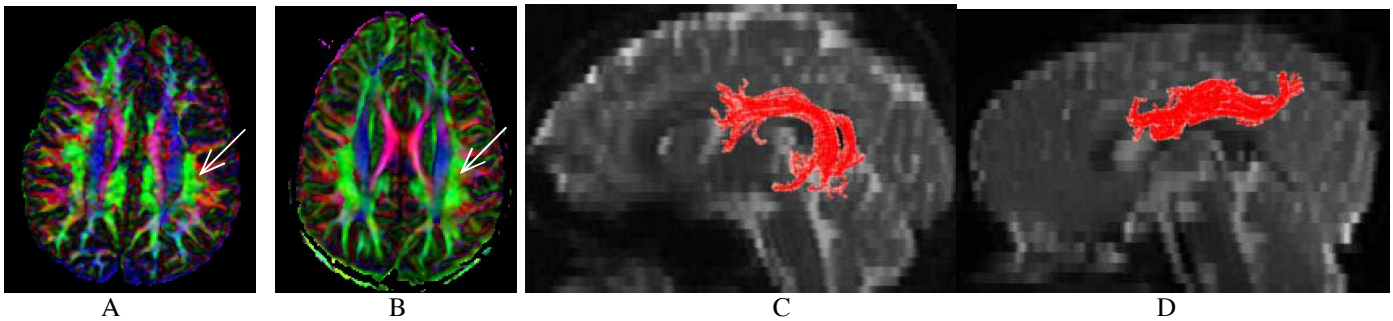

Figure 1: Axial FA color maps showing areas corresponding to the arcuate fasciculus pointed by white arrows. (1.A) represents a typically developing child, (1.B) corresponds to a developmentally delayed child. The color maps look identical, thus the absence of the arcuate fasciculus in (B) can not be appreciated. (1.C) shows that the fibers of arcuate fasciculus from posterior inferior frontal region descend into superior temporal gyrus in the typically developing child.(1.D) shows that the fibers from the posterior inferior frontal region do not descend into the superior temporal gyrus of the developmentally delayed child.

Conclusion: Agenesis of arcuate fasciculus and inadequate maturation of inferior longitudinal fasciculus (ILF) may be important mechanisms contributing to global developmental delay. DTI can be used to identify poor/absent development of major cortical association tracts in children with global developmental delay in whom comprehensive diagnostic evaluation has failed to identify the etiology. These DTI findings could help in understanding the abnormal patterns of brain connectivity in the developmentally delayed children.

References: (1) Yeargin-Allsopp M. et al., Am J Public Health 85;3(1995); (2) Reese TG et al., MRM 49(2003).