

New DTI marker characterizing white matter maturation in perisylvian language network: color-coded orientation component analysis

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Introduction: Diffusion tensor imaging (DTI) has the promise that it may aid the prognosis of language deficits in children with developmental delay (DD) and Angelman Syndrome (AS) by visualizing abnormally developed white matter in the perisylvian language network. Although our previous DTI studies [1,2] have suggested global impairment of white matter related to DD and AS by demonstrating quantitative reduction in diffusivity parameter such as fractional anisotropy (FA), determining whether a single DTI scan contains sufficient information to classify and make decision about an individual patient remains a critical challenge due to many experimental confounds, mainly depending on chronological age. The present study introduced new objective marker to quantify developmental maturation of the arcuate fasciculus based on the anterior-posterior (AP) component in colored coded orientation map which quantifies the first eigenvector of the diffusion tensor at every voxel. We first assessed a life-span maturation curve of new marker from healthy controls and examined its feasibility to discriminate the children with DD and AS from typically developing children without age-related confounds. **Materials and Methods:** 92 normal controls with typical development (TD group, age range: 0 month-30 years old 46 males) including 46 children (available from www.lban.med.jhmi.edu which is sponsored by NIH 1RO1 AG20012-01/P41 RR15241-01A1), 11 children with a diagnosis of DD (age range: 24-60 months, 6 males) and 7 children with a diagnosis of AS (age range: 42.7-106.2 months, 5 males) were studied. Whole brain DTI acquisition was performed using a 3T Signa EXCITE scanner (GE Healthcare, Waukesha, WI) equipped with an eight channel phased-array head coil at a diffusion weighting of $b=1000$ s/mm² and 55 diffusion gradient directions, TR/TE = 1250/88.7 ms, voxel size = 1.88×1.88×3mm. An additional acquisition without diffusion weighting at $b=0$ s/mm² was also obtained. The entire DTI data set was visually inspected and affine corrected for motion and other imaging artifacts. Correction for eddy induced distortions was performed using a mutual information-based registration of all images to the mean non-diffusion-weighted images (FMRIB software library from www.fmrib.ox.ac.uk/fsl). Six diffusion tensor images of individual subjects were generated using an in-house implemented software incorporating a signal-to-noise-ratio weighed multivariate least square fitting approach [3] and spatially normalized into the MNI space where the tensor field was properly reoriented according to local deformation [4]. The reoriented tensor images were finally utilized to produce the maps of FA and AP in MNI space using conventional principal component analysis of diffusion tensor matrix. Two investigators manually delineated a single ROI to cover all voxels of the perisylvian area in MNI space (Fig. 1). For individual subject an average value of AP component was sampled from the voxels of the ROI having FA > 0.2 and used as a marker to approximate the maturation of arcuate fasciculus. The entire sample of normal controls was fitted using the Pearl-Reed logistic growth curve ($y(t) = A/(1+B*\exp(-C*t))$) in order to estimate an asymptotic maturation of typical development [5]. **Results and Discussion:** A maturation curve of the proposed marker and its 95% confidence at the perisylvian network and posterior limb of internal capsule were presented in Fig 2. Compared with age-matched normal controls in the estimated maturation curve, most children in DD and AS groups showed significantly reduced AP components in the perisylvian ROI, underlying their impairment in language generation and comprehension (i.e., 6 of 11 DD and 4 of 7 AS were located outside 95% confidence curve). Those reductions were not observed in posterior limb of internal capsule demonstrating that the results are not associated with global effect (right plot of Fig. 2). Absent or delayed language function is one of the striking feature of AS and DD. The present study illustrated that by individually analyzing the AP components in the color coded orientation map, we can feasibly quantify abnormality in perisylvian area without performing complex tractography. Furthermore, it might be possible to predict the developmental age of delayed white matter maturation that is responsible for the language impairment in children with DD and AS. **Reference:** [1] Wilson BJ et al. *Pediatr Neurol*, 2011. [2] Jeong JW et al. *Am J Neuroradiol*, 2011. [3] Basser PJ et al. *J Magn Reson B*, 1996. [4] Xu D et al. *Magn Reson Med*. 2003. [5] Nico UF et al. *Science*. 2010.

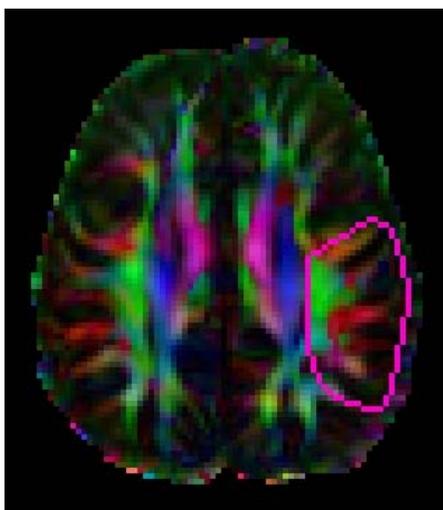


Figure 1: ROI used to average the value of AP component (green) in color-coded orientation map.

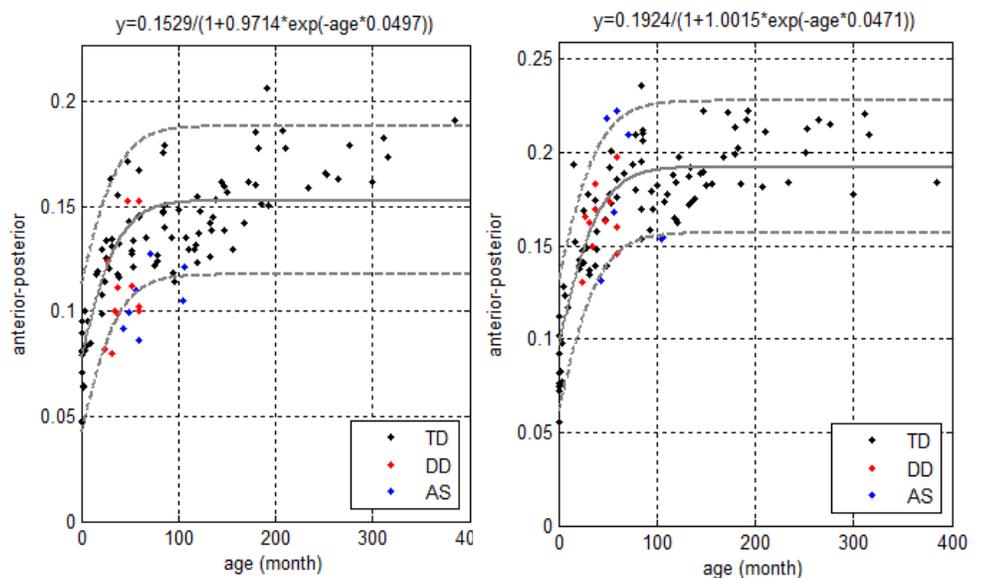


Figure 2: Maturation curve of the AP component of the perisylvian ROI (left) and posterior limb of internal capsule (right). Chronological age is shown on the x-axis and the average AP component on the y-axis (black: TD, red: DD, blue: AS). The fit and 95% confidence limits are shown with solid and dashed lines.