Diffusion Tensor Imaging of normal white matter maturation from late childhood to young adulthood: voxel-wise evaluation of mean diffusivity, fractional anisotropy, radial and axial diffusivities

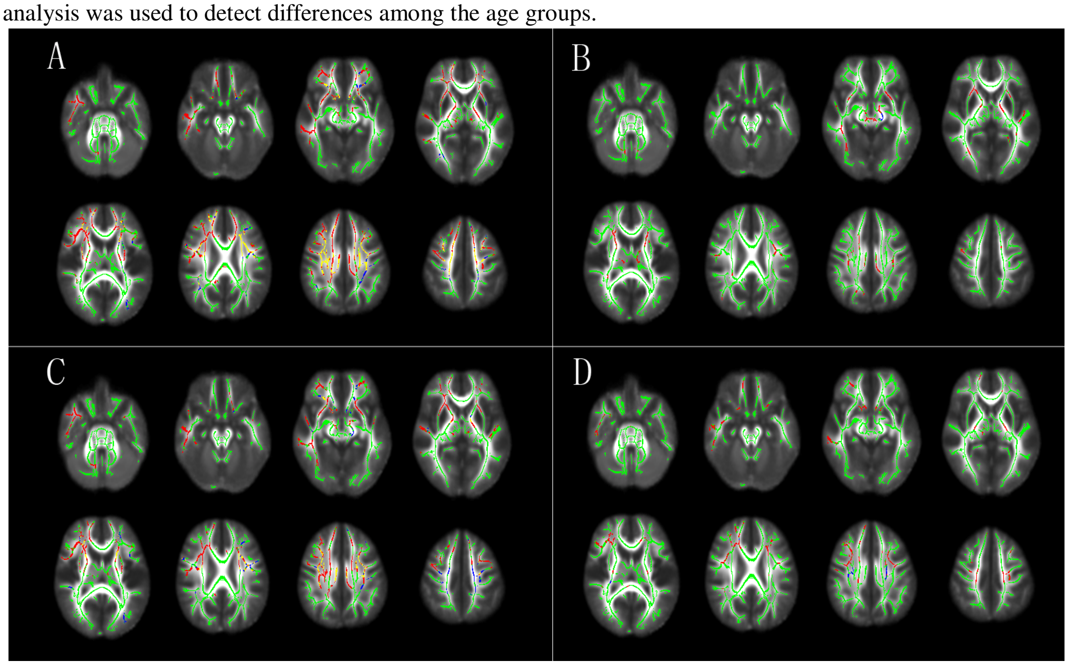
D. Qiu[1], L-H. Tan[2], and P-L. Khong[1]

[1]Diagnostic Radiology, The University of Hong Kong, Hong Kong, Hong Kong, China, People's Republic of, [2]Linguistics, The University of Hong Kong, Hong Kong, Hong Kong, China, People's Republic of

Introduction: Using diffusion tensor MR imaging(DTI) and advanced voxelwise analysis tools, we aim to study changes of diffusivities and anisotropy of white matter in three stages of critical language development from late childhood to young adulthood.

Methods: Seventy-five normal healthy school going students and young adults of three age groups were recruited (Group 1, 1st grade students who were learning to read, n=24, mean±SD = 7.4±0.3 years; Group 2, 4th grade students who had obtained substantial reading skills, n=27, mean±SD = 10.3±0.5 years; Group 3, college students who were sophisticated readers, n=24, mean±SD = 22.8±2.3 years). DTI was performed on a 3T scanner using the following parameters: TR/TE=6000/84ms, FOV=192mm, Matrix=64 × 64, slice thickness=3mm, one image without diffusion weighting, DWI in 6 directions with b = 1000 mm^{-2}s, 4 repetitions. Voxelwise analysis was performed using Tract-Based Spatial Statistics (TBSS) to localize regions of white matter showing significant changes of mean diffusivity(MD), fractional anisotropy(FA), radial and axial diffusivities between groups. Images were nonlinearly normalized to a standard space, the center of the white matter tracts was located and mapped to a common white matter skeleton. Non-parametric permutation test was subsequently performed for each voxel in the common skeleton to detect regions of significant difference of diffusion indices among the three age groups. This was followed by ROI analysis of specific regions of white matter tracts to obtain quantitative diffusion indices. ANOVA analysis was used to detect differences among the age groups.

Results: The figure shows regions of significantly decreased MD (A), increased FA (B), decreased radial diffusivity(C) and decreased axial diffusivity(D). Green color indicates the white matter skeleton where no significant difference was found while blue color indicates significant increase/decrease in Group 2 as compared with Group 1, red color indicates significant increase (or decrease) in Group 3 as compared with Group 2, and yellow color indicates overlap of the above two contrasts. Changes were more widespread between Group 2 and Group 3 than between Group 1 and Group 2. Among the four indices, significant change was much more widespread in mean diffusivity and radial diffusivity than FA or axial diffusivity.



- **MD:** Decreased MD was found in Group 2 compared to Group 1 in small clusters in the external capsule, superior corona radiata, cingulum, temporal, occipital and the superior frontal lobes. This was much more extensive in Group 3 compared to Group 2 in the frontal lobes, and in the right anterior temporal lobe white matter, cerebral peduncles, anterior and posterior limbs of the internal capsule, and small clusters in the cerebellar white matter and the splenium of the corpus callosum. No region was found to have significant increase in MD.
- **FA:** Increased FA was found in Group 3 compared to Group 2 in multiple regions including cerebellum, cerebral peduncles, mid and posterior right temporal lobe, anterior limb, genu and rostral part of the posterior limb of the internal capsules, anterior part of the external capsule, superior corona radiata, cingulum, and parts of the frontal and parietal lobes, more widespread in the frontal lobe.
- **Radial diffusivitiy:** Areas of decreased radial diffusivity closely mirrored decreased MD. On further inspection of the superior frontal and parietal lobes, a gradient of change is evident in that significant regions between Group 2 and Group 1 were posterior while significant regions between Group 3 and Group 2 were distinctly in the anterior i.e. frontal regions.
- **Axial diffusivity:** Mainly regions of significant decrease with several clusters of increase were found. Decreased axial diffusivity was found in the right temporal lobe, internal capsule, a small cluster in the splenium of corpus callosum and widespread areas in the frontal lobes whilst increased axial diffusivity was found in the cerebellar hemisphere, occipital lobes and left corona radiata (which may include fibers of the superior longitudinal fasciculus).
- **ROI analysis**: confirmed our result of voxelwise analysis (due to limited space, figures are not shown here).

Discussion: The findings of continual brain development during the period when complex cognitive functions such as language, executive function and attention are maturing suggest that these changes may be the neural substrate of maturing cognitive functions. For example, the frontal lobes has been associated with executive functions while left frontal lobe, temporal lobe and superior longitudinal fasciculus have been shown to be involved in language functioning. The evaluation of radial and axial diffusivities could provide more information with respect to the underlying physiological processes. We propose that the growth of glial cells would decrease axial and radial diffusivities proportionally, while myelination would decrease radial diffusivity preferentially. Changes of DTI indices likely also reflect other biological processes during brain development including axonal growth and cohesive fiber organization.

References: ***1***. Huang H, et al, 2006. Neuroimage. 33:27-38. ***2***. Huppi, PS, 2006. Semin.Fetal Neonatal Med. 11:489-497.
3. Snook, L, et al, 2005. Neuroimage 26:1164-1173.