Assessment of Age-Related Microstructural Changes in the Thalamus by Diffusional Kurtosis Imaging

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INTRODUCTION: The thalamus is a major subcortical relay station that filters incoming primary sensory input and modulates processed cortical information through reciprocal cortico-thalamic connections. Therefore, it is a key region for fronto-temporal communication and is crucial for modulating emotion and cognition in humans [**1, 2**]. In the thalamus, an age-related decrease in volume [**3**] along with age-related MR diffusion changes have been reported [**4, 5**], however with somewhat inconsistent results. Diffusional kurtosis imaging (DKI) quantifies the non-Gaussian nature of the water diffusion process resulting from diffusion barriers due to tissue microstructure [**6-9**] and can provide a measure of the degree of tissue microstructural complexity. We have previously demonstrated [**10**] age-related changes in the pre-frontal cortex with the mean kurtosis (MK) yielding useful and distinct information from the mean diffusivity (MD) or fractional anisotropy (FA) obtained using conventional DTI. Due to the intrinsic relationship between pre-frontal cortex and thalamus, we applied DKI to investigate the age-related non-Gaussian patterns of microstructural change in the thalamus.

METHODS: Imaging was conducted on a 3T Siemens Trio MR system. DKI scans with 30 gradient encoding directions and 6 b-values (0-2500 s/mm^2) were performed on a total of 25 normal subjects consisting of three groups: 1) adolescent (ages 12-18 yrs; n=9); 2) young adult (ages 26-47 yrs; n=8) and 3) cognitively intact elderly (ages 63-85 yrs; n=8). Other imaging parameters were: TR/TE=2300/108 ms, FOV=256×256 mm^2, 15 oblique axial 2 mm slices. The DKI dataset was used to calculate parametric maps for the mean diffusivity (MD), fractional anisotropy (FA), axial diffusivity (D_{ax}), radial diffusivity (D_{ra}), mean kurtosis (MK), axial kurtosis (K_{ax}), and radial kurtosis (K_{ra}) [**8, 9**]. Rectangular regions of interest were drawn on both right and left thalamus on the b=0 images, on three consecutive slices. To assure the same anatomical level in all subjects, the central slice was determined to be at the level of the anterior horns of the lateral ventricles, adding one slice before and one after. To minimize partial volume effect, voxels with MD > 2 were excluded from the analysis. Group means (+/- s.d) for all diffusion metrics were calculated. Unpaired t-tests were performed to compare groups' means ($p < 0.05$) of the diffusion metrics. The relationship between mean diffusion metrics and age was evaluated by Pearson's correlation ($p < 0.05$).

RESULTS and DISCUSSION: The DKI data set contains all the information necessary to calculate all of the aforementioned diffusion matrices. The group comparison showed a significant MK and K_{ra} mean increase for the young adult group when compared with the adolescent group (p=0.02 and 0.004 respectively), and K_{ra} showed a significant mean increase for the elderly group when compared with the adolescent group (p=0.01). **Figure 1** illustrates the significant group differences for K_{ra}. Additionally, a significant D_{ax} mean increase for the elderly group when compared with the young adult (p=0.05) was detected. No significant mean difference was detected for FA, MD, D_{ra} and K_{ax} between all three groups. For all groups, only the adolescent group showed a negative age-related correlation for D_{ax} (-0.76; p= 0.02), and a positive correlation for K_{ax} (0.84; p= 0.005).

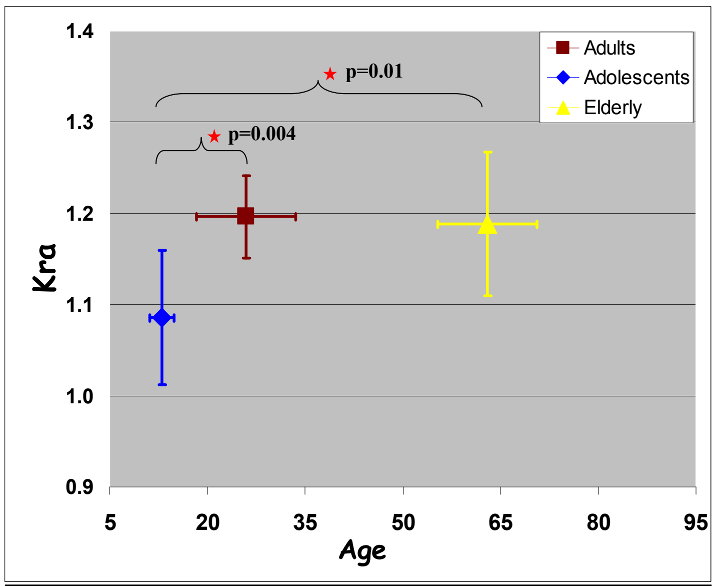

Figure 1. Significant (*) group mean differences were detected for K_{ra} when compared the adolescent group with the young adult (p=0.004) and elderly group (p=0.01). The increase of K_{ra} represents an increase in the microstructural complexity of the thalamus, possibly related to ongoing myelination and increase in fiber packing density.

The thalamus is a morphologically heterogeneous grey matter region with several major nuclear groups traversed by a band of myelinated fibers that forms the cortico-thalamic connections. Previous studies have shown that the thalamus undergoes structural changes during childhood and adolescence [11]. The data presented here shows that adolescence, and the transition between adolescence to adulthood, is a period with dynamic changes in water diffusion in the thalamus, with decrease in diffusivity and increase in kurtosis values (MK and K_{ra}), which are possibly related to ongoing myelination and increase in fiber packing density. These results are consistent with an overall increase of the degree of microstructural complexity that represents the normal maturation of the thalamo-cortical pathways associated with attention and motor improvements during this age transition.

In summary, our preliminary results suggest that significant changes in diffusional non-Gaussianity occur during adolescence and early adulthood. The information provided by the DKI metrics (MK and K_{ra}) yield complementary but distinct information from the diffusion indices obtained using conventional DTI in detecting developmental changes in neural tissue. Even though the number of subjects was small, this study still represents the first demonstration of statistically significant age-related changes in diffusional non-Gaussianity within the thalamus.

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