Diffusional Kurtosis Imaging of White Matter in the Aging Brain

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INTRODUCTION: White matter (WM) develops and degenerates in a manner that parallels cognitive trajectories through the human lifespan[1]. Thus, WM is an ideal biological target for the study of cognitive aging. Diffusional Kurtosis Imaging (DKI) is a clinically viable technique that can quantify age-related WM changes[2-3]. Moreover, DKI may identify regions associated with fluid cognitive functions that decline with age, such as executive functions[4]. To our knowledge, detailed examination of DKI metrics throughout the aging brain and its neurocognitive correlates have not been reported. *Purpose*: This study reports the associations between DKI metrics, age, and a neurocognitive test of executive functions (i.e. Trailmaking Test-Part B [TMT-B]) using Tract-Based Spatial Statistics (TBSS). *Target Audience:* Cognitive aging researchers interested in imaging biomarkers.

METHODS: 27 cognitively healthy older adult subjects were recruited from the NYU AD Center (19F, mean age = 77.54 ± 4.01, range = 55-82). MRI data were acquired using a 3T Trio MR system (Siemens). DKI acquisition was performed with 3 b-values (0, 1000, 2000 s/mm^2) along 30 diffusion encoding directions using single-shot twice-refocused-EPI. Other imaging parameters were: TR = 5900 ms, TE = 96 ms, averages = 2, FOV = 222×222 mm^2, matrix size = 82×82, parallel imaging factor of 2, slice thickness = 2.7 mm, 45 oblique axial slices. DKI post-processing using Diffusional Kurtosis Estimator (http://nitrc.org/projects/dke) provided parametric maps of the diffusion metrics. Voxelwise analyses were performed with TBSS[6] running in FSL with statistical analyses performed only in the voxels of the WM skeleton. All parametric maps were normalized to the 1×1×1mm^3 MNI152 standard space. Permutation-based statistics were computed using *randomise* (1,000 permutations). Linear regression analyses were first run for age, and secondly for TMT-B raw scores (mean = 78.11 ± 29.19) with age as a covariate. Voxels were tested for metrics decreasing with increasing age and increasing TMT-B scores (as higher scores indicate worse performance, i.e. a longer time taken to complete the task), applying threshold-free cluster enhancement[7] to correct for familywise error from multiple comparisons (p<0.05).

RESULTS: First, as depicted in Figure 1, mean kurtosis (MK), radial kurtosis ($K_\perp$), and axial kurtosis ($K_\parallel$) were negatively associated with age in widespread WM regions (i.e. greater age corresponds with decreased kurtosis), less pervasively so for $K_\parallel$. Second, MK, $K_\perp$, and $K_\parallel$ were all negatively associated with TMT-B (i.e. worse performance corresponds with decreased kurtosis). Figure 2 illustrates an example of these correlations with $K_\perp$. Significant voxels were in bilateral fronto-parietal regions, including sections of the body and splenium of corpus callosum, the superior and inferior longitudinal fasciculi, cingulum, superior corona radiata, corticospinal tract, thalamic radiations, and the posterior limb of the internal capsule.

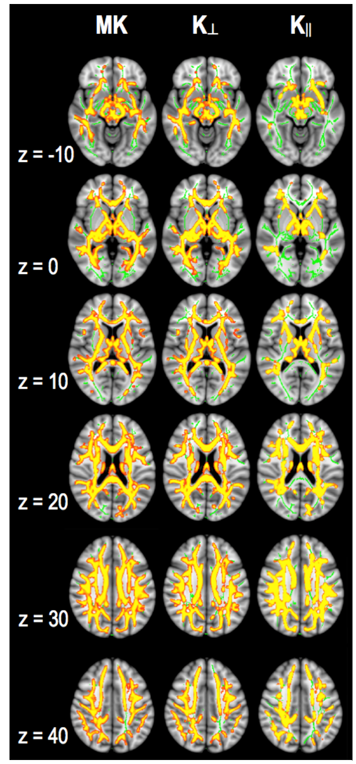

Figure 1. Negative association between DKI metrics and age (p<.05). All images are in radiologic convention (R=L).

DISCUSSION: Our results show that DKI metrics reflect pervasive WM degeneration in the aging brain, where aging corresponds with decreased kurtosis. In addition, decreased kurtosis corresponds with worse performance on a neurocognitive test of executive functions, within anatomically relevant fronto-parietal regions. *Conclusion:* DKI can quantify WM decline in the aging brain, and provide a non-invasive metric of a cognitive function known to decline with age.

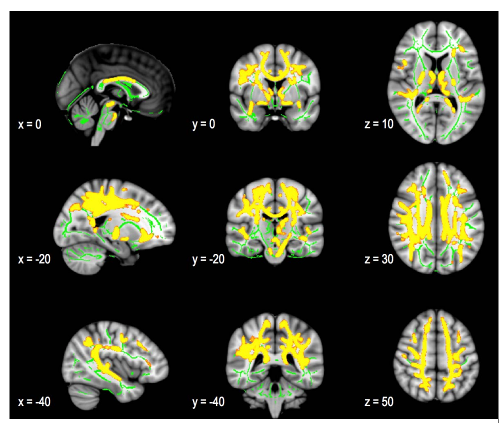

Figure 2. Positive association between $K_\perp$ and TMT-B (p<.05). All images are in radiologic convention (R=L).

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