

# Diffusion kurtosis metrics as biomarkers of microstructural development: a comparative study of a group of children and a group of adults

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## Target Audience

In this work diffusion kurtosis imaging (DKI) is used to evaluate water diffusion properties in anatomically defined regions in a group of children and a group of adults; this is of interest to scientists investigating development and healthy ageing.

## Purpose

WM plays a vital role in information transfer between various grey matter regions. DTI, an indispensable tool in brain research, has enabled the examination of WM connectivity and microstructural changes across the lifespan and has improved our understanding of the link between microstructure and function in development and ageing. Cognitive changes in early maturation are associated with changes in brain integrity and circuitry, and cerebral decline in the late age is correlated with cognitive changes/deficits. Numerous DTI studies helped to establish the patterns of cerebral maturation and decline. In particular, Kochunov et al.<sup>1</sup> have shown that fractional anisotropy (FA) of cerebral WM follows a quadratic trajectory, which peaks in early-to-middle adulthood, with age-of-peak being different for different tracts (between 23 and 40 years old). On the other hand, many WM fibres have been shown<sup>2</sup> to reach 90% of their FA (or mean diffusivity, MD) asymptote adult values by age 8-15. Methodically, a vast majority of the studies has been based on the tensor directionality and FA, the latter being considered as an overall neuroimaging index of microstructural WM integrity. In particular, FA is considered to be sensitive to axonal myelination and permeability levels. The magnitude of the changes with age is associated with more early development of projection fibres followed by commissural and then associational fibres. Recently, advanced non-Gaussian diffusion methods, such as DKI, have shown promising results<sup>3,4</sup> in elucidation of microstructural changes in development and healthy aging. In this work we investigate DKI metrics in the whole brain and in the anatomically defined regions in a group of school children and a group of adults. We hypothesize that DKI is more sensitive to age-related microstructural changes along specific fibres than DTI and examine the following question: what regions of the brain continue to develop through late childhood into the adulthood as revealed by DKI metrics?

## Materials and Methods

Two groups of healthy volunteers, that is, 20 school children (range, 9-12 years) and 21 adults (range, 38–64 years) underwent DKI. DTI/DKI metrics including MD, axial diffusivity (AD), radial diffusivity (RD), FA, mean kurtosis (MK), axial kurtosis (AK), radial kurtosis (RK), and kurtosis anisotropy (KA) were determined on the voxel-by-voxel basis in the whole brain and averaged over 20 anatomical structures provided by JHU white-matter tractography atlas (<http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/Atlases>). We performed voxelwise statistical intergroup comparison of the DTI and DKI data using the Tract-Based Spatial Statistics (TBSS), Fig.1. For each anatomically defined structure we performed a) intragroup linear regression analysis with age; b) intragroup correlation analysis for various pairs of metrics such as MD vs. FA, MD vs. MK, etc.; c) an intergroup t-test comparison ( $p < 0.01$ ); d) an intergroup histogram analysis of the averaged DTI/DKI metrics.

## Results

Intragroup changes of DTI/DKI metrics with age did not reach significance in either of the individual groups with the exception of a few regions at the threshold of significance ( $p < 0.05$ ). The intergroup TBSS analysis revealed significant ( $p < 0.01$ ) differences in DKI metrics throughout the most of the brain regions; far less brain regions showed significant differences in MD or FA. As an overall trend, the magnitude of changes of DKI metrics in anatomical regions was much larger than that of DTI metrics. The observed average changes in FA (increased in adults) and MD (decreased in adults) did not exceed more than 3% ( $p < 0.01$ ) for any of the investigated regions. On the contrary, the changes in MK (increased in adults) were much larger, ranging from about 10% in corticospinal tract to 15% in superior longitudinal fasciculus and 24% in cingulum. The data were supported by the regional histograms of the kurtosis metrics showing a clear shift (not observed in FA and MD histograms) towards higher values for the adults (Fig. 2).

## Conclusions

Within the same age group DTI and DKI parameters varied depending on the anatomical region. In an intergroup comparison using both TBSS and averaged atlas-based regional data analysis, DKI metrics showed significantly larger changes than DTI metrics. Our findings showed a high sensitivity of DKI metrics as biomarker of age related microstructure development.

## References

- [1] Kochunov P, Williamson DE, Lancaster J, et al. (2012) Fractional anisotropy of water diffusion in cerebral white matter across the lifespan. *Neurobiol Aging*. 33:9–20; [2] Schmithorst, V., and Yuan, W. (2010) White matter development during adolescence as shown by diffusion MRI. *Brain Cogn*. 72, 16–25; see also references therein; [3] Falangola MF, Jensen JH, Babb JS, et al. (2008) Age-related non-Gaussian diffusion patterns in the prefrontal brain. *J Magn Reson Imaging* 28:1345–1350; [4] Lätt J, Nilsson M, Wirestam R et al. (2012) Regional values of diffusional kurtosis estimates in the healthy brain, *J Magn Reson Imaging*, 37:610–618.

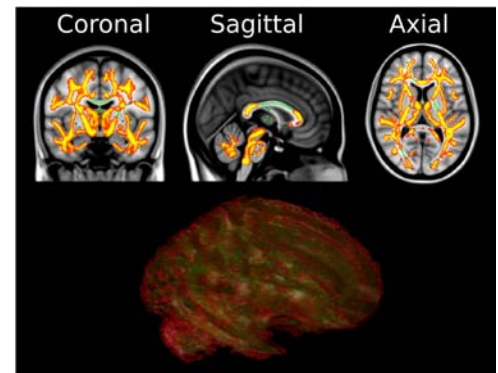


Figure 1. Example of the TBSS analysis for a selected slice (upper panel) and in the whole brain (3D rendered, lower panel). The highlighted regions are where MK is significantly ( $p < 0.01$ ) larger in adults than in children.

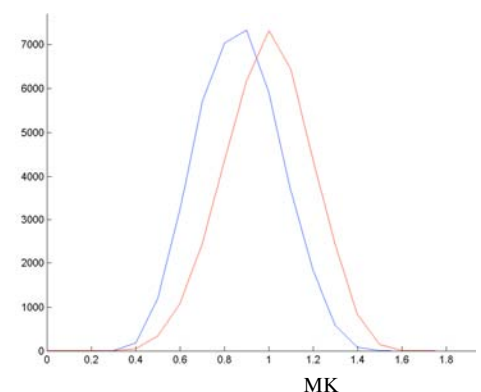


Figure 2. The representative MK histograms averaged over the group of children (blue) and adults (red) shown for anterior thalamic radiation as an example.