White matter changes of neurite density and fiber orientation dispersion during human brain maturation

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Introduction

Diffusion tensor imaging (DTI) studies of human brain development have consistently shown widespread, nonlinearly increasing white matter (WM) anisotropy through childhood, adolescence, and into adulthood. However, despite its sensitivity to changes in tissue microstructure, DTI lacks the specificity to disentangle distinct microstructural features of white and gray matter. Neurite orientation dispersion and density imaging (NODDI) is a recently proposed multi-compartment biophysical model of brain microstructure that can compute the non-collinear properties of neurite orientation dispersion index (ODI) and neurite density index (NDI) [1]. In this study, we apply NODDI in healthy controls aged 7-63 to investigate changes of ODI and NDI with brain maturation, with comparison to standard DTI metrics.

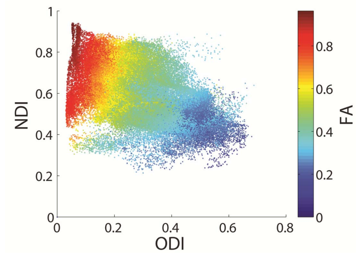

Figure 1. The relationship between DTI and NODDI: NDI vs ODI, colored by FA, for every voxel along the mean white matter skeleton across subjects.

Methods

High resolution 3T structural MRI was acquired in 67 healthy subjects (ages 7 - 63), as well as whole-brain diffusion-weighted MRI using 30 directions at b=1000 s/mm^2 and 64 directions at b=3000 s/mm^2. DTI and NODDI fitting were performed to calculate maps of fractional anisotropy (FA), radial diffusivity (RD), axial diffusivity (AD), ODI and NDI. Using Tract-Based Spatial Statistics in FSL, the diffusion metric maps from all subjects were registered to and skeletonized using FSL's FMRIB58 FA template. Analyses of age trajectory over regions of interest (ROIs) within the skeletonized WM were characterized and compared for core tract groups derived from the JHU-DTI81 atlas, as well as WM regions adjacent to grey matter ROIs derived from the Harvard-Oxford (HO) atlas, denoted regional termination zones (RTZs). Voxel-wise analyses were also performed to elucidate regional differences in development. Additionally, partial least squares regression (PLSR) was employed separately with NODDI and DTI in several WM groups to create and compare models for the prediction of age.

Results

We find that NDI exhibits striking increases throughout the studied age range following a logarithmic growth pattern, while ODI rises later in life, following an exponential growth pattern. Regional variations in change of ODI and NDI are both consistent with existing literature on DTI of brain development, while providing more physiologically specific interpretation of these regional differences. Using PLSR, we further demonstrate that NODDI better predicted chronological age than DTI. The predicted root mean square error (PRMSE) of the model created using NODDI metrics was minimized using one PLS component with a PRMSE of 8.1 years, while the model created using DTI metrics was minimized using four PLS components with a PRMSE of 9.9 years.

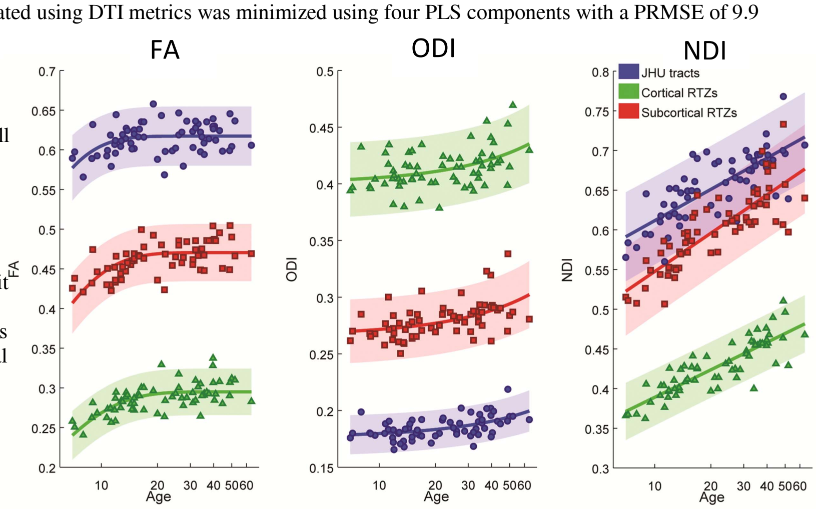

Figure 2. Subject FA, ODI, and NDI age trajectories in all core tracts (JHU) averaged (blue), all cortical RTZs averaged (green), and all subcortical RTZs (red). FA is fit by an exponential decay model, ODI is fit by an exponential growth model, and NDI is fit by a logarithmic growth model.

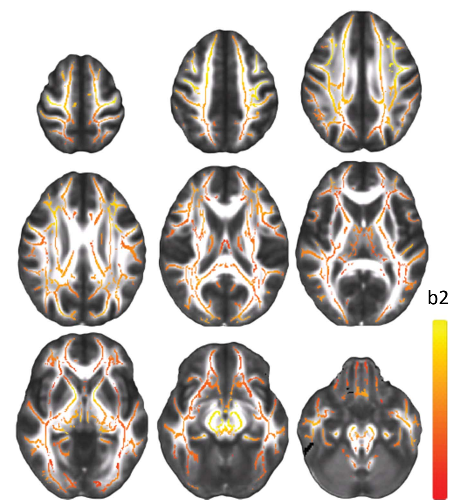

Figure 3. Rate of logarithmic growth (b2) in NDI along the WM skeleton, for voxels which are fit significantly by a logarithtmic curve, with threshold free cluster enhancement correction.

Discussion

Our results reveal that, while neurite density increases rapidly in childhood and more slowly in adulthood, fiber orientation dispersion increases more slowly in childhood, and accelerates in adulthood. This novel finding is consistent with well-established age-related changes of FA over the lifespan that show growth during childhood and adolescence, plateau during early adulthood, and accelerating decay in late adulthood. Our results suggest that the rise of FA during the first two decades of life is dominated by increasing NDI, while the fall in FA during late adulthood is driven by the exponential rise of ODI that overcomes the slower increases of NDI.

Conclusion

NODDI reveals biologically specific characteristics of brain development that are more closely linked to the microstructural features of WM than are the empirical metrics provided by DTI. As a result, the NODDI metrics are better correlated with chronological age.

References

[1] Zhang H, Schneider T, Wheeler-Kingshott CA, Alexander DC. NODDI: practical in vivo neurite orientation dispersion and density imaging of the human brain (2012). Neuroimage 61: 1000–1016.