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NEUROIMAGING

A Comparison of DTI-Based Measures as Predictors of Future Cerebrovascular Degeneration

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Abstract

Background: There has been a recent proliferation of various quantities based on single shell Diffusion Tensor Imaging (DTI) for capturing overall cerebrovascular health, especially Small Vessel Disease (SVD) as a single number. The existing literature has gaps in the comparison of these measures, so we evaluated them as predictors of both current and future White Matter Hyperintensity (WMH) as a proxy of SVD.

Method: Using baseline 3T MRI examinations (T1, DTI, FLAIR scans) of 598 participants (>60 years, amyloid negative, to limit to those on the SVD pathway) from the Mayo Clinic Study of Aging, we calculated five summary DTI quantities with varying degree of complexity. We estimated their partial R^2 from cross-sectional linear regression models and computed semi-partial R^2 from mixed models predicting WMH volume as a percentage of Total Intracranial Volume (TIV). All models were adjusted for age, sex, and scanner model, and the WMH and based were log-transformed before fitting. We also conducted subset analyses with high (WMH+) vs. low (WMH-) baseline WMH load (cut at 1.62%) to compare the performance of the measures in early vs. widespread WMH.

Result: All MD-based quantities computed on the whole brain, including FWF, performed similarly to each other, but Genu FA underperformed at explaining WMH variance (Table 1). PSMD (skeletonized or atlas based) was more sensitive in WMH+ but dramatically less so in WMH-. In WMH- and overall cohort, FWF and JHU MD (which is a simple averaging of MD in the JHU atlas) performed well.

Conclusion: All MD-based measures performed similarly to each other in the whole dataset but dichotomizing by WMH load showed interesting differences. PSMD measurements are driven by the extreme end (95^{th} percentile) of the MD distribution and therefore more sensitive in WMH+. Genu FA, a regional measure, was not useful for predicting whole brain WMH change. We noticed some variation in how

the quantities are affected by scanner model (GE Signa HDxt and Discovery 750) which needs broader investigation. Simply averaging MD over WM avoids additional processing and is more sensitive to WM degeneration that is not (yet) severe.

Fig 1. **Neuroimaging methods used to characterize SVD in WM**. L to R: WMH (green outline) on FLAIR. FA from 0 to 1 in native space with the JHU "Eve" genu in red outline, MD from 0 to 0.003 mm^2/s in native space with the JHU "Eve" mask, FWF warped by FNIRT to the FMRIB 1mm template, and the WM skeleton (in FMRIB template space) overlaid on warped MD (0 to 0.003 mm^2/s) and colored by skeletonized MD.

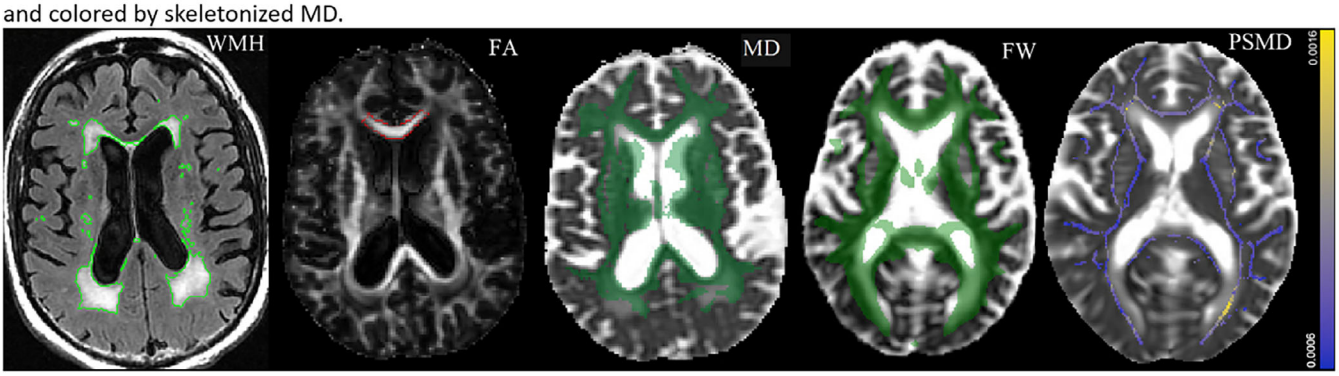

Fig. 2: WMH load with respect to the diffusion quantities for the entire dataset.

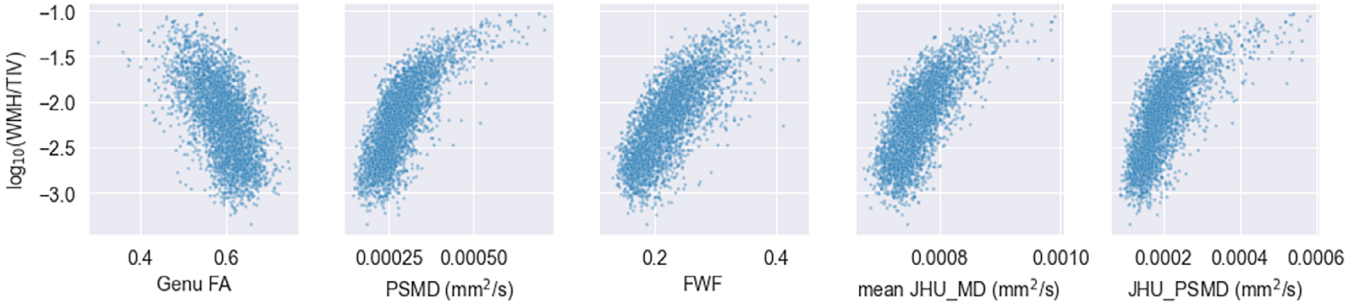

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Table 1: DTI-based quantities and their efficacy at predicting WMH

DTI Quantity		*Partial R^2 for estimating current log(WMH/TIV%)*			*Semi-partial R^2 of baseline diffusion measure for predicting follow-up log(WMH/TIV%)*		
Label	**Description**	**WMH-** n=529	**WMH+** n=69	**All** n=598	**WMH-** n=529	**WMH+** n=69	**All** n=598
Genu FA	Fractional Anisotropy of the genu of the corpus callosum	0.027	0.153	0.079	0.021	0.175	0.054
PSMD	Peak width (95%ile – 5%ile) of the Skeletonized Mean Diffusivity	0.091	0.589	0.269	0.049	0.418	0.135
FWF	Free Water Fraction averaged over a nominal WM mask, from the MarkVCID kit.	0.145	0.307	0.301	0.084	0.252	0.168
JHU_MD	Mean Diffusivity (MD) averaged over the JHU "Eve" regions	0.153	0.342	0.292	0.096	0.259	0.165
JHU_PSMD	95%ile – 5%ile of MD in the JHU "Eve" regions	0.108	0.431	0.249	0.055	0.363	0.135