Comparing NODDI Implementations for Evaluating Brain Microstructure with ADNI3 Diffusion MRI

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Introduction:

The Alzheimer's Disease Neuroimaging Initiative (ADNI3) is collecting multi-site diffusion MRI (dMRI) with protocols optimized for different scanner vendors across 47 sites [1]. Of 7 protocols, currently one is multi-shell. Whereas standard diffusion tensor imaging (DTI) microstructural measures [2], such as fractional anisotropy and mean diffusivity (MD), are nonspecific, multi-shell protocols can be used to fit biophysical models, such as neurite orientation dispersion and density imaging (NODDI), to disentangle signal contributions from the extracellular, intracellular, and CSF compartments. There are several publicly available implementations of NODDI that vary in their parameter estimates and optimization schemes: the original Zhang NODDI Toolbox [3], DMIPY [4], and AMICO [5]. We set out to better profile white matter (WM) differences in cognitively normal (CN) elderly individuals compared to those with mild cognitive impairment (MCI), by comparing the sensitivity of measures derived from each NODDI implementation. In addition to assessing effects of clinical diagnosis on WM microstructure, we compared amyloid positive (Aβ+) and negative (Aβ-) individuals.

Methods:

Clinical and dMRI data were downloaded from the ADNI database (https://ida.loni.usc.edu/): 39 CN (mean age: 73.2±7.2 yrs; 25M/14F) and 17 with MCI (76.8±7.5 yrs; 14M/3F). Aβ-status, determined with amyloid-β–specific PET, was also downloaded from the database: 9 Aβ+ (75.4±4.2 yrs; 4M/5F), and 23 Aβ- (71.0±6.2 yrs; 13M/10F) [6]. Siemens Prisma 3T multi-shell dMRI data, from 9 sites, included 13 b0 images, 48 b=1000, 6 b=500, and 60 b=2000

s/mm^2 diffusion-weighted images (DWI). After DWI were corrected for eddy, motion, and EPI distortions, MD was estimated by fitting DTI to the subset of b=1000 s/mm^2 DWI, while intracellular volume fraction (ICVF), orientation dispersion index (ODI), and the isotropic volume fraction (ISOVF) were estimated by fitting each NODDI implementation to the multi-shell data. Using ANTs' multi-channel registration [7], dMRI scalar maps were registered to the JHU DTI atlas [8], and mean measures extracted from 24 WM ROIs. Using random-effects linear regressions, we tested for associations between MCI diagnosis or Aβ-status and dMRI measures, covarying for age, sex, and their interaction, and grouping data by acquisition site. We corrected for multiple comparisons using FDR (q=0.05) [9].

Results:

MCI diagnosis was significantly associated with higher MD (18 ROIs), higher ISOVF (AMICO and DMIPY: 7 ROIs, Zhang: 5 ROIs), and lower ICVF (AMICO: 22 ROIs, Zhang: 21 ROIs, DMIPY: 20 ROIs; Fig. 1). Effect sizes did not differ across NODDI implementations (within the standard error). Aβ+ status was significantly associated with higher MD (11 ROIs), higher ISOVF (AMICO: 8 ROIs; DMIPY and Zhang: 7 ROIs), and lower ODI (DMIPY, Zhang, and AMICO: 1 ROI; Fig. 2). AMICO ODI was also significantly higher in 4 ROIs.

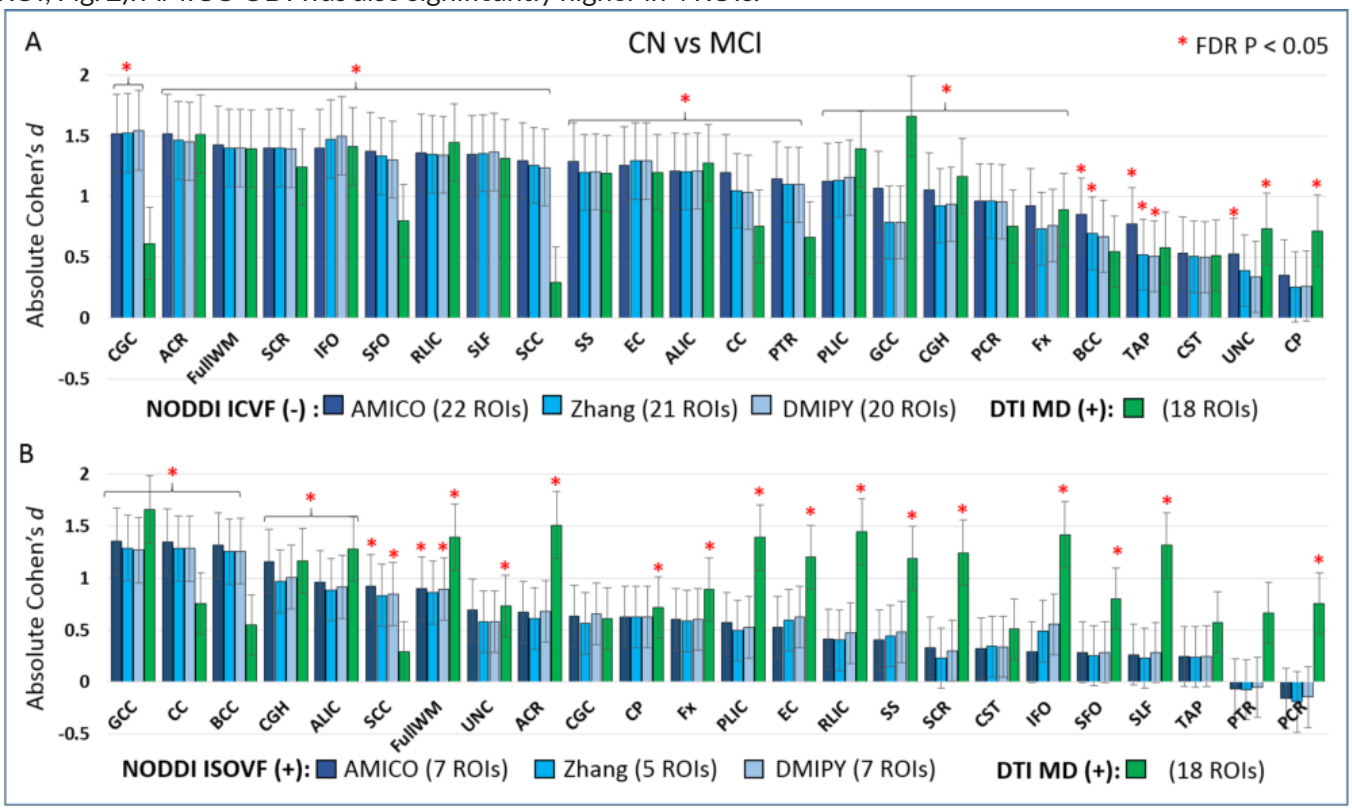

Figure 1. Absolute effect sizes (Cohen's *d*) for white matter microstructural differences between MCI individuals compared to CN in 24 ROIs. MCI individuals showed **(A)** lower ICVF and **(B)** higher MD and ISOVF compared to CN (FDR *q*=0.05). While a different number of significant associations were detected for each measure (as noted), similar effect sizes were detected across NODDI implementations (*blue*). MD associations are shown twice for effect size comparisons.

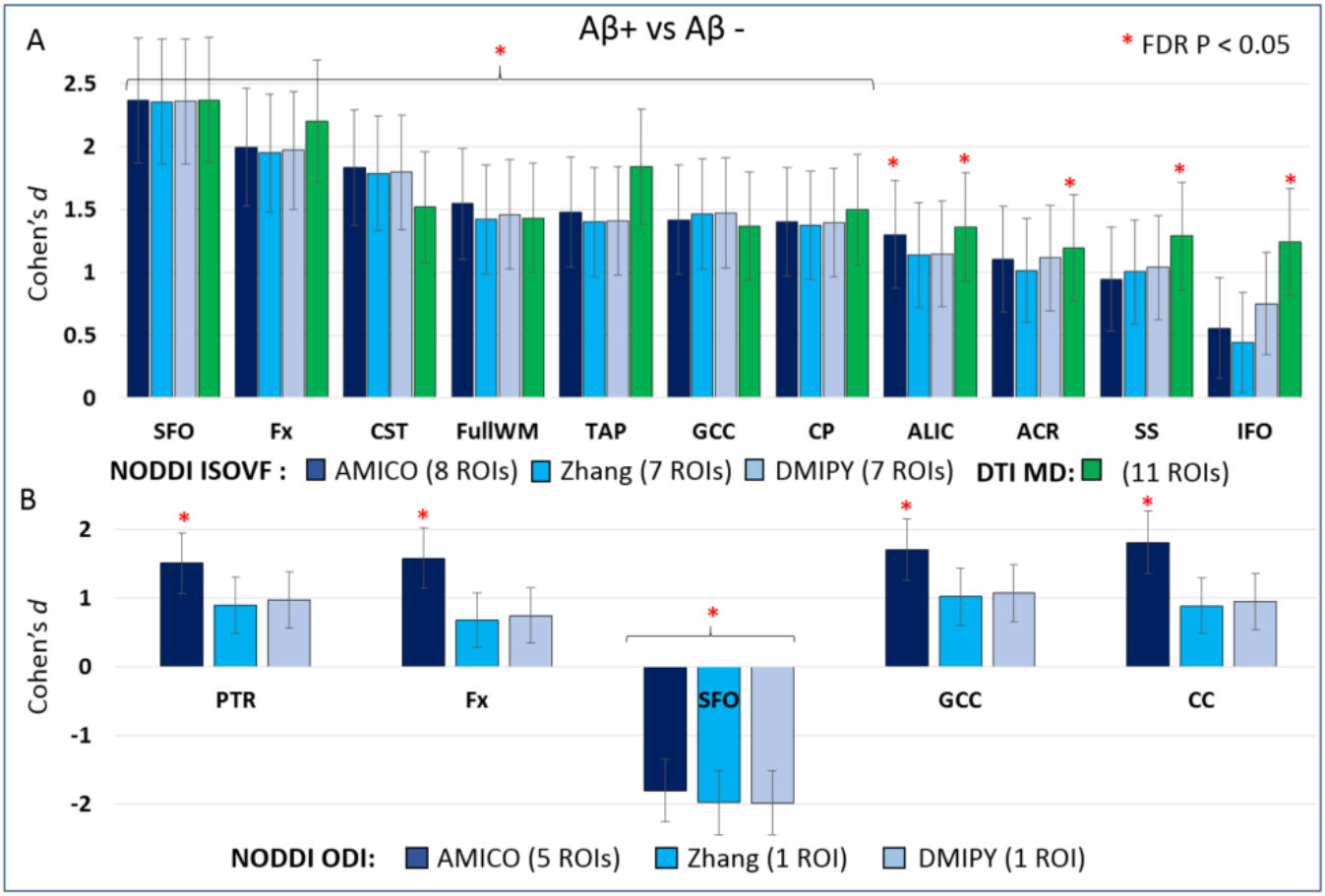

Figure 2. Effect sizes (Cohen's *d*) for the subset of ROIs where white matter microstructural measures were significantly associated with amyloid status (FDR q=0.05). Aβ+ individuals showed **(A)** higher ISOVF and MD and **(B)** both lower and higher ODI compared to Aβ-.

Conclusions:

Similar associations were detected across NODDI implementations. For associations with clinical diagnosis, AMICO ICVF detected significant effects in the greatest number of ROIs, while MD showed the largest effect size overall. NODDI measures, however, may offer greater insight into underlying pathology. Like MD, the largest ISOVF effect sizes were detected in the genu of the corpus callosum (GCC; MD Cohen's d=1.66; ISOVF AMICO d=1.35), suggesting increased free-water from CSF or inflammation, while for ICVF the largest effects were in the cingulum (CGC DMIPY d=-1.55), a region not significantly associated with MD or ISOVF, suggesting neuronal loss. Clinical vs histopathological diagnosis revealed differential WM patterns and processes. For example, the largest effects for Aβ+ status were consistently detected in the superior-frontal occipital fasciculus (SFO) across measures (MD d=2.37; DMIPY ODI d=-1.99; AMICO ISOVF d=2.37). Instead of ICVF, ODI associations were detected suggesting differences in orientation dispersion in these regions.

Disorders of the Nervous System:

Alzheimer's Disease and Other Dementias [2]

Imaging Methods:

Diffusion MRI

Modeling and Analysis Methods:

Diffusion MRI Modeling and Analysis [1]

Keywords:

White Matter
WHITE MATTER IMAGING - DTI, HARDI, DSI, ETC
Other - Alzheimer's disease

[1|2]Indicates the priority used for review

My abstract is being submitted as a Software Demonstration.

No

Please indicate below if your study was a "resting state" or "task-activation" study.

Other

Healthy subjects only or patients (note that patient studies may also involve healthy subjects):

Patients

Are you Internal Review Board (IRB) certified? Please note: Failure to have IRB, if applicable will lead to automatic rejection of abstract.

Yes

Was any human subjects research approved by the relevant Institutional Review Board or ethics panel? NOTE: Any human subjects studies without IRB approval will be automatically rejected.

Yes

Was any animal research approved by the relevant IACUC or other animal research panel? NOTE: Any animal studies without IACUC approval will be automatically rejected.

Not applicable

Please indicate which methods were used in your research:

Diffusion MRI

For human MRI, what field strength scanner do you use?

3.0T

Which processing packages did you use for your study?

FSL
Other, Please list - ANTs
LONI Pipeline

Provide references using author date format

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