Brodmann revisited: Using diffusion MRI to characterize functionally distinct gray matter regions in development

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Target audience: This research is intended for those interested in bridging the gap between technological development and practical application of neuroimaging methods.

Purpose: In 1909, anatomist Korbinian Brodmann defined gray matter regions in the brain based on the local cytoarchitectonic neuronal organization. While Brodmann's areas (BA) have been contested and refined, the crux of his discovery holds true – functionally defined regions are differentiated by the underlying neuronal cytoarchitecture and columnar organization. Diffusion MRI (dMRI) allows for the non-invasive in vivo mapping of brain microstructure through quantification of water molecule diffusion. Neurite orientation dispersion and density imaging (NODDI) is a novel multi-shell dMRI technique that uses biophysical tissue models to estimate microstructural parameters[1], including orientation dispersion index (ODI) and the intra-neurite volume fraction (v_{in}). Here, we measure ODI, v_{in}, and the diffusion tensor (DT) parameter, mean diffusivity (MD) in several gray matter regions in the brain to (1) determine if the regional structural neural organization can be differentiated by diffusion imaging-derived parameters and (2) evaluate how these cortical measures change with age.

Region	Best fit	BIC
L caudal middle frontal	vin + MD	-48.966185
R caudal middle frontal	vin + MD	-41.532007
L inferior parietal	vin + MD + odi	-18.68264
R inferior parietal	vin + MD + odi	-27.413662
L middle temporal	NA	-
R middle temporal	vin + MD	-1.7145046
L pars orbitalis	NA	-
R pars orbitalis	odi + MD	52.812665
L pericalcarine	NA	-
R pericalcarine	NA	-
L postcentral	vin + MD	-35.517463
R postcentral	vin + MD	-31.665459
L precentral	NA	-
R precentral	vin	-58.636395

Table 1: Model of best fit for predetermined segmented regions in predicting cortical thickness with Bayesian Information Criteria (BIC) listed for each preferred model. Regions marked with "NA" did not reach significance with any of the tested models.

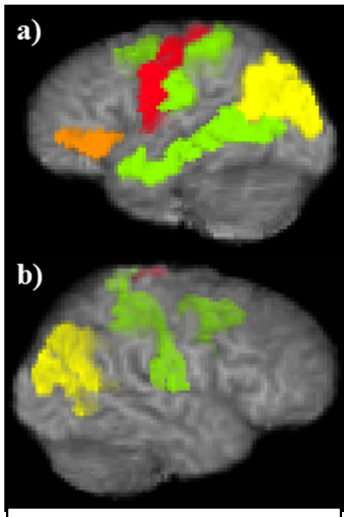

Figure 1: Best fit models to predict cortical thickness are color coded for each region. a) right hemisphere and b) left hemisphere. Red= vin; orange= ODI + MD; yellow= vin + MD + ODI; green= vin + MD.

Methods: *Subjects* 92 healthy volunteers (50% female) aged 2 to 18 years (8.9 ± 4.4 years) participated in the study through the Cincinnati MR imaging of Neurodevelopment (C-MIND) consortium study.

Image Acquisition Scans were obtained on a 3T Philips scanner. Two high-resolution T1w images were obtained with the following parameters: 1 mm^3 isotropic voxels, TR = 8.1 ms, and TE = 3.7 ms. Two diffusion-weighted images (DWI) were acquired using a spin-echo EPI method with the following parameters: 61 diffusion-encoding directions plus 7 b0 images, 2 mm^2 isotropic voxel size, TR=6614 ms, TE=81 ms. The two DWI scans differed in the following parameters- Scan 1: b-value=1000 mm/s^2, Δ=40.3, ms δ=20.9; Scan 2: b-value=3000 mm/s^2, Δ=50.93, δ=32.7.

Cortical segmentation Surface-based cortex reconstruction and volumetric segmentation was completed on the T1w images using Freesurfer image analysis software[2]. The following regions were selected for analysis in each hemisphere: caudal middle frontal gyrus, inferior parietal lobule, middle temporal gyrus, pars orbitalis, pericalcarine cortex, postcentral gyrus, and precentral gyrus. Cortical thickness was extracted and averaged within each region.

dMRI models Fitting was performed with the NODDI Matlab Toolbox to generate values for ODI and v_{in}. MD was calculated using the tensor model.

Statistical Analysis Linear models were used to predict regional cortical thickness using combinations of MD, ODI, and v_{in} as covariates. Best-fit models were determined using Bayesian information criteria (BIC). For development, linear and non-linear functions were tested. All tests of significance were corrected for multiple comparisons (p = .00357).

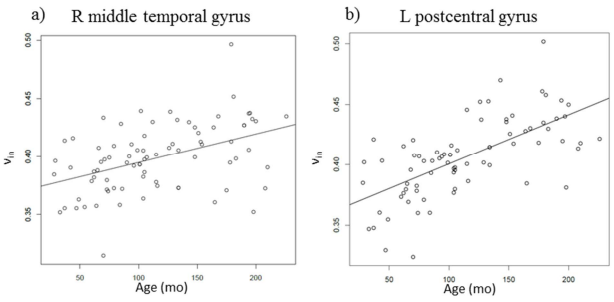

Figure 2: Plots of the relationship between neurite density and age in a) right middle temporal gyrus ($\beta=2.9\times10^{-4}$, $p=3.9\times10^{-8}$) and b) left precentral gyrus ($\beta=4.1\times10^{-4}$, $p=1.4\times10^{-10}$) to highlight different regional developmental trajectories.

Results Best-fit models to predict cortical thickness are reported in Table 1 and Figure 1. The v_{in} accounted for most of the cortical thickness variance in the bilateral caudal middle frontal gyrus (left effect size=.15; right effect size=.12), left inferior parietal lobule (effect size=.26), right pars orbitalis (effect size=.13), and the left postcentral gyrus (effect size=.12). Developmentally, v_{in} was significantly and linearly correlated with age in all analyzed regions (Figure 2).

Discussion and Conclusion Our results suggest that dMRI parameters have regional influences on cortical thickness and can be used to discriminate between anatomically-defined cortical regions. These age-related differences in parameter contributions likely reflect the underlying structural organization of these regions.

References

1. Zhang, H., Schneider, T., Wheeler-Kingshott, C. a, & Alexander, D. C. (2012). NODDI: practical in vivo neurite orientation dispersion and density imaging of the human brain. *NeuroImage*, *61*(4), 1000–16. doi:10.1016/j.neuroimage.2012.03.072

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