Predicting Myelin Content from Functional Connectivity in the Developing Brain

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Target Audience: MR Image Analysts, Pediatric Imaging Neuroscientists, Neuroimaging Scientists

Purpose: The development of functional cortical networks in humans as reported using functional magnetic resonance imaging (fMRI) overlaps *in time* with a dramatic period of white matter development. The progressive myelination firstly in central subcortical structures and later in cortical areas overlaps *in space* with the development of focal and sensory systems to distributed cortical functional networks in the infant and toddler brain[1,2]. Here we test their relationship directly by investigating whether individual difference in myelin volume fraction (VF_M) relate to individual differences and development in functional connectivity in a large cohort of 80 children aged 3 to 54 months old.

Methods:

Imaging An *in-vivo* surrogate measure of myelin-associated water, the myelin volume fraction (VF_M), was measured using multi-component relaxometry (mcDESPOT)[3], which derives the VF_M using a three-pool model fit to a series of T1-weighted SPGR and T2/T1- weighted bSSFP imaging data, with additional correction for B0 and B1 magnetic field inhomogeneities[4]. Functional resting state fMRI data were collected using a gradient echo-planar imaging sequence (TR=2.5, TE=34, FA=80^o) with resulting resolution of 3mm in-plane over 32 3.6mm slices. All data were acquired in 1 session on the same 3T Siemens scanner with a 12-channel head coil.

Sample Only children scanned during natural sleep are included in this analysis. An age matched set of 35 female (mean age 753 days) and 45 male (mean age 740 days) children who had (a) both fMRI and VF_M data available and (b) had minimal interscan motion on fMRI were included in this analysis.

Analysis After standard preprocessing and confound regression (motion and CSF signals), fMRI volumes were parcellated into 400 random regions of interest and inter-regional functional connectivity matrices were constructed. These matrices were used as multivariate predictors of myelin or age for each subject using Gaussian Process Regression (GPR)[5]. Leave one out cross validation and permutation testing was used to assess classification accuracy and significance. Using normalised mean squared error for both models, a permutation test was performed to compare prediction accuracy of both models.

Results: Using GPR, functional connectivity significantly predicted both age ($p<0.001$) and myelin ($p<0.001$) (see figure 1). Functional connectivity explained 63% of the variance in age and 77% of the variance in individual VF_M. Model comparison indicated that functional connectivity better predicted VFM than age ($p<0.01$).

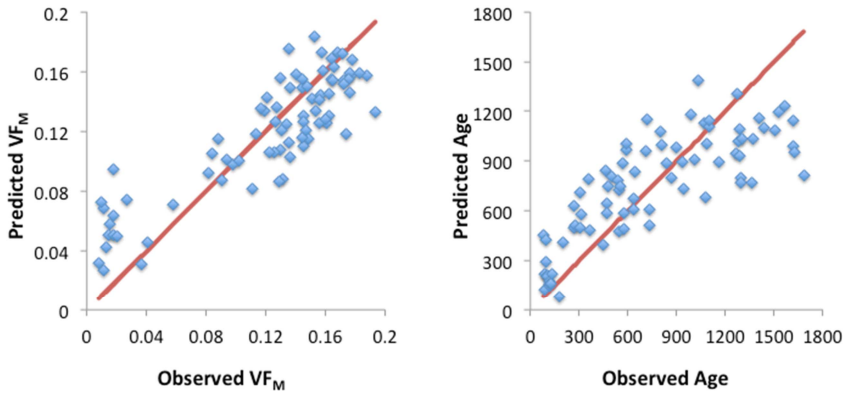

Figure 1: Figure: Scatterplots of predicted versus observed myelin water fraction (VFM) and age respectively. The red line represents a perfect classification.

Discussion and Conclusions: This work indicates that developing functional connectivity is linearly associated with developing myelin. Importantly, we show that VF_M provides information on the developing functional brain over and above that which would be provided simply by age. These two connectivity-based imaging techniques provide complementary information about brain maturation in the typically developing child.

References: 1. Fransson et al (2011), Cerebral Cortex, 21, 145-154 | **2.** Paus et al. (2001) Brain Research Bulletin, 54, 255-266 | 3. Deoni et al (2008), MRM, 60, 1372-1385 | **4.** Deoni et al (2012) Neuroimage; 63, 1038-1053 | 5. Rasmussen and Williams (2006) Gaussian Processes for Machine Learning. MIT Press.