Imaging Myelin in Autism

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Introduction Autism is a complex neurodevelopmental disorder characterized by impairments in social interaction and communication. A hypothesized substrate of the disorder is aberrant white matter maturation and abnormal myelination. Evidence for this has been suggested by volumetric, spectroscopic and diffusion tensor magnetic resonance imaging studies [1]. However, these methods provide only anecdotal information related to myelin content, hindering specific investigations of myelin content, changes in which are believed to underlie the observed gross white matter changes. Multi-component Driven Equilibrium Single Pulsed Observation of T_1 and T_2 (mcDESPOT) is a recently proposed magnetic resonance imaging (MRI) method which allows whole-brain myelin analysis through the acquisition of spoiled and fully-balanced steady-state free precession (SPGR and SSFP) imaging data. With mcDESPOT, the MR signal is decomposed into contributions from water in the intra- and extracellular compartments, and water trapped between the lipid layers of the myelin sheath, allowing quantification of each compartments volume fraction [2]. Here we report on the first quantitative study of myelin content throughout the brain in people with Autism Spectrum Disorders (ASD) and healthy controls using mcDESPOT.

Objective To *quantitatively* compare myelin content in people with ASD and healthy controls using the mcDESPOT multi-component relaxometry imaging method.

Methods *In-vivo* data from 15 healthy controls (aged 19-40) and 15 individuals with autism spectrum disorder (ASD) (aged 19-34) were collected; all subjects were right-handed males, of normal intelligence (IQ>70) and not using medication. Sagitally oriented mcDESPOT data were acquired with a 128x128x88 matrix over a 22cmx22cmx15cm FOV with specific acquisition parameters: SPGR: TE/TR=1.9ms/5.3ms, α={3,4,5,6,7,9,12,17}°, BW=±23kHz; SSFP: TE/TR=1.6ms/3.2ms, α={12,16,21,27,33,40,51,68}°, BW=±65kHz, acquired with phase-cycling increments of 0 and 180° (to correct for off-resonance effects [3]). An inversion-prepared (IR-)SPGR image was also acquired with TE/TR/TI/α=1.9ms/5.3ms/450ms/5° and BW=±23kHz in order to correct for transmit flip angle inhomogeneity [4].

Following acquisition, data for each participant were linearly co-registered and mcDESPOT model fitting [2] performed to derive the voxel-wise myelin water fraction estimates. Myelin fraction maps from all participants were then non-linearly co-registered to MNI standard space for comparative analysis. Regions of interest (ROI)s corresponding to the major white matter regions and tracts were drawn and superimposed onto the co-registered data and mean values obtained and compared between the normal and ASD groups. Further, voxel correlations between the MWF estimates and Autism Quotient (AQ) scores (a screening measure for autism traits, [5]) was investigated using randomise [6].

Results Between-group ROI analysis revealed significantly reduced mean myelin water fraction in the body of the corpus callosum, and in frontal, temporal, parietal and occipital regions (Figure 1). Between-group 'tracts of interest' analysis showed significant MWF reductions in the left and right uncinate, the left inferior occipitofrontal tract, the left inferior cerebellar peduncle, the left arcuate, the right anterior segment, the left inferior and superior longitudinal fasciculus, and the posterior segments bilaterally (see Figure 2). Finally, correlation analyses investigating the relationship between Autism Quotient scores and mean MWF values controlling for age in the whole group, i.e. pooled data of individuals with ASD and healthy controls, revealed significant inverted correlations in the cerebellum (r=-.34, p=0.043) and in frontal regions (r=-.44, p=0.034): MWF decreased with increasing ASQ score.

Conclusions This work presents the first evidence of decreased myelin content in adults with ASD in brain regions previously implicated in autism, albeit on a small sample, intimating the investigative potential of mcDESPOT in ASD. While aberrant myelination has been proposed to underlie ASD symptoms, to date this hypothesis has been difficult to directly test due to the absence of a suitable myelin imaging technique. Our method provides a new quantitative technique for measuring brain myelination in people with autism.

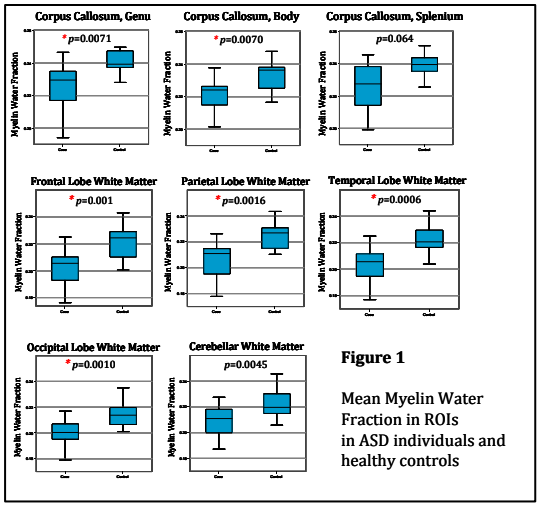

Figure 1

Mean Myelin Water Fraction in ROIs in ASD individuals and healthy controls

References

1. Amaral et al. Trends Neurosci, 2008;137.
2. Deoni et al. MRM, 2008. 60: 1372.
3. Deoni et al. JMRI 2007; 26:1106.
4. Deoni et al. Proc ISMRM 2009; 4609
5. Woodbury-Smith et al. J Autism Dev Disord 2005;331.
6. Nichols et al. HBM 2002;15:1.

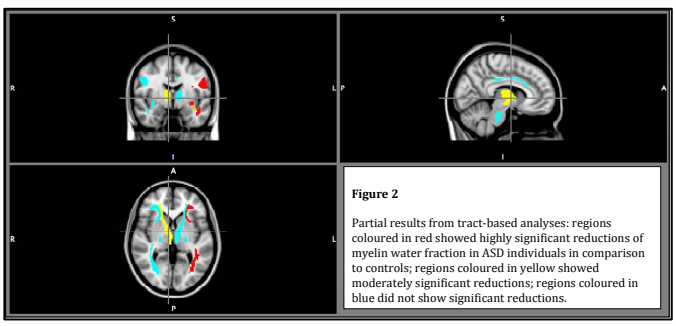

Figure 2

Partial results from tract-based analyses: regions coloured in red showed highly significant reductions of myelin water fraction in ASD individuals in comparison to controls; regions coloured in yellow showed moderately significant reductions; regions coloured in blue did not show significant reductions.