

Regional Specificity and Magnitude of Differences in DTI Metrics between Autistic and Typically Developing Children

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Introduction

Diffusion tensor imaging (DTI) shows promise for studying potential structural abnormalities in the brains of autistic children [e.g. 1-2]. The most consistent finding in the literature is reduced fractional anisotropy (FA) and increased mean diffusivity (Trace(D)) in autistic subjects compared to healthy subjects. However, the regional distribution of the abnormalities is inconsistent across studies. Further, the magnitude of the changes is rarely reported in the literature, but when reported, it is very small. Our goal is to investigate potential structural differences between the brains of autistic children as compared to age and gender matched typically developing children using high quality DTI data, and to measure the regional magnitude of differences in various DTI metrics.

Methods

39 children who met DSM-IV criteria for autism (aged 2.2 – 8.7 years, mean 4.6 ± 1.7 years, 28 male), and 39 age and gender matched typically developing children (aged 2.0 – 8.1 years, mean 4.7 ± 1.8 years, 26 male), were scanned on a 1.5T GE scanner. DTI data consisted of 60 b=1100s/mm², 10 b=300s/mm² and 10 b=0s/mm² volumes at 2.5mm isotropic resolution. Autistic subjects were sedated for scanning, while typically developing subjects were scanned without sedation. Data was preprocessed using TORTOISE to correct for motion, eddy current distortions and EPI distortions [3]. TBSS analysis [4] was performed on FA, Trace(D), axial diffusivity (AD) and radial diffusivity (RD) to compare to literature data. In addition, all autistic and typically developing subjects were registered using a fully deformable diffeomorphic tensor based registration technique (DTITK) [5]. An average tensor was then calculated for the autistic subject group and the typically developing subject group separately, to create an average brain representative of each population. From these average tensors, FA and Trace(D) were computed for each group. Subtraction maps of FA and Trace(D) were computed (autistic minus typically developing) to investigate the magnitude of differences between autistic and typically developing subjects.

Results

TBSS analysis showed a reduction of FA in autistic children compared to typically developing children in many white matter regions, including the cerebellum, genu, splenium and body of the corpus callosum, brain stem, posterior limb of the internal capsule, superior frontal and temporal parietal regions (blue regions on Fig 1a). Trace(D) was greater in autistic compared to typically developing children in most white matter regions, but only in the posterior half of the brain (red regions on Fig 1b). AD and RD results had a similar pattern to Trace(D). Subtraction of average FA and Trace(D) maps showed very small magnitude differences in regions where TBSS was significant, e.g. FA difference in the genu of the corpus callosum is less than 1%, and Trace(D) in the splenium of the corpus callosum is about 1%.

Discussion

The general trend of decreased FA and increased Trace(D) in autistic subjects compared to typically developing subjects is consistent with previously reported studies. However, we find more regions with reduced FA than most previous studies, and a pattern of Trace(D) that does not match the literature, thereby adding to the heterogeneity of the existing regional inconsistencies in the literature. Also, the magnitude of the differences is small, which might obscure meaningful between-group differences that fail to reach the threshold set for statistical significance. The small magnitude of these differences also renders the analysis vulnerable to the effects of minor confounds, such as motion and artifacts, which are common in DTI data [6]. For example, the anterior-posterior gradient of significance in Trace(D) that we observed may simply be the result of a small difference in subject motion between groups, due to the fact that only the autistic subjects were sedated. While DTI is promising as a method for revealing anatomic abnormalities in autism, caution must be exercised in interpreting between-group differences. Replication of published findings is a crucial first step to understanding true anatomical differences in the brains of autistic children.

References: [1]Groen, WB, et al, J Psychiatry Neurosci. 2011, [2]Alexander, A, et al, NeuroImage, 2007 [3]www.tortoisediti.org, [4]Smith, S. et al., NeuroImage, 2006, [5]Zhang, H., et al, IEEE Trans on Med Img 2007, [6]Pierpaoli, C in Jones, DK, *Diffusion MRI: Theory, Methods, and Applications*, Ed. 1, 2010.

