Application of High Angular Resolution Diffusion Imaging to a Child with Autism Spectrum Disorder and Comparison with his Unaffected Identical Twin

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Introduction

Autism Spectrum Disorders (ASD) are a group of complex neurodevelopmental disorders characterized by social and communication impairments with restricted and repetitive interests. The use of brain Diffusion Weighted Imaging (DWI), has led to the hypothesis that children with ASD show abnormally connected brain. Disrupted connectivity was found in particular at the level of the prefrontal cortex, the anterior cingulate, the temporal-parietal junction, the superior temporal sulcus and the corpus callosum. The significance of these findings is still questioned, as differences among the studies are present in terms of definition of ASD, severity, patient’s age and imaging method. Especially, a key issue is whether abnormal connectivity can be identified at single subject level, as this would greatly increase the clinical utility of this approach.

Aim of the present study was to determine the differences in brain connectivity between one ASD child and his identical twin, by using an advanced DWI approach.

Methods

Two identical twins (males, age 5 years) were scanned using a 1.5T GE scanner, sedated. A high-resolution T1 structural image was acquired for each participant together with a high angular resolution diffusion imaging (HARDI) sequence (30 directions, b = 1000 s/mm2). Data pre-processing included correction for head movement and intensity inhomogeneities. Cortical parcellation was performed on structural images with the Freesurfer image analysis suite, which parcellates the cortex into 33 units per hemisphere based on gyral and sulcal structure. The fibre orientation distribution was estimated using constrained spherical deconvolution imaging with MRtrix software. Fibre tracking was performed with MRtrix. Five million probabilistic streamlines were generated over the entire brain volume to create a whole-brain tractogram. Information from the cortical parcellation with Freesurfer was combined with tractography information to obtain a connection matrix.

Figure 1 outlines the automated image-processing pipeline used in this study.

Results

The diagnosis of ASD associated with mild mental retardation was confirmed in the proband while a mild expressive and receptive language disorder was diagnosed in the non-ASD twin. No abnormalities of brain morphology were detected in either child.

Parcellation of the two brains was effective and HARDI protocol could be successfully applied. Comparison between twins showed differences in areas as shown in Figure 2.

Conclusions

Our results support the underconnectivity theory of ASD, and in particular those reports showing a reduced connectivity in the long-range fibers, and increased connectivity in the frontal short-range fibers. More advanced DWI protocols such as the HARDI are new and powerful tools to explore the structural connectivity in ASD, potentially allowing the detection of abnormalities at a single-subject level. Investigating identical twins with different clinical presentations might represent an ideal model to study structural and functional differences in ASD subjects, and to deepen our understanding in the genetic and epigenetic mechanisms of the disorder.

REFERENCES