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2D Voxel-based Morphometry Shows Less White Matter Concentration in Autism

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Introduction

Autism is a neurodevelopmental disorder with the abnormal reduction in anterior, midbody and posterior part of the corpus callosum (CC) [2]. We applied 2D version of the voxel-based morphometry (VBM) in quantifying the dynamic pattern of the CC and show less white matter concentration in the high functioning autistic (HFA) group at the genu and spleninum removing the effect of age using the general linear model (GLM). Further it is shown that the less white matter concentration is due to hypoplasia rather than atrophy.

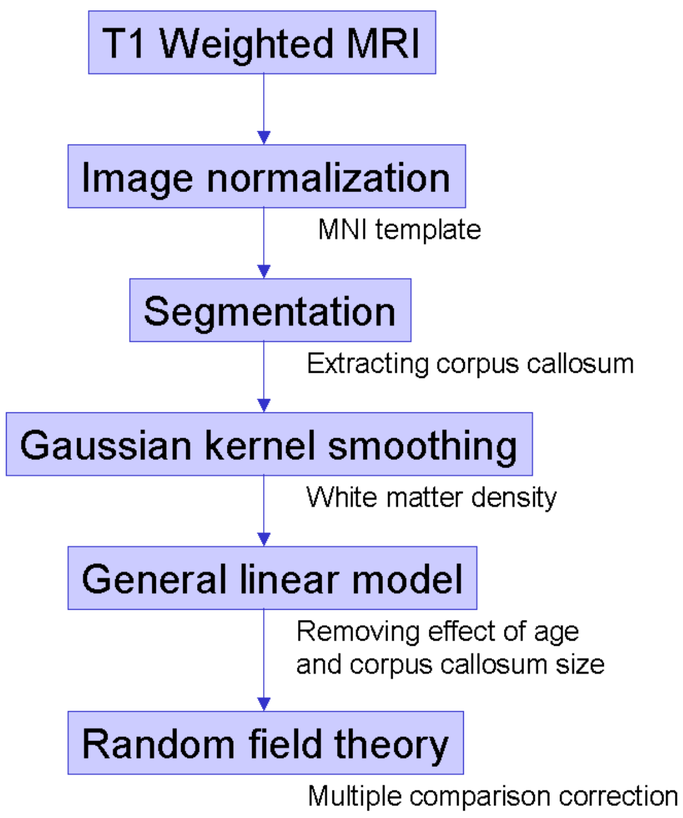

Figure 1: Data analysis flow.

Methods

Gender and handedness affect the corpus callosum anatomy [4] so 16 HFA (age 16.1 ± 4.5) and 12 control subjects (age 17.1 ± 2.8) used in this study are right-handed males. Diagnoses were confirmed with the Autism Diagnostic Interview-Revised (ADI-R) or clinical interview administered by a certified psychologist. T1-weighted MRI data were collected on a 3T GE scanner. The 2D version of VBM was performed on the midsagittal images based on SPM'99 [1]. Based on Gaussian mixture model, CCs are segmented automatically. The advantage of VBM is hat it avoids artificial Witelson partition [5]. Afterwards, 2D-Gaussian smoothing with 12mm FWHM was performed on the resulting white matter density (Figure 2).

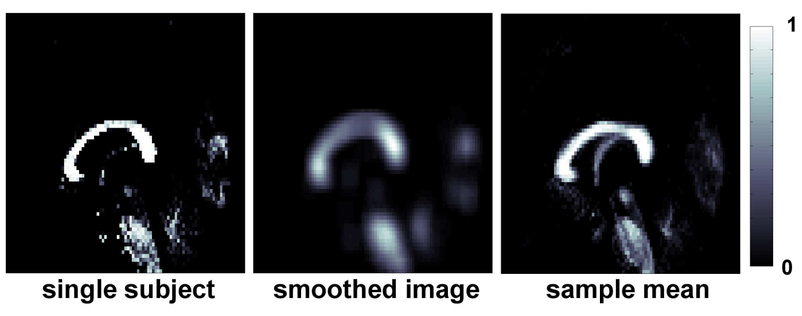

Figure 2: Left: white matter segmentation using SPM'99. Middle: 2D Gaussian kernel smoothing of the white matter segmentation with 12 pixel wide FWHM.

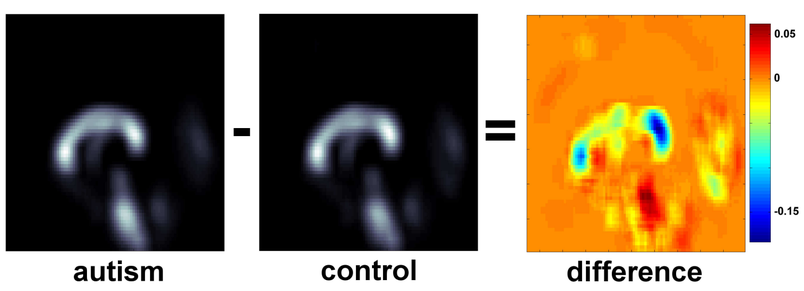

Figure 3: The sample mean of the white matter density of the autistic group, the control group and their difference respectively. We are interested in determining if this difference is statistically significant.

Linear growth model of white matter density over age was fitted in the least-squares fashion for each group to show different dynamical pattern of white matter concentration change. To remove the effect of age and corpus callosum size difference, the following general linear model (GLM) was used:

$$\texttt{density} = \lambda_1 + \lambda_2 \texttt{age} + \lambda_3 \texttt{area} + \beta \texttt{group}$$

where the dummy variable `group` is 1 for autism and 0 for control and `area` is the relative total corpus callosum area. Then we are interested in testing if there is any group difference, i.e. $H_0 : \beta = 0$. Afterwards, the multiple comparison problem is solved thresholding F-random field [6].

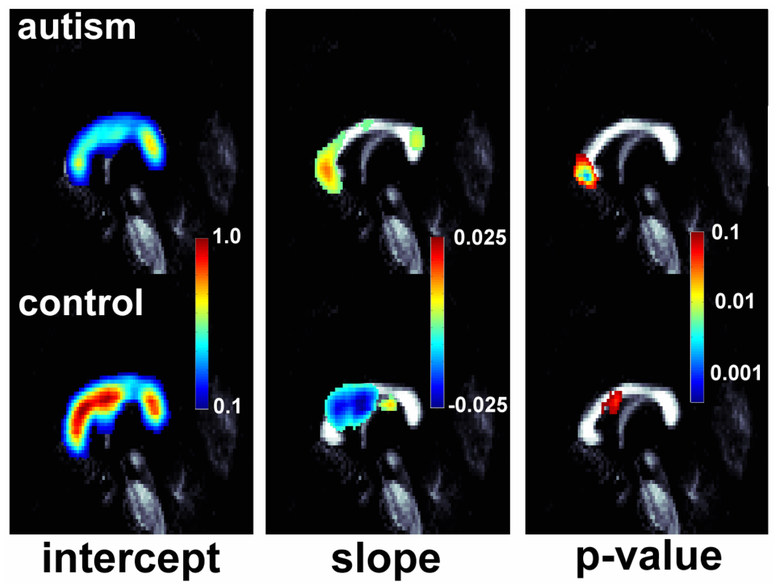

Figure 4: Linear regression of the white matter density on age. Linear growth model is fitted for each group separately. P-value map measures the fit of linear regression.

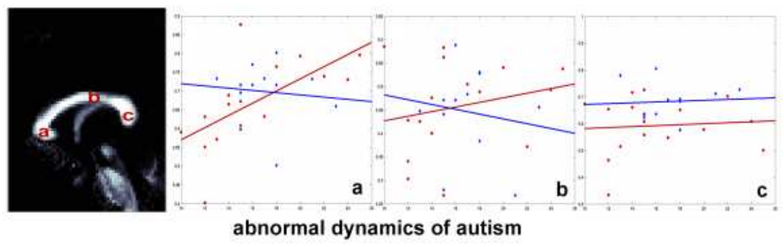

Figure 5: The simple linear fit correlating the white matter density to age at the genu (a), midbody (b) and the splenium (c). Red color is the autism group and blue color is the control group.

Results

Simple linear growth model shows that the white matter increase of 2.5% per year in the genu of the autistic group is statistically significant. Although the autistic group exhibits less white matter concentration at the early age in the genu, the concentration seems to catch up with the normal subjects at the rate of 2.5% per year. On the other hand both autistic and control subjects exhibit increasing white matter in the selenium over the years but there seems to be a gap of about 14% less white matter in the autistic (Figure. 5-C). To test the hypothesis of less white matter in the HFA removing the age effect, GLM was used. The statistical significance for the genu and the rostrum region is P-value < 0.16 (corrected) while the selenium is P-value < 0.097 (corrected) (Figure 6). The orbital frontal cortex projects through the rostrum while occipital and inferior temporal cortex projects through the splenium. Since the white matter density can be taken as an index for inter-hemispheric connectivity, our results suggest impaired connectivity in prefrontal and especially in temporal and occipital regions. The detailed analysis result can be found in [3].

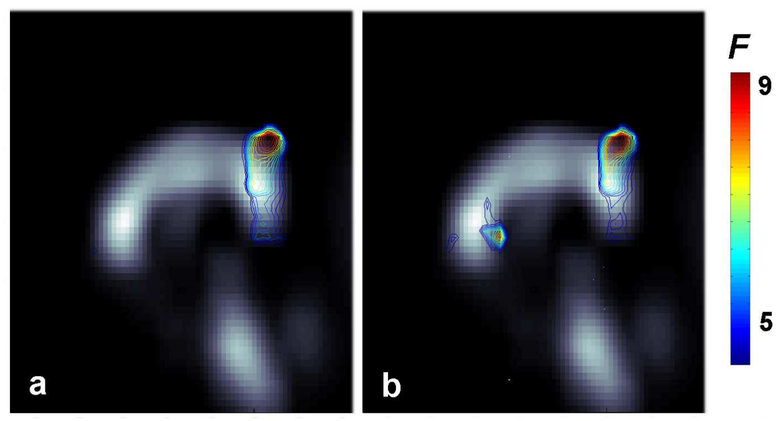

Figure 6: F-map showing the statistically significant white matter density difference (a) after controlling for age only and (b) after controlling for both age and total corpus callosum area.

Acknowledgements

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