Tissue-Specific, Smoothing-Compensated Voxel-Based Analysis of DTI Data.

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Introduction

Voxel-based analysis (VBA) is commonly used for statistical analysis of image data including the detection of significant signal differences between groups. Typically, images are co-registered and smoothed with an isotropic Gaussian kernel to compensate for image misregistration, improve SNR and reduce the number of multiple comparisons in statistical analysis. The smoothing is also used to constrain the image data to conform better to Gaussian random field theory [1]. Problems with typical implementations of VBA include anatomical misregistration, poor tissue specificity from the misregistration and the image smoothing. In this study, we developed a new VBA method with improved tissue specificity and compensation for image misregistration and smoothing. The technique was applied to a DTI study of white matter in autism. Results from our tissue-specific, smoothing-compensated (T-SPOON) VBA were compared with conventional VBA with isotropic smoothing. Results in the corpus callosum were compared with manual ROI measurements from the same data set [2].

Methods

1. Data acquisition: DTI data of 43 autism and 34 normal subjects were acquired using a single-shot spin echo EPI sequence with diffusion-tensor encoding (12 directions, b=1000s/mm^2, identical slice locations, voxels = 2x2x2.5mm, 3 NEX, 23 cm FOV). Subjects were matched for age, handedness, IQ, and head size. Data were corrected for the eddy current and field inhomogeneity distortions using the *AIR* (http://bishopw.loni.ucla.edu/AIR5) and in-house field mapping software.

2. White matter segmentation: To minimize the effects of partial voluming between different tissue types, white matter was first segmented using the *mFAST* algorithm in the FMRIB software library (http://www.fmrib.ox.ac.uk/fsl/). The major (λ1) and minor eigenvalues (λ3) were used for the input channels in the *FAST*. These two inputs were found more robust than using the MD (mean diffusitivity) and FA (fractional anisotropy) to generate the segmented white matter maps. With this 2nd step, each subject had the white matter segmented FA, MD, three eigenvalues and binary mask for these maps.

3.Template creation: One subject with the mean age of the entire population was co-registered to the 152-MNI white matter template using affine spatial normalization.

4. Normalization: All DTI data sets were spatially normalized using a 12-parameter transformation that best matched the template created in step 3. The FA maps were used for the co-registration. The 4x4 affine transformation matrix using *FLIRT* (http://www.fmrib.ox.ac.uk/fsl/) were subsequently applied to the white matter masks and maps of the mean diffusivity (MD) and eigenvalues.

5-A. Spatial smoothing: Isotropic Gaussian smoothing (8 mm FWHM) was applied to the masked DTI data and also the white matter mask.

5-B. Correction: Smoothed DTI data then were divided by the white matter mask that was smoothed using the same Gaussian kernel in the step 5-A to compensate the blurred image intensity of DTI data. The process is depicted in Fig 1. Fig 1-a is an example of a normalized FA map from one subject. Fig 1-b is a normalized white matter mask. Fig 1-c is a smoothed FA map of Fig 1-a with 8 mm Gaussian kernel. Fig 1-d is a smoothed white matter mask map with the same smoothing as Fig 1-c. Fig 1-c divided by Fig 1-d results in Fig 1-e, which is the T-SPOON FA map.

6. Statistics: A two sample *t* test was performed on maps of both of isotropically smoothed data (FA, MD, and eigenvalues) and blurring corrected data. Age and IQ were covariates as a nuisance. Cluster inference was performed (P<0.05) using the software package *FMRISTAT*. (http://www.math.mcgill.ca/keith/fmristat/).

Results

Figures 2 and 3 depict mid-sagittal corpus callosum regions with statistically significant differences in autism using conventional VBA and T-SPOON VBA, respectively. The T-SPOON method revealed more extensive differences in the corpus callosum for FA, MD, and λ3, which is consistent with manual ROI measurements that were previously reported [2]. Note that the FA and WM mask maps show similar regions of group-wise difference for conventional VBA (Fig 2), which suggests that these effects are predominately caused by misregistration.

Discussion and Conclusions

The effects of isotropic smoothing may be compensated by using a regional mask with the same smoothing parameters. We also investigated whether T-SPOON compensation effected the distributions of residuals. Although the number of the voxels that did not have Gaussian residuals was bigger (45% for FA) with T-SPOON than the isotropic case (15% for FA) [Fig 4], non Gaussian residual voxels were mostly located at the edges of the brain, which would not affect the analysis of interest. Future studies will investigate the effects of filter size [3].

Reference

[1] Worsley et al., J. Cereb. Blood Flow Metab. 12, pp. 900-918. [2] Alexander et al., NeuroImage, in press. [3] Jones et al., 2005 NeuroImage vol. 26, pp.546-554

Fig 1. Blurring correction process

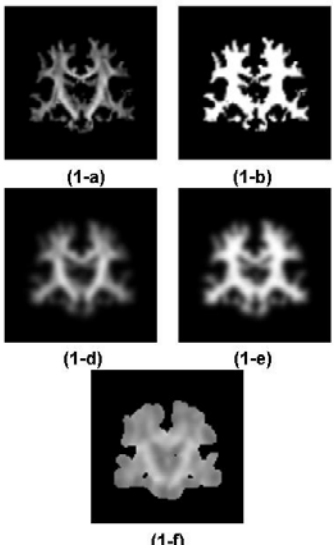

Fig 2. *t* maps without smoothing compensation correction

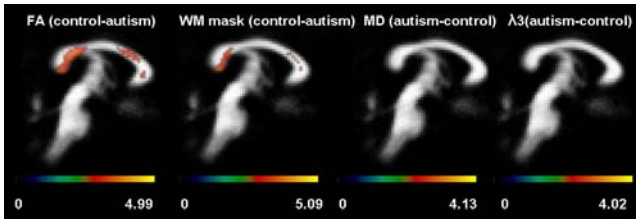

Fig 3. *t* maps with smoothing compensation correction

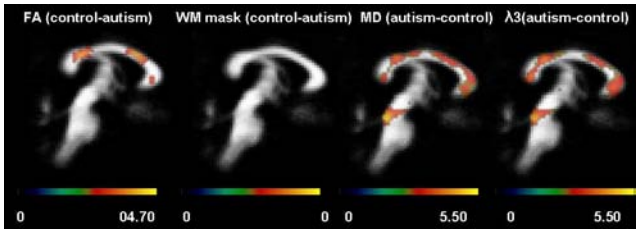

Fig 4. Voxels with non-Gaussian residuals from FA analysis (Bera-Jarque test, P<0.05). Top : without correction. Bottom: with correction