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

Jee Eun Lee [1], Mariana Lazar [1], Andrew L. Alexander [1] Erin Bigler [2], Moo K. Chung [1], Terrence. R. Oakes [1], David Hsu [3], Janet Lainhart [4]

1. Waisman Laboratory for Brain Imaging and Behavior, University of Wisconsin, Madison, WI, United States
2. Department of Psychology, Brigham Young University
3. Department of Neurology, University of Wisconsin, Madison, WI, USA
4. Department of Psychiatry, Salt Lake City, UT, USA

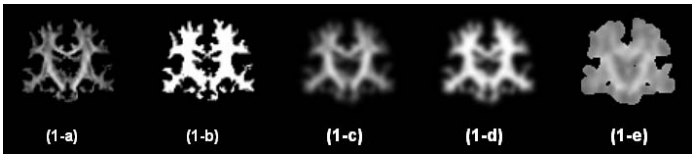
INTRODUCTION

Voxel-based analysis (VBA) is a method for statistical image analysis that is performed at each voxel location in the brain or structure of interest. VBA does not require *a priori* anatomical hypotheses but sacrifices some statistical power due to the large number of comparisons. 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. **The co-registration and smoothing steps alter the values in the DTI maps, particularly at the edges and in narrow structures, which may alter the statistical results.**

Tissue-specific, smoothing-compensated (T-SPOON) is an improved VBA method with improved tissue specificity and compensation for image smoothing. The technique was applied to a DTI study of white matter in autism. Results from T-SPOON VBA were compared with conventional VBA.

METHODS

Fig 1. Blurring Correction process



1. Data acquisition: DTI data of 43 autism and 34 normal subjects were acquired with 12 DW directions, b=1000s/mm^2, voxels = 2x2x2.5mm, 3 NEX, 256 mm 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. DTI maps of FA, MD and eigenvalues were generated using custom in-house software.

2. White matter segmentation: To minimize the effects of partial voluming between different tissue types, white matter (WM) 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. These two inputs were found more robust than using the MD and FA to generate the segmented white matter maps. The segmented WM mask was used to mask the DTI maps.

3. Normalization: The FA map from one subject (the 'template') was co-registered to the 152-MNI WM template using affine spatial normalization. All other FA maps were spatially normalized using a 12-parameter transformation to the template. The 4x4 affine transformation matrix using *FLIRT* (http://www.fmrib.ox.ac.uk/fsl/) were subsequently applied to the WM masks and maps of the MD and eigenvalues.

4. Spatial smoothing: 8 mm isotropic Gaussian smoothing was applied to all maps.

5. Correction: Smoothed DTI data were divided by the smoothed WM mask to compensate for the effects of blurring with non WM regions (see Fig 1). Fig 1-a is normalized FA map from one subject. Fig 1-b is normalized WM mask. Fig 1-c is smoothed FA map with 8 mm kernel. Fig 1-d is smoothed WM mask. Fig 1-c divided by Fig 1-d results in Fig 1-e, which is the T-SPOON FA map.

6. Statistics: Two-sample *t* tests were performed the segmented but uncorrected (SEG), the unsegmented whole-brain (UNSEG) and the T-SPOON data. Age and IQ were 'nuisance' covariates. False discovery rate (FDR) < 0.05 was used and cluster inference was performed (P<0.05) using the software package *FMRISTAT*. (http://www.math.mcgill.ca/keith/fmristat/).

RESULTS

Figures 2 depicts mid-sagittal corpus callosum regions with statistically significant differences in autism using conventional VBA(UNSEG), VBA on segmented WM data (SEG) and T-SPOON VBA, respectively. UNSEG and T-SPOON t-stat images were threshold using both FDR <0.05 and cluster extent P<0.05. The SEG images were displayed as uncorrected P <0.05 since no signals survived the FDR threshold. 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 in these subjects [1]. Note that FA and WM mask maps show similar regions of difference for SEG VBA, which may be caused by either morphological or registration differences.

Fig 2. *t*-maps of DTI measurements

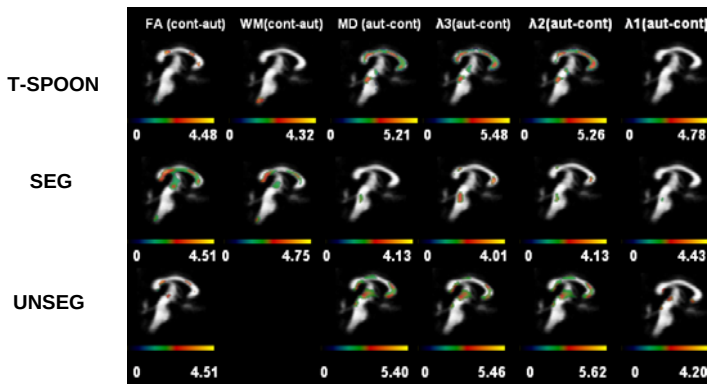
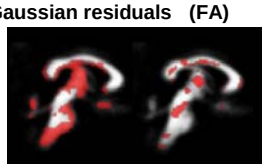


Fig 3. Voxels with non-Gaussian residuals (FA)



We also investigated whether T-SPOON compensation effected the distributions of FA t-stat residuals. Although the number of the voxels that did not have Gaussian residuals was bigger (43% for FA, Fig 3 Left) with T-SPOON than the UNSEG or SEG case (15% for FA, Fig 3 Right), non Gaussian residual voxels with T-SPOON were mostly located at the edges of the corpus callosum, which did not affect the analysis of interest.

DISCUSSION

The proposed T-SPOON method appears to be effective for correcting the effects of blurring that result from spatial normalization and image smoothing. The tissue segmentation step reduces the problems associated with misregistration and signal mixing (from interpolation and blurring) between different tissues (e.g., WM and GM). It also minimizes the confounds from differences in morphology that are not compensated by the spatial normalization. As the SEG results show, the FA and WM mask results are similar, which leads to ambiguity in the interpretation. The T-SPOON method removes the effects of morphometry from the analysis. In this study, a simple affine transformation was used. Improved image normalization methods (e.g., nonrigid warping) may require less blurring, which will further improve the anatomic specificity.

REFERENCES [1] Alexander et al., NeuroImage, 2007

Grant support NIH MH62015 and HD35476