Sensitivity of voxel-based analysis of DTI images to the warping strategy

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Introduction: The voxel-based approach has become a popular method for the objective analysis of various parameters. It essentially relies on the warping of the MR images to a common space in which the parameter-of-interest can be compared in a voxel-wise manner. The original implementation was applied to the analysis of volume changes (voxel based morphometry, VBM (1)) but the methodology has found increasing use in the analysis of DTI data (voxel based diffusion, VBD). From a survey of the ever increasing quantity of papers published using this analysis method applied to diffusion, it is clear that there is no consensus as to how to perform the warping step in spite of the significance of this step in the voxel-based methodology. The sensitivity of VBD results to this procedure is explored in a study of patients with hippocampal sclerosis (HS). HS is characterized by focal areas of diffusion changes (2,3).

Methods: Subjects: 13 patients with unilateral left HS were compared with a control group of 98 healthy subjects (mean age: 33 years; 52 men).

Imaging: DTI was performed with a 28 direction spin echo EPI sequence (3T GE scanner). The imaging parameters were as follows: TR/TE=5.8sec/83ms, 96×96 matrix, voxel size: 2.5×2.5×2.5mm, 50 contiguous slices, 3 pass interleaving, b=1100s/mm^2, 5 repeats of b=0 image, 28 directions. T1-weighted structural imaging was performed with a inversion-recovery prepared FSPGR sequence (voxel size: 0.5×0.5×2mm).

Image analysis: The DTI images were analysed with the FSL package (fMRIB, Oxford). The fractional anisotropy (FA) and trace (Tr(D)) were obtained as invariant measures of anisotropy and mean diffusivity respectively.

Voxel-based analysis: The following warping strategies were implemented for the warping of the appropriate images to standard space:

(a) Simple approach: b0 (i.e., b=0) EPI images non-linear-normalised to SPM2 EPI template; normalisation parameters applied to DTI images.

(b) Customized b0 template (FSL): b0 images affine-normalised to a target b0 image in FSL. The registered images were averaged, smoothed (to 8mm) and used as the new target of a second pass; b0 images then affine-normalised to the b0 template and parameters applied to the DTI parameter maps.

(c) Customized FA template (FSL): The same procedure as in (b) but with creation of a FA template to which all the FA images were normalised.

(d) Customized b0 template (SPM): Template creation using b0 images in SPM with subsequent non-linear normalisation of images to this template.

(e) Customized FA template (SPM): The same procedure as in (d) but with template creation from FA images.

(f) Coregister FA to WM-T1 (SPM): Coregistration of FA image to white matter (WM) component of the segmented T1-w image (WM-T1). Coregistered images then warped to standard space using parameters from warp of WM-T1 to SPM WM template.

(g) Coregister FA to GM-T1 (SPM): As in (vi) but coregistration of FA image to grey matter segment (GM-T1).

(h) Segment b0 and coregister to WM-T1 (SPM): Segmentation of b0 image and subsequent coregistration of WM segment (WM-b0) to WM-T1 scan. Images then warped to standard space via non-linear warp of WM-T1 to SPM WM apriori template.

In all cases, spatially normalised images were smoothed with a 6mm kernel (approx. hippocampal lesion size). For statistical analysis, age and gender were included as covariates. Areas of significant FA decrease and Tr(D) increase in the patient group were calculated (P<0.05 FWER). Masks of several anatomical areas were generated and were used to compare counts of significant voxels.

Results: Figure 1 and 2 show SPM glass brain images from each of the 8 warping schemes for the FA and Tr(D) analysis respectively. Tr(D) changes were apparent at a lower statistical threshold than the FA changes. Table 1 shows the count of significant voxels for each analysis. The extent of temporal Tr(D) changes was relatively consistent between the different analysis streams although the extent of secondary extra-temporal changes varied. The FA changes displayed a more significant degree of variability with warping strategy. The creation of customized templates did not improve the detection yield and the expected FA change in the uncinate fasciculus (3) was not seen. A greater degree of FA change was observed for the schemes that relied on coregistration to T1-w scans. It should be noted that the commonly implemented basic scheme (a) was associated with a diminished extent of FA and Tr(D) changes.

Discussion & Conclusions: This study has demonstrated the sensitivity of VBD analysis to the chosen warping method. Results reported with this technique should be interpreted in this light and appropriate regard taken as to the chosen warping procedure. It should be noted that the underlying basis of the voxel-based approach applied to diffusion data is quite different to the original VBM approach applied to volume. In VBM, the volume of brain structures is limited to a brain segment (commonly, GM) and modified by the normalisation whereas for VBD, the parameters of interest are continuous, whole-brain measures.

References: (1) Ashburner J et al, NeuroImage, 11:805 (2000); (2) Arfanakis K et al, MRI, 20:511 (2002); (3) Pell GS et al, ISMRM 2005 (#1202)

Tr(D) ↑	(a)	(b)	(c)	(d)	(e)	(f)	(g)	(h)
HC	719	494	0	0	36	602	112	478
PHC	142	673	1230	478	994	69	29	413
TL	235	1787	2279	4061	3841	1080	2061	818
FA ↓								
CC	0	0	0	0	0	16	1698	16
TL	0	0	0	4	5	12	47	8

Table 1 Counts of significant voxels (p=0.05 FWER) for the 8 warping schemes (a-h, see Methods) implemented for preprocessing in the VBD analysis. Voxel counts were obtained in masks of ipsilateral hippocampus (HC), parahippocampal area (PHC), temporal lobe (excluding mesial area, TL) and corpus callosum (CC).

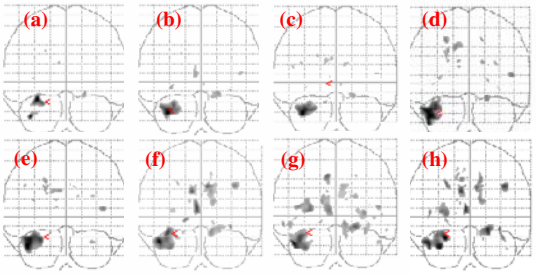

Fig 1 Glass brain sections for each of the 8 warping schemes (a-h, see methods) used in the analysis of Tr(D) increase. Results are shown for p<0.05 (FWER correction)

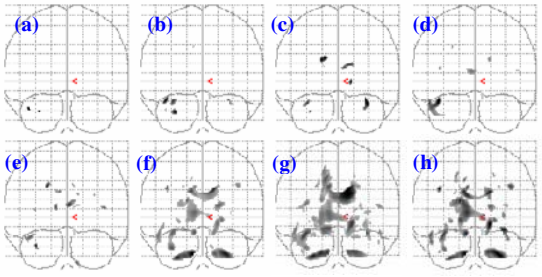

Fig 2 Glass brain sections for the 8 warping schemes used in the analysis of FA decrease. Results are shown for p<0.00005 (uncorrected).