Optimization of VBM parameters for the detection of hippocampal sclerosis

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Introduction: Voxel based volumetry (VBM) (1) has become the technique of choice for group analysis of volume changes in MR imaging. Its approach based on the normalisation of the appropriate images to a standard space enables simple voxelwise comparison between different subject groups. However, there are a large number of parameter choices to be made when setting up a VBM analysis, which may influence the outcome of the analysis. These include the choice of smoothing kernel, the degree of spatial normalisation and the choice of user-generated template images. This report examines the sensitivity of the VBM result to the choice of these parameters in a homogenous group of patients in which a focal area of volume loss in expected.

Methods Thirteen patients with right hippocampal sclerosis (HS) were recruited from our comprehensive epilepsy surgery program at Austin Health. Their structural scans were compared with a control group of 109 healthy subjects. Structural scanning was performed on a 3T GE scanner using a T1-prepared high-resolution FSPGR sequence (voxel size: 1×2×2mm).

VBM analysis: The VBM parameters that were manipulated in this study and their scope of variation were as follows:

(a) smoothing kernel: (i) 4mm (ii) 6mm (iii) 8mm (iv) 10mm (iv) 12mm

(b) covariates of no-interest: (i) without covariates (ii) total intracranial volume (TIV) (iii) TIV + age + gender

(c) VBM methodology: (i) optimized VBM (segmentation+normalisation+segmentation+modulation) (2) ; (ii) regular VBM (normalisation+segmentation)

(d) template choice: (i) SPM templates (ii) user-created templates generated from all subjects in analysis (controls+patients) (iii) user-created template generated from the control subjects only (iv) user-generated templates with tailored template for each subject group (i.e. separate control and patient templates for each groups' normalisation).

(e) normalisation scheme: (i) non-linear (ii) linear (affine 12 parameter)

Each of these choices were combined with each of the other choices to generate 120 alternative analysis pathways for the analysis of left or right HS subjects. All analyses were carried out using SPM2 (http://www.fil.ion.ucl.ac.uk). Results were compared at a statistical threshold of p=0.0005 (uncorrected). Comparison of the analysis pathways was undertaken by the assessment of the number of significant voxels in the areas of expected focal volume loss (ipsilateral hippocampus). This was compared to an estimate of measurement error, which was taken as the number of active voxels in the extra-temporal area of the brain. Binary masks were thereby generated of the ipsilateral hippocampal volume and the extra-temporal volume. A detection ratio was defined as the ratio of the hippocampal to the extra-temporal voxel counts, and all results given are based on this ration (figures 1-3).

Results and Discussion: In different analysis pathways a-d are first shown separately, so that changes in one pathway (eg (a) above) can be appreciated by keeping the other pathways (eg b-d) stable. Covariates-of-no-interest generally improved the detection efficiency for optimized VBM with the combination of 3 covariates proving to be the most effective (Fig. 1). However, the inclusion of covariates in regular VBM tended to deteriorate the result (Fig. 1). In general, a smaller smoothing kernel was found to be more efficient at detecting the hippocampal lesions (Fig. 2). Optimized VBM provided significantly more detection efficiency that regular VBM, this was found with different co-variates (Fig 1) and with different smoothing (Fig. 2). A user-generated template for normalisation and smoothing did not in general lead to a significant improvement in detection ratio with respect to the SPM template (Fig.3). The poorest results were obtained with the use of separate control and patient templates. This is most likely a result of small registration differences between the two templates which become magnified by their repeated use in each subject. The use of affine rather than non-linear normalisation tended to reduce the detection effectiveness of optimized VBM, but to slightly increase the effectiveness of regular VBM. Second, we identified the optimal combination over all of the 120 analysis pathways. This optimal combination was: 6mm smoothing, optimized VBM, no covariates, non-linear normalisation, user-generated template from average of controls.

Conclusions: This study has demonstrated the sensitivity of the VBM analysis method to the choice of several important parameters. The parameters choices are likely to be closely related to the size and characteristics of the region of volume change. In particular a small smoothing kernel should be used reflecting the small size of the assessed structure (hippocampus). For comparison of the different analysis pathways, we used the detection ratio with the approximate presumption that extratemporal changes represent false positives. True extra-hippocampal volume loss may be present in HS patients, but pre-dominantly affects the ipsilateral temporal lobe. Therefore, we expect only minimal contamination of true extra-temporal volume loss to our measurement error estimate.

References: (1) Ashburner J. et al., NI 8 :1105 (1997) ; (2) Good C. et el, Neuroimage, 14:21-36 (2001)

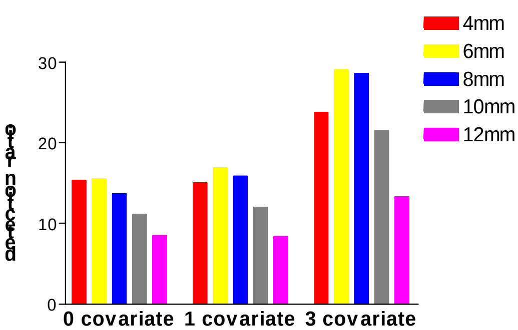

Fig.1: The effect of the number of covariates and the smoothing kernel on the detection ratio (fixed standard optimized VBM)

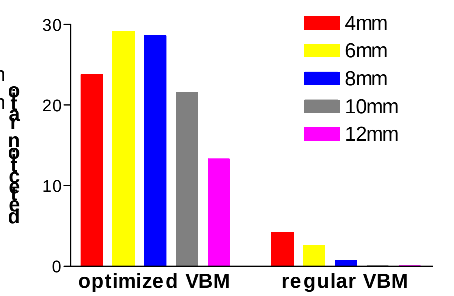

Fig.2 : The effect of the VBM method and the smoothing kernel (fixed 3 covariates)

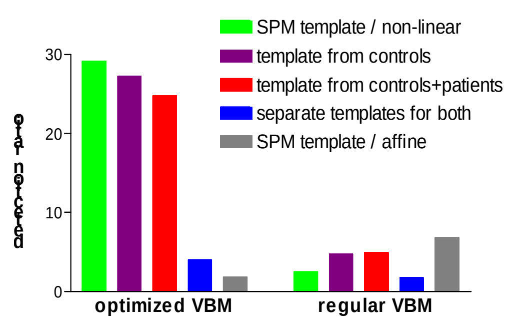

Fig.3 (left): The effect of template and normalization schemes for both optimized and regular VBM (fixed 0 covariates, 6mm smoothing)