Investigation of sources of variance in the analysis of structural data with voxel based morphometry

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Introduction: Voxel based morphometry (VBM) has become a popular technique for the structural analysis of volume changes in MR imaging (1). Its approach based on the normalisation of the appropriate images to a standard space enables simple voxelwise comparison between different subject groups. The technique relies on the ability to discern "real" group-based structural variance from the underlying variation caused by factors such as the expected anatomical variability. As a statistical method, the technique therefore requires a significant number of subjects in each group for an optimal detection of volume different. For these reasons, the VBM technique is believed to be limited to the study of groups of subjects that have been scanned at the same site and with identical imaging sequences and imaging parameters. This limitation severely hampers the utility of the method especially for patient groups that are limited in number and that cannot practically be scanned in the same location. The aim of this study is to investigate the potential of pooling structural data from multiple sources by quantifying the variance in images of subjects scanned with repeated imaging parameters. The sources of unwanted variance investigated include intra/inter-session variation, contrast changes from different flip angles, partial voluming effects and the influence of different RF coils.

Methods: Structural scanning was performed on a 3T GE scanner using a T1-prepared high-resolution FSPGR sequence with voxel size: 0.5×0.5×2mm. Two healthy volunteers were scanned on 10 separate occasions, each time with 4 different combinations of hardware and parameter choices: (a) Baseline scans: coronal plane, flip angle (FA)=20°, GE head coil; (b) Contrast variation: coronal plane, FA=25°, GE head coil; (c) Partial voluming variation: sagittal plane, FA=20°, GE head coil; (d) RF coil variation: coronal plane, FA=20° but using a dome RF coil. In addition, in order to discern sources of variance from underlying inter-session variance, the subjects were scanned 10 times in one session with parameters as in experiment (a) (the "intra-session repeat scan").

VBM analysis: Each set of 10 scans from the same subject (a-d) was compared with VBM to two sets of "control" groups: (i) the intra-session repeat scan of that subject, and (ii) a group of 109 healthy subjects (mean age: 30 years; 53 men). Optimized VBM (2) was used with a 10mm smoothing kernel and results were reported at a statistical threshold of p=0.05 (FWER correction).

Variance analysis: The variance of each set of 10 scans was computed from the set of the normalised grey matter segments. Statistical differences between the variance maps were assessed by using the intra-session variance as a baseline and comparing variance with an F-test (p=0.05). A statistical map was thereby calculated indicating the probability (as a p-value) of a significant difference in variance.

Pooled VBM analysis: In order to assess the effect of "mixing" the variance sources, the images from the 4 sets of scans (a-d) were pooled together and compared to each of the two controls groups in turn using VBM. In addition, the pooled data was also split into two groups containing half of the scans from each scan set, and these two groups were compared using VBM.

Results and Discussion: VBM analysis using the intra-session repeat scan as the control group indicated that the inter-session variance in repeating structural scans (a) is not significantly different to the intra-session variance (Fig. 1). The contrast-change induced by changing the flip angle also does not contribute significantly to the measurement variance. However, the effects of voxel orientation and the RF coil as additional source of variance are readily apparent (c,d). A consistent conclusion was reached by examination of the VBM analysis using the 109 subject control set. Figure 2 shows the variance maps for each set of 10 scans. Table 1 lists the mean p-value in two regions indicating the likelihood of a significant difference in variance distribution between each scan set (a-d) and the intra-session repeat scan. This data indicates the significance of the variance contribution from voxel orientation and RFcoil choice. VBM analysis on the pooled data indicated that the grouping of the data in this way diminished the contaminating effects of the different sources of variance. Comparison of the pooled group with the intra-session repeat scan showed no apparent volume changes, and comparison with the 109 controls showed a similar pattern of changes to that observed when comparing the intra-session repeat scan to the same set of 109 controls although the statistical threshold to see only these changes was increased. Finally, no significant volume changes were detected when comparing the pooled data that had been split into two groups.

Discussion & Conclusions:

This study has demonstrated the contribution of several sources of extraneous variance in the analysis of structural data for volume differences using VBM. The most serious factors affecting the VBM comparison of structural images from different acquisition strategies has been shown to be differing voxel orientations and therefore likely different voxel sizes, and different RF coil homogeneity profiles. However, if the data from the different sources are pooled together and preferably present in approximately equivalent numbers in the two groups, then the contribution of the extraneous variance to the VBM measurement is diminished. This is likely to be the best approach for VBM using multiple acquisition schemes and scanners.

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

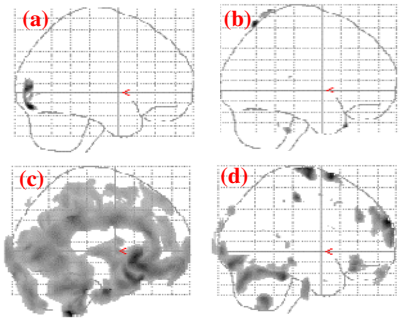

Fig 1 Glass brain sections depicting the negative contrast from the VBM analysis comparing the intra-session repeat scan with each of the four repeated scan sets (a: inter-session, b: contrast change, c: voxel orientation change, d: RF coil change, see Methods). Results are shown for one of the subjects and for p<0.05 (FWER).

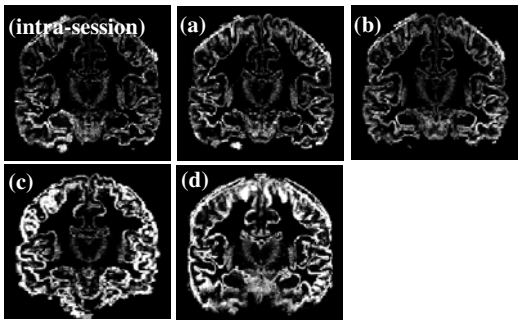

Fig 2 Variance maps from the GM segments for the intra-session repeat scan and for the four scan sets (a-d, see Methods). The maps are shown with the same windowing.

	(a)	(b)	(c)	(d)
WB	0.152 ±0.194	0.151 ±0.193	0.120 ±0.230	0.112 ±0.210
TL	0.175 ±0.192	0.160 ±0.192	0.116 ±0.229	0.113 ±0.204

Table 1 Averaged p-value measurements obtained from the statistical map produced by the F-test. This tested for differences between the variance distributions from each scan set (a-d, see Methods) and the baseline intra-session repeat scan. A lower value indicates a more likely difference in variance. Values are shown with standard deviations. Results are reported for the whole brain (WB) masked by grey matter, and also for a mask of the left temporal lobe (TL)