Impact of Smoothing Weights on Voxel-Based Quantification (VBQ) analysis

Submission No:

1077

Submission Type:

Abstract Submission

Authors:

Geoffrey Salvoni[1], Siawoosh Mohammadi[2], Nadège Corbin[3], John Ashburner[3], Martina Callaghan[3], Christophe Phillips[1]

Institutions:

[1]University of Liège, Liège, Belgium, [2]University Medical Center Hamburg-Eppendorf, Hamburg, Germany, [3]University College London, London, United Kingdom

Introduction:

Voxel-based group analyses enable hypothesis-free analyses over the entire brain[1]. In such analyses, data for each participant are spatially normalised to group space, using non-linear warping[2]. While these algorithms can achieve a high degree of spatial correspondence across individuals, smoothing is still useful to compensate for any residual misalignment between participants, enhance the study's sensitivity, and reduce the multiple comparisons problem. However, for quantitative data with distinct values in different tissue classes, smoothing can introduce deleterious partial volume effects at the tissue boundaries. Like the TSPOON method[3], voxel-based quantification (VBQ)[4] has been proposed to minimise partial volume effects by using participant-specific weights derived from the spatially normalised tissue probability maps while accounting for the original tissue volume. Here we investigate whether these weights might introduce spurious effects due to participant-specific morphology by looking at a cohort where differential atrophy can be expected.

Methods:

A previous analysis of a cohort, age range 19-75 years, identified distinct patterns of age-related differences in quantitative MRI data using the VBQ approach[5]. The identified effects were consistent with demyelination (via MT) and iron accumulation (via R2*). The VBQ approach used to smooth the maps is given by Eq. 1 (Fig.1). These data were reanalysed with one change: participant-specific VBQ smoothing weights were applied to a single parameter map according to Eq.2 (Fig.1). Our hypothesis was that, since the parameter map was identical and only the smoothing weights changed across participants, any age-related effects identified by this analysis would be spurious and driven by age-related changes in morphometry, most notably atrophy, captured by the Jacobian determinants.

Figure 1

Equation (1) : $p_j = \frac{g*(w_j s_j) m_{\mathrm{TPM}}}{g*w_j} m_j$

Equation (2) : $p_j = \frac{g*(w_j s) m_{\mathrm{TPM}}}{g*w_j} m_j$

where:

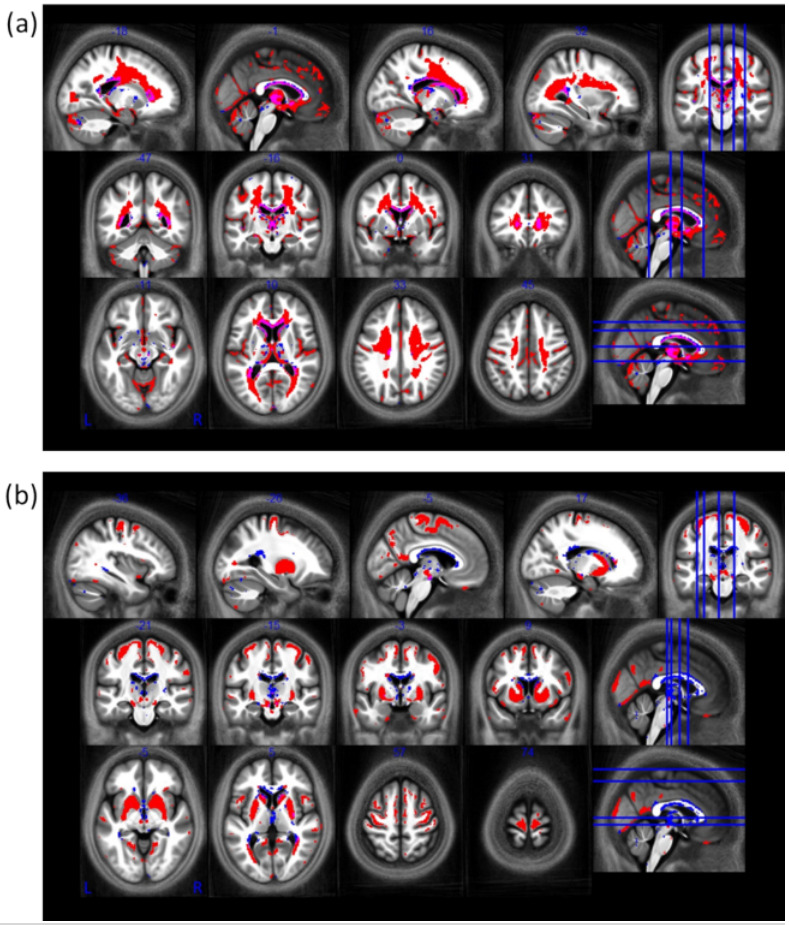
Parameter	Meaning
p_j	Parameter map for subject indexed by j after VBQ smoothing
s_j and s	Participant-specific and single-participant parameter map warped to group space by deformation Φ_j
w_j	Participant-specific weights given by $J_j t_j$
Φ_j	Participant-specific deformation mapping from native to group space
J_j	Jacobian determinants of deformation Φ_j
t_j	Participant-specific tissue probability map warped by deformation Φ_j
m_{TPM}	TPM-specific mask identifying voxels with probability > 5%
g	Gaussian smoothing kernel (FWHM of 3mm used here)
m_j	Participant-specific mask defined as $g * w_j > 5\%$, where * denotes convolution

·Equation 1 and 2 with the description of their parameters.

Results:

Fig.2a shows voxels deemed to have a significant (p<.05 FWER) correlation with age in MT. This reproduced the previously reported pattern of age-related change consistent with demyelination with 43552 voxels identified across grey and white matter (red; Eq.1). The analysis using a single MT map identified spurious significant age-related effects in 8619 voxels (blue; Eq.2). These were primarily localised to the boundary of the ventricles. Fig.2b also reproduced the previously reported age-related effects, now in R2*, with the majority of significant voxels (18608) in the cortex and basal ganglia (red; Eq.1). The analysis using a single R2* map also identified spurious significant age-related effects (6792 voxels, blue; Eq.2), again primarily located at the boundary of the ventricles. The spatial distribution of the spurious effects was largely consistent regardless of the map used (R2* or MT) or which individual was analysed (cohort mean, younger or older adult). These spurious effects showed some overlap (magenta, Fig.2) with age-related effects identified by the standard VBQ analysis: Dice's coefficients of .21 (MT) and .03 (R2*). The larger Dice's coefficient in the MT case stems from the fact that age-related effects in MT were predominantly in WM, including adjacent to the ventricular walls.

Figure 2: Age-related effects identified in MT (a) and R2* (b) using the standard VBQ approach with participant-specific parameter maps and smoothing weights (red voxels exceeded the significance threshold) or a single parameter map but participant-specific weights (blue voxels exceeded the significance threshold). The magenta voxels showed significant age-related effects in both analyses. The combined results for grey and white matter are presented and overlaid on the mean MT map in MNI space.



·Statistical map of age-related effects identified in MT (a) and R2* (b).

Conclusions:

The VBQ smoothing approach is often adopted when analysing quantitative MRI data[4-8]. The results presented here indicate that despite using morphologically-informed weights, this approach introduces only limited spurious effects, which appear to be mostly localised to the ventricular walls, where the morphological differences can be expected to be greatest. Interestingly, few spurious correlations were identified in the cortex despite its convoluted morphology. The VBQ[9] or similar[3] approaches to smoothing should be adopted when analysing quantitative data in a voxel-wise fashion in order to prevent partial volume effects being introduced. While this approach may introduce some spurious effects, it appears to be rather robust to differential morphometry across the cohort, particularly in the cortex.

Imaging Methods:

Anatomical MRI [1]
Imaging Methods Other

Modeling and Analysis Methods:

Image Registration and Computational Anatomy [2]

Keywords:

MRI
STRUCTURAL MRI
Other - quantitative MRI

[1|2]Indicates the priority used for review