Single subject VBM analysis

Joao M. S. Pereira[1], Julio Acosta-Cabronero[2], Peter J. Nestor[2], Guy B. Williams[3], and Miguel Castelo-Branco[4]

[1]Laboratory of Biostatistics, IBILI - Faculty of Medicine, University of Coimbra, Coimbra, Portugal, [2]German Centre for Neurodegenerative Diseases (DZNE), Magdeburg, Germany, [3]Department of Clinical Neurosciences, University of Cambridge, Cambridge, United Kingdom, [4]Visual Sciences Laboratory, IBILI - Faculty of Medicine, University of Coimbra, Coimbra, Portugal

Target Audience

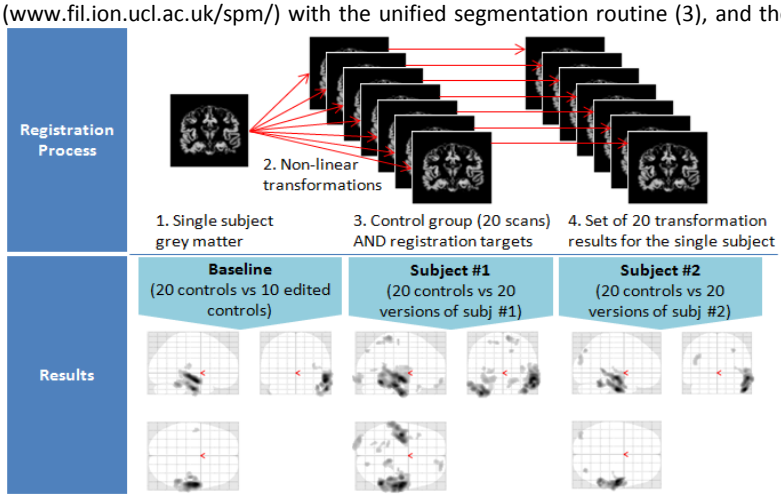
The application of a research tool such as Voxel Based Morphometry (VBM) in a clinical setting is of importance to both clinicians and radiologists, as well as to image processing scientists.

Purpose

VBM is a common brain imaging tool used in research to detect differences in the volume of brain tissues between groups (1). Its application to a clinical setting has been hampered by its inability to assess single subjects. This work presents a proof of concept of single subject VBM, using a nonlinear registration algorithm to simulate normal anatomical variability and thus generate a sample of subjects out of a single scan.

Methods

Twenty healthy controls had magnetic resonance (MRI) scans acquired with a 1.5-T GE Signa MRI scanner (GE Medical Systems, Milwaukee, WI, USA) using a T1-weighted 3-dimensional inversion-recovery fast spoiled gradient-echo sequence with voxel size 0.86×0.86×1.5mm. Of these, a subset of ten scans was re-sampled to 256×256×256 (1mm isotropic) using sinc interpolation. The GUI tkmedit in FreeSurfer v.3.04 (http://surfer.nmr.mgh.harvard.edu/) was used to manually mask grey matter (GM) voxels in the temporal lobe and insula of the subjects of this subset, the removal being more intense on the right side (2). All scans, original and edited, were processed in SPM8 (www.fil.ion.ucl.ac.uk/spm/) with the unified segmentation routine (3), and the modulated GM (mGM) segments were obtained in standard space. Each mGM segment of the edited subjects was then non-linearly registered to each of the 20 mGM segments from the original controls, using a viscous fluid registration method (4), as described in the Figure. Each original mGM of the edited subjects was therefore non-linearly registered 20 times to 20 different targets (control mGMs), resulting in 20 transformed mGMs, differentiated only by the control mGM used as target and their differences thus represent normal anatomical variability. In short, each single subject mGM became a *simulated patient group* with 20 mGM scans. Segments, both the originals and the edited ones registered to the controls, were smoothed with an 8mm Gaussian kernel and contrasted. Results were obtained with an uncorrected threshold of p=10^-15 for the single cases and p=0.001 for the baseline analysis (basic VBM), and the extent threshold was set at *k*=20.



Results

The baseline result obtained when comparing the twenty control subjects to the ten edited subjects shows the right region as "atrophic", but it missed detecting the left simulated atrophy (Figure). The two subjects presented reveal the individual editing on the right side (subject #2), and on both sides (Subject #1). All other subjects have shown similar results, with varying degrees of false positives. The right region always presented more simulated atrophy, as expected, with the left being harder to detect.

Discussion

The p-values of the single subject analyses have no statistical meaning due to the simulated "healthy" anatomical variability of the single subject group, much lower than the real anatomical variability of the control group. The presented method detects the simulated atrophy with great sensitivity and, visually, with a low number of false positives on a single subject basis. The results were consistent across subjects, and in some cases (such as Subject #2 in the Figure), minute details of the editing process could be easily observed.

Conclusions

The presented method is a solution to the use of VBM for single cases. It is easy to implement and fast to execute (2mins per target, i.e. 40 minutes per single subject on an Intel Xeon Dual-Core CPU with 8Gb of RAM). Additional target (control) scans should improve the results further while adding more computational time, but the registration method used can also be further optimised. Further work will assess these findings in patient data and will explore the impact of using different registration methods. This approach may have important applications on the clinic by providing a first automated assessment of atrophy to guide the diagnosis.

References

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