Effects of the Modulation in the White Matter Voxel Based Morphometry

O. Ozmen Okur[1], C. Ozturk[1], and K. Aydin[2]

[1]Bogazici University Biomedical Engineering Institute, Istanbul, Turkey, [2]Istanbul Medical School, Istanbul University, Instanbul, Turkey

INTRODUCTION

Voxel Based Morphometry (VBM) aims to reveal the differences between different populations' brains by making voxel based comparisons on MR brain images. SPM is used extensively for VBM analyses (the newest version is SPM5 and it is freely available at http://www.fil.ion.ucl.ac.uk/spm). Before making statistical comparisons, all images have to be normalized (registered) to a common template and segmented into three tissues: grey matter, white matter and cerebrospinal fluid. Optionally, the data might also be modulated so that the total amount of tissue remains the same after the normalization. The normalization should not be perfect; otherwise no differences would be detected, but it should be good enough to eliminate the normal variances across the individuals. However, so far, "the degree of the goodness of this normalization" and its effects on the final results have not been fully investigated. There are some studies which investigate the effects of normalization onto VBM results, but to our knowledge, not any of them presented their results with the quantitative evaluation of the registration. They evaluated the VBM results with the performance of VBM in finding artificial lesions. These lesions can either be made by hand[1], or automatically in arbitrary shapes[2], or they can be created automatically but according to an atrophy model[3]. The third option seems more attractive, but it uses segmented images; an appropriate evaluation of SPM5's registration performance becomes impossible, since in SPM5 segmentation and registration processes are unified into a single process[4]. In this study, we employed the second option by placing artificial lesions into the white matter regions of linearly aligned brain MR images. Unlike the previous studies, we computed a mutual information based goodness metric of our non-rigid registration in order to reveal the relationship between the registration quality and VBM results for two cases: with and without modulation. Additionally, we registered the images onto the groups' own template (group average); and repeated the VBM analysis.

METHODS

$$I(A,B) = H(A) + H(B) - H(A,B)$$

where

$$H(A) = \sum_{a \in A} p(a) \log p(a)$$

$$H(B) = \sum_{b \in B} p(b) \log p(b)$$

$$H(A,B) = \sum_{a \in A, b \in B} p(a,b) \log p(a,b)$$

The cranial MR images have been taken from 25 normal male adults (age: 38.3 ± 6.9). The images acquired by MP-RAGE sequence (TR=11 ms, TE=4ms, TI=300ms, flip angle=15^0, FOV=256x256mm, 128 sagittal slices, with a voxel size of 0.5x0.5x1.3 mm) on 1.5T superconducting whole body MRI system (Symphony Maestro, Siemens Medical Systems, Germany). All images have been first realigned and resliced with respect to the MNI template (avg152T1). Then, identical lesions (where certain size volumes were digitally deleted) were placed at the same coordinates as seen in the Figure 1. At the third step, all normal and lesioned image sets underwent a unified segmentation and normalization process, without changing any default parameter of SPM5. Finally, all images were smoothed by 8mm kernel. The registration metric utilized here is mutual information (I^5) as described on the left where A and B are the images, H represents entropy, and p is the probability. The metric has been calculated for only normal (without lesions) images. For the group comparisons, the groups are consisted of the normal images and their lesioned counterparts. We had two categories of group specific templates: The group averages of nonmodulated images and modulated images. Four different sizes of lesions have been placed: 36mm, 28mm, 20mm, and 12mm in diameter, yielding four different lesioned data sets for each location (For the sake of simplicity and clarity, Figure 2 shows the results only for one coordinate and a sample case for the other coordinate). For each group, after the VBM preprocessing, a t-test has been applied and mutual information has been calculated between each image and the mean image of each group.

RESULTS

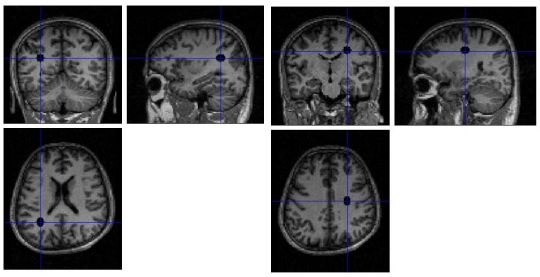

Figure 1: The placement of lesions in two different coordinates.

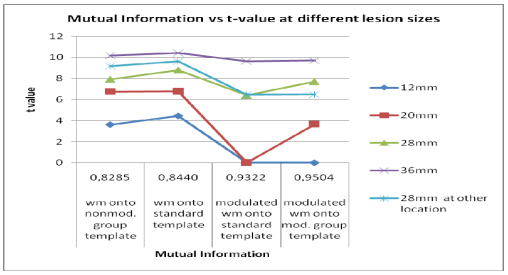

Figure 2: Effects of modulation on the t-test results of the VBM analysis between lesioned and normal groups.

The low t-test values at the modulated cases show that the modulation weakens the ability of VBM to find the lesions. It might even become impossible to detect smaller lesions (lesions with 12mm and 20mm in diameters) if the modulation is used. It seems that t-tests inversely related to the mutual information between the images and the group means. This might mean that, the more the images resembles to each other after the registration, the less chance VBM has to find the differences. The effects of the use of group specific template seem not to be significant.

DISCUSSION

The relationship between the registration quality and the VBM statistical results using mutual information metric is explored. This can be further investigated in other aspects of the registration process and also by using other metrics. We have focused here only on the white matter VBM analysis, grey matter VBM should also be studied. Our simulated lesions were not similar to the real clinically encountered lesions or atrophies; methods to create more realistic lesions/atrophies should be developed. We believe, knowing the full effects of all those parameter choices during currently widely used VBM analysis will give us a better understanding to its final results.

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