Assessing the accuracy of detecting mouse brain structure changes from MRI using simulated deformations

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Introduction

The use of image registration techniques to investigate shape differences in mouse brain MRIs have become a significant area of interest [1-3]. The ability of these techniques to bring brains into alignment have been well documented [4,5], however, it is unknown how accurately structural changes between groups can be detected or whether this sensitivity varies with brain geography or structure shape. Here we present a novel method to simulate deformation fields with known structural tissue shrinkage or growth and subsequently attempt to recover the induced changes in 21 structures of the mouse brain.

Methods

A simulated deformation field inspired by [6] was created as follows: using a 3D atlas of the mouse brain with 62 structures identified [7], a target Jacobian determinant map was created, in which any voxel of one structure received a reduced determinant (less than 1, i.e., tissue shrinkage), while the remaining part of the brain was assigned a determinant of 1 (no change). Concurrently, a tolerance map was created to indicate areas outside of the brain which were permitted to deform (i.e., grow/shrink) to accommodate the induced changes in the brain. A deformation field with zero vectors was initialized and iteratively adjusted by updating the vectors of each voxel's six nearest neighbours until the resulting vector field yielded the same determinant map as was inputted, using the tolerance map to park volume changes in areas outside the brain. To test the ability of a registration algorithm to recover induced structural changes, 21 of the relatively larger structures of the mouse brain were chosen and deformation fields simulated which featured a structural tissue loss of 0.5 to 10 percent. A set of 20 identical wild type fixed brain MRI scans were then selected and the simulated deformation field applied to half of them. An iterative registration procedure, previously applied to multiple phenotyping studies [3,8,9], was then applied to these 20 brains and the resulting Jacobian determinants of the deformation fields analyzed for structural group differences. Multiple comparisons were accounted for using the False Discovery Rate (FDR) [10].

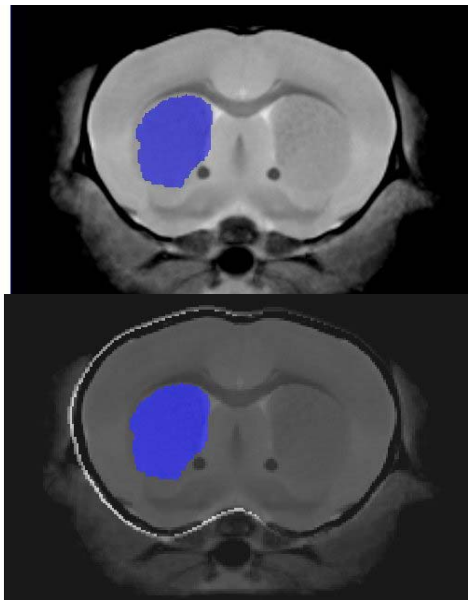

Figure 1: The top figure shows a target determinant for the left striatum overlaid on an anatomical mouse brain. The bottom figure shows the determinant of the created deformation field. The white rim outside the brain indicated areas that will grow to compensate the change in the striatum.

Results

Using a 5% FDR threshold, 20 out of 21 structures which had a 10% change in volume were recovered with 1 false positive. When the changes in volume of the structures were reduced by 5%, 17 out of 21 were found with 1 false positive. In all cases the registration process slightly underestimates the size difference in the effected structures. Furthermore it seemed that elongated structures (e.g., dentate gyrus) were more poorly detected than spherical structures (e.g., striatum). To test this hypothesis, we tested the correlation between the discrepancy in the detected and incuded change and the surface to volume ratio in structures. We found that volume changes in more compact and spherical shapes which have a lower surface/volume ratio can be more accurately detected (see Figure 3).

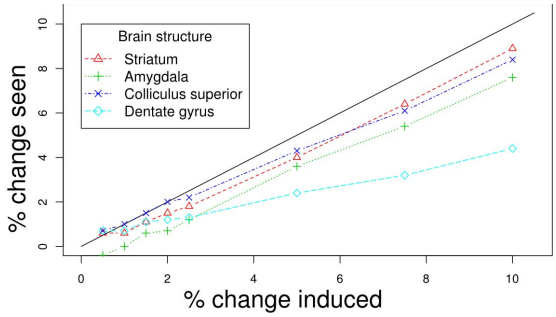

Figure 2: The relationship between induced changes and changes detected after image registraion in several structures.

Conclusion

From this investigation it is demonstrated that image based registration algorithms can reliably detect structural shape differences down to 5% in the structures with a lower surface to volume ratio, and reliably down to 10% in all others. A possible explanation for the correlation we see in Figure 3 is that a volume change in a structure with a higher surface to volume ratio will have a smaller impact on the displacement of the boundaries of that structure, and since image registration algorithms depend on local boundaries, it will be more prone to detection errors than a structure with a low surface to volume ratio. The ability to simulate deformation fields proves to be a powerful technique for assessing the structural varying sensitivity of registration algorithms to localize structural differences in the mouse brain.

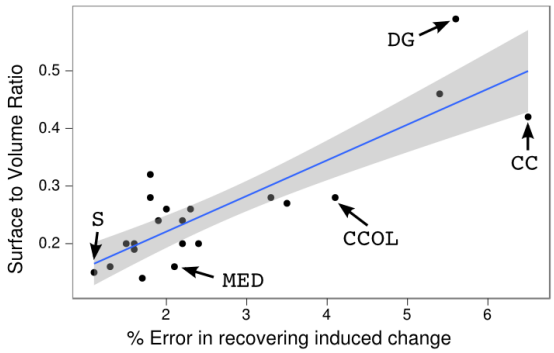

Figure 3: The relationship between the error in recovering the induced change and the surface to volume ratio for the 21 structures. (S = Striatum, MED = Medulla, CCOL = Cerebral Cortex Occipital Lobe, DG = Dentate Gyrus, and CC = Corpus Callosum)

References

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