

Automated segmentation of 3D histological mouse brains using a MRI-based 3D digital atlas

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Introduction

MR atlases are a new generation of digital atlases that can be easily recorded, annotated and are not biased by sample slicing such as histological atlases¹. Thus, several MRI-based 3D digital rodent brain atlases have recently become available. However, most descriptions of neuroanatomy and brain function in small animal research are based on histological and autoradiographic studies that remain the gold standards. These *post mortem* data are classically analyzed by manual delineations of regions-of-interest (ROI). Such analysis is time-consuming and subject to operator bias. To overcome these limitations, ROIs defined on digital atlases can be mapped on histological and autoradiographic images. This paper provides a method to register MRI-based 3D digital atlas on *post mortem* mouse brain images in order to automatically segment those data. We investigated the reliability of this method by qualitatively and quantitatively comparing the MR atlas-based segmentation with manual segmentation, regarded as the reference.

Material and Method

The selected atlas was derived from T1 and T2-weighted 3D MR images of 6 9-week-old C57BL/6J mice². We tested our method on autoradiographic and corresponding histological sections of 4 APP/PS1 mouse brains (Alzheimer's disease model strain, right hemisphere, 64±1 week-old) and 3 PS1 mouse brains (control strain, right hemisphere, 65±2 week-old). The blockface photographs captured prior to each section allowed providing co-registered and spatially consistent 3D *post mortem* volumes³. The hippocampus, the cortex and the striatum were manually delineated by an expert on the histological volume of one APP/PS1 and one PS1 mouse.

To co-register the atlas with *post mortem* data to be segmented, the T1-weighted MR image was first deformed to match with 3D reconstructed *post mortem* volumes. Deformation parameters were estimated by successively applying rigid, affine and elastic (Free Form Deformation) registration techniques. The reference image was the blockface volume for the first two transformations and the autoradiographic volume for the last one. The deformation parameters were then used to warp the 3D digital atlas.

Registration accuracy was qualitatively assessed by visual inspection of the superimposition of the contours of MR image on *post mortem* data. The agreement between atlas-based and manual delineated ROIs was also evaluated by measuring the Dice coefficient: $\kappa = 2 \times V(A \cap M) / (V_A + V_M)$, where V_A and V_M are the volumes of the Atlas-based and Manual segmentations, respectively.

Results

Figures 1 and 2 illustrate results obtained on an APP/PS1 mouse. Figure 1 shows the superimposition of the contours of the T1-weighted MR image on the 3D reconstructed histological volume before (A) and after (B) registration. Both the external contours (1) and those defining inner structures such as the corpus callosum (2) or the hippocampus (3) are correctly superimposed. Figure 2 presents the studied part of the 3D digital atlas (A) and displays that even if both volumes were not initially aligned (B), atlas outer edges (red transparent) are fitting with those of the blockface volume (blue transparent) after registration (C). Moreover, the atlas-based segmentation of the hippocampus (red) presents, after registration (C), a good matching with the manual segmentation (blue).

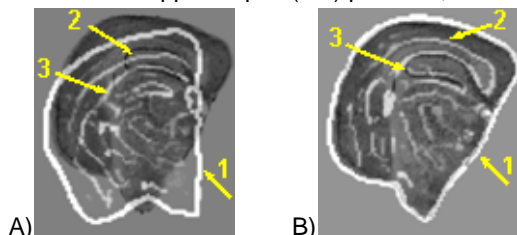


Figure 1 : Superimposition of the T1-weighted MR image contours on the histological volume before (A) and after (B) registration. Arrows 1, 2, 3 indicate external contours, corpus callosum and hippocampus, resp.

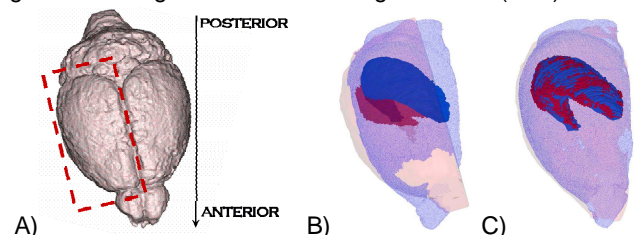


Figure 2 : Studied part of mouse brain (right hemisphere, dashed line in A). Superimposition of the hippocampus atlas-based segmentation (red) on the manual segmentation (blue), before (B) and after (C) registration.

Tables 1 - 2 display Dice coefficients computed for the cortex, the hippocampus and the striatum of one PS1 and one APP/PS1 mouse before and after registration. In both cases, overlapping scores are higher after registration and close to the maximal overlapping (1).

PS1 mouse (control)	ROI	κ before registration	κ after registration
	Cx	0,45	0,82
Hc	0,38	0,86	
Striat	0,45	0,79	

Table 1 : Dice coeff. (κ) computed for the cerebral cortex (Cx), the hippocampus (Hc) and the striatum (Striat) of one PS1 mouse.

APP/PS1 mouse (alzheimer model)	ROI	κ before registration	κ after registration
	Cx	0,56	0,84
Hc	0,41	0,90	
Striat	0,47	0,78	

Table 2 : Dice coeff. (κ) computed for the cerebral cortex (Cx), the hippocampus (Hc) and the striatum (Striat) of one APP/PS1 mouse.

Conclusion and Discussion

Our method was able to successfully co-register MRI image from a wild type mouse strain with 3D reconstructed *post-mortem* data from transgenic mouse strains. The visual inspection of the superimposition of atlas-based segmentations on manual tracings as well as the computation of overlapping scores have demonstrated that a MRI-based atlas could be used as a template for fully-automated mouse brain structures segmentation. This approach is promising to investigate histological and/or autoradiographic datasets, yielding more objective, easier and faster morphometric and metabolic comparisons between different strains relevant to neurodegenerative diseases. Furthermore, our approach could be easily extended to *in vivo* data segmentation in small animal imaging studies.

References

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