Automated Image Analysis of Many Mouse Brains

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Introduction

With the growing interest in mouse MR imaging, two issues have become apparent. Firstly, genetic and biological experiments typically require large cohorts of animals and imaging, by neccessity, has to be high throughput. Secondly, with this increased output of data, automated image processing techniques are of utmost importance to analyze and interpret the results. We address the first problem by imaging mice in parallel [1]. To address the second problem, we have developed an image analysis pipelining tool to register and average together many mouse brains in order to facilitate efficient brain structure measurements in large numbers of mice.

Methods

Using a 7-T, 40-cm bore magnet (Magnex Scientific, Oxford, UK) controlled by a Unity^{INOVA} console (Varian, Inc. Scientific Instruments, Palo Alto, CA), we performed two imaging experiments with the murine brain. In the first experiment we used age- and sex-matched animals of the inbred strain, 129Sv/cp/imj (n = 9). The brains were excised and perfusion-fixed in formaldehyde. We used custom-built solenoid coils and imaged two brains at a time. We used 3D spin echo imaging with sequence parameters: TR 1600 ms, TE 35 ms and a voxel resolution of $(60\ \mu m)^3$, resulting in an imaging time of 18:30 hours.

In the second experiment, we imaged the heads of live age-matched mice of the inbred strain, C3H/HeSnJ (n = 5). The imaging techniques were as in [2] with the exception of using $MnCl_2$ as a brain contrast agent [3]. The 3D spin echo sequence had imaging parameters of TR 300 ms, TE 10 ms and a voxel resolution of $(156\ \mu m)^3$, resulting in imaging time of 2:45 hours.

We applied our image analysis pipeline to both datasets. The pipeline starts by registering the brains to create an unbaised average brain with intensity averaging. The average brain image represents the entire group of mouse brains and is better delineated than the individual input images (Fig 1). The average image, therefore, enables precise anatomical interpretation such as manual segmentaion by an expert anatomist. The final step of the pipeline transforms the anatomical knowledge back onto the individual input images and calculates the corresponding statistics across the whole group.

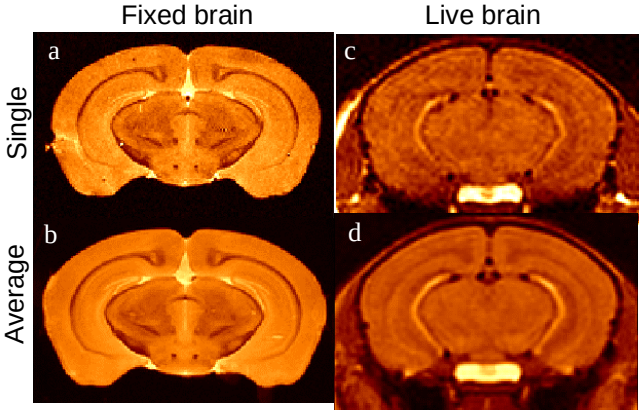

Figure 1. Coronal slices in both the live and excised brains. **(a)** A single excised mouse brain, **(b)** the average image from the excised brains, **(c)** a single live brain and **(d)** the average image from the live brains.

Table 1. The average volume and standard devation (in mm^3) of total brain volume and the cerebellum in the two datasets.

	Excised 129Sv brain (n = 9)	Live C3H brain (n = 5)
Total brain volume	487 ± 21	415 ± 24
Cerebellum	63 ± 4	53 ± 4
Cerebellar vol. as % of total brain vol.	13.0 ± 0.4	12.7 ± 0.3

Results and Discussion

We applied the imaging analysis pipeline to the data from the two imaging experiments described above. In both cases we manually segmented the cerebellum and the whole brain of the average model. The corresponding volumetric measurements in individual images were obtained by back registering the segmentation and the statistics across the two groups are given in Table 1.

This work demonstrates a robust and automated pipelining method for image analysis. The method has been successfully applied to two significantly different image datasets. We have reduced the time it takes to obtain volumetric data on a cohort of mice. Compare this to a typical situation of an observer who spends many hours manually segmenting numerous MRI brain scans. While we only present two structures measured in two strains, many more labels can be identified. The scope for further reasearch is broad as these tools not only provide a measure of variability within a strain of mouse brains but also enables analysis of potential morphological mutants.

References

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