Virtual Mapping of Cyto-architectonic Distinct Structures with MRI

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Introduction

Cytoarchitecture and myeloarchitecture are histological features that are used to segment the brain into neuroanatomical regions. Those histological procedures are the base of brain atlases used for neurosurgical navigation and brain mapping research. These procedures are based on the brain sample of a single subject and suffer from deformation artifacts (due to fixation shrinkage), and therefore, their correspondence with in-vivo brain mapping is limited. Recently we proposed a multi-parametric MRI acquisition and analysis framework called virtual.com imaging (virtual definition of tissue by cluster analysis of multi-parametric MRI) [1]. This framework includes 4 main analysis steps: 1) acquisition of multi-parametric data set (>3 MR based contrasts); 2) Contrast enhancement and dynamic range stretching; 3) principal component transformation to increase variability; 4) clustering. With this procedure we have shown that the human thalamus can be segmented into its sub-nuclei masses. In this work we further validated the virtual.com framework by comparing its segmentation of the rat thalamus with cyto-architecture mapping of the same sample.

Methods

Three Wistar male rats (4-6 months old) were scanned in a 7T/30 spectrometer (Bruker) under ~2.5% isofluorane anesthesia. The experimental protocol consisted of: Spin-echo images (TR=3500ms, TE incremented from 6 to 72ms in steps of 6ms) from which T2 maps were calculated; Gradient echo images (TR=1000ms, TEs of 3.5ms and 15 ms to produce T1 and T2* weighted images respectively, flip angle of 15^0), Spin-echo (TR=1000ms, TE=3.5ms) with and without magnetization transfer pulse to produce T1 and magnetization transfer (MT) weighted images. The Geometerical parameters were: Field of view: 30X25 mm^2, 18 slices with a thickness of 0.4mm, matrix dimensions of 192x160 resulting in a resolution of 0.156x0.156x0.400 mm^3. The brains of the rats were removed and fixed in 4% formalin and embedded in paraffin. Coronal cuts of 20 microns were obtained of the whole brain with 100 microns separation between slices. Silver staining of cell bodies was used for cyto-architecture mapping. The MRI volume data sets and clusters were coregistered to the histological slices using an in-house software and SPM2 (UCL, UK).

The input images for virtual.com algorithms were: proton density weighted image (the shortest TE in the spin echo acquisition), Calculated T2 map, T2* weighted image, gradient echo T1 weighted image with and without MT, and spin-echo T1 weighted image (total of 6 contrasts). The virtual.com algorithm was implemented with the k-means clustering algorithm and executed with an increasing number of clusters (k) until the clusters were not statistically different from one another.

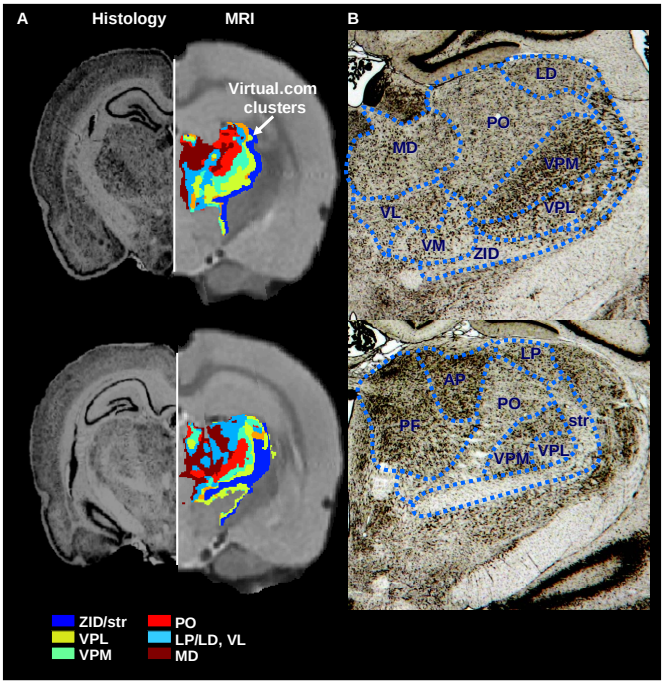

Figure 1: (A) Cyto-architectonic staining of the rat brain (left side) and T2 weighted MRI of the same brain (right side) with the virtual.com clusters superimposed. Each color represents different MR contrast cluster. Note the MRI brain is slightly bigger than the histology brain due to shrinkage following histological preparation. (B) Enlargement of the thalamus region of the histological section with the different nuclei mass marked with blue borders. Note the correspondence between the MRI clusters and the cyto-architectonic arrangement of the nuclei.

Results & Discussion

Virtual.com found 7 statistically different clusters in the rat's thalamus. Figure 1A shows cyto-architectonic maps of the rat brain on the left, and the MRI (T2 weighted image) of the same rat with the virtual.com clusters superimposed on the right. Figure 1B shows an enlargement of the thalamus region of the histological section depicting the different nuclei with their borders marked in blue. The visual correspondence between the MRI clusters and the cyto-architectonic mapping allows the assignment of clusters to different nuclei (see Figure 1). In addition, the difference in cyto-architecture of the different nuclei, corresponded with their MRI contrast profile. For example, the VPL nucleus that had the highest cellular density (Figure 1B) also had higher contrast on PD and T1, (light green in Figure 2), whereas the ZID/str nucleus is composed mostly of white matter fibers (blue in Figure 2).

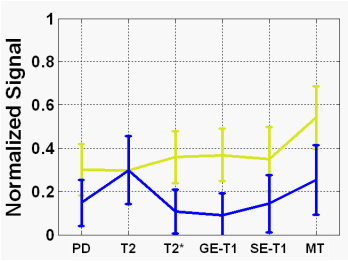

Figure 2: MRI contrast "finger prints" for two clusters shown in figure 1 (The VPL and ZID/str). These two regions differ in the fiber and cell composition and it is reflected in their cluster contrast profile which is higher in PD and T1 for the denser tissue.

Conclusions

In general, virtual.com and multi-parametric MRI clustering allows segmentation of neuronal tissue to its cyto-architetonic components. The advantage of using many contrast mechanisms is that fine morphological differences between tissue compartments become significant. This methodology can evolve into an in-vivo cyto-architectonic mapping procedure that can be applied on the single subject level.

References

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Acknowledgements: We wish to thank Prof. Katrin Amunts and Ms. Ferdag Kocaer for their help with the histological procedure. This work was financed by the German-Israel Science (GIF) foundation grant.