Virtual Definition of Tissue by Cluster Analysis of Multi-parametric MR imaging (Virtual-dot-com imaging)

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Introduction

Resolution and contrast limits of MR images are the main factors that restrict our current ability to segment and define certain tissues. While typical human brain image resolution lies in the order of 1-2 mm, some CNS structures are much smaller than that. In addition to that, contrast differences within a specific region might be close to noise level and prevent us from accurately defining sub-regions within it. In this work we devised an algorithm (virtual-dot-com imaging) that detects and define small sub-cortical regions based on contrast enhancement and cluster analysis.

In order to test the algorithm we applied it on the thalamus**.** Histology shows that the thalamus is composed of at least 9 different nuclei. These nuclei have different cytoarchitectonics and different functions. It is expected that the different cyto and myelo-architecture of the thalamus nuclei will be differentially weighted in a multi-contrast MRI protocol. These contrast differences combined with clustering algorithm might allow us to reliably and accurately define the sub-nuclei.

Methods

9 healthy male subjects aged 25-30 underwent MRI in a 3T scanner (GE) using an 8-channel head coil. Each volunteer was subject to 10 different image contrasts (summarized in Table 1). All images were created in an axial plane with FOV of 20x20 cm^2, slice thickness of 1.5 mm, image matrix of 128x128 giving cubic resolution of 1.5x1.5x1.5 mm^3. The total MRI protocol lasted for 40 minutes.

The 10 different contrast volumes were realigned to correct for head movements and co-registered to obtain similar slice locations across subjects using SPM (UCL, London, UK). Following the co-registration, the thalamus was semi-automatically segmented. On the segmented thalamus, we used basic contrast enhancement in order to exclude outlier pixels thus stretching the dynamic range of the image. Next we performed cluster analysis based on the multi-parametric data including the following steps: 1. Normalizing the data to create a uniform scale between the different imaging methods. 2. Transforming the data into its P.C.A (principle component analysis) space to increase the variance. 3. Running a clustering algorithm such as "K-means". Statistical difference between the clusters was calculated using the ANOVA test.

Table 1	TR (ms)	TE (ms)	Exp. Time	Misc.
1. FLAIR	9000	140	4:50	TI= 2100ms
2. T2 weighted	7000	150	3:00	ETL = 32
3. Proton Density	7000	6	3:00	ETL = 32
4. T1 weighted	550	8	5:00	
5. T1 + MgT	550	8	6:20	IF = 1.2kHz
6. $T2^*$	600	2	5:00	$FA=20^0$
7. $T2^*$	600	15	5:00	$FA=20^0$
8. $T2^*$	600	32	5:00	$FA=20^0$
9. STIR	5000	25	3:00	TI=130ms
10. SPGR	400	2	2:30	$FA=12^0$

MgT = Magnetization transfer, TI = inversion time, ETL = echo train length, IF= irradiation frequency, FA = flip angle

Results

The clustering algorithm was able to detect as many as 7 significantly different clusters in the thalamus. In addition, high symmetry between the two thalami of the same subject was observed. These clusters were assigned to the different thalamus nuclei based on two thalamus atlases [1] [2] that were digitized and co-registered to our template (see Figure 1). The position of the clusters found by our algorithm and the nuclei positions according to the atlas was very similar in all subjects.

For each cluster we could calculate the normalized signal intensity across all acquired image methodologies. This provided a contrast finger print per cluster. Obviously the contrast finger prints were significantly different between the clusters but were highly correlated across subjects. This is shown in Figure 2 where different contrast finger-prints are shown for 4 different clusters. The small standard deviations indicate the resemblances of these contrast finger prints across subjects.

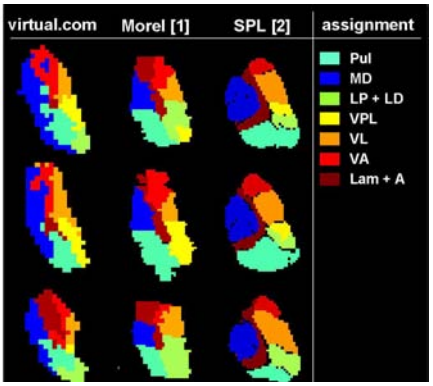

Figure 1: Left column – cluster analysis of the segmented thalamus using the virtual.com algorithm for 3 different slice locations. The middle and right columns represent two atlas based thalamus segmentations of the same slices.

Discussion and Conclusions

We found that using advanced image processing routines one can extend the use of MRI to study and define sub-structures for individual subjects. The use of the virtual.com imaging algorithm enables not only to detect the sub thalamic nuclei but also to characterize them in terms of contrast finger-print. For instance we could shows that cluster 7 defined as the internal lamina has high contrast in the T1 weighted sequences and low in the T2 suggesting that it is composed mainly from white matter fibers as known from histology. By contrast, cluster 2, defined as the medio-dorsal nucleus has the opposite contrast characteristics suggesting that it is composed mainly for cellular structures (neurons and glia).

The potential implementations of virtual.com imaging are many: first the methodology should be tested on diseases on thalamus (e.g. Creurtzfeld-Jacob disease). Second it can be applied on smaller cortical and sub-cortical area (e.g. defining contrast finger-print to the different Brodmann cortical areas), segmenting other sub-cortical nuclei such as the amygdala and the hypothalamus. Furthermore, the presented methodology might be used to define the specific characteristics of certain tumors and help in the diagnosis of those.

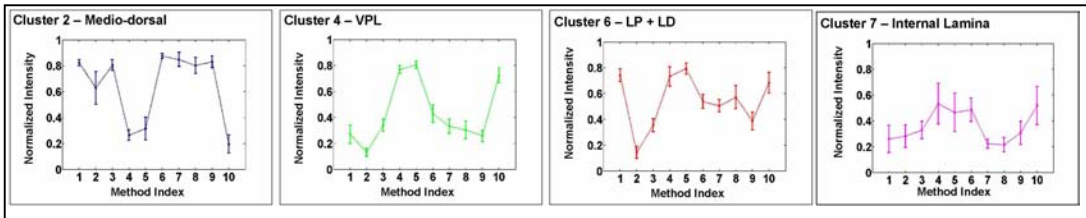

Figure 2: Contrast finger-prints for 4 clusters representing the medio-dorsal, the VPL, the LP+LD and the internal lamina nuclei. The method index is the same as in Table 1.

References

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