Characterization of the Substantia Nigra in Elderly Subjects by Multi-modality MRI

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Introduction

The segmentation and characterization of small brain structures (e.g. thalamus sub-nuclei) by MRI is restricted by contrast and resolution limits. Recently, the virtual.com (virtual definition of tissue by cluster analysis of multi-parametric MRI) image acquisition and analysis framework has been suggested for characterization, and segmentation of brain structures (1). The essence of virtual.com is that it attributes a specific contrast finger print (i.e. a vector of the mean intensity in each MR contrast methodology) to every region that it segments. Using this framework, segmentation of the thalamus to its sub-nuclei using high resolution, conventional MR sequences, was achieved.

The sunstantia nigra (SN), lies within the midbrain and controls aspects of movement inhibition and supervision. It is composed of two compartments that have different morphology and different function, called the SN-compacta (SNc) and the SN-reticula (SNr)., It is well known that the SN degenerates during Parkinson's disease and during normal aging, and that the degeneration is different in the two compartments. The SN has high levels of a substance named Ferritin which gives it its black color. Ferritin contains large amounts of iron ions. Iron deposition is known to occur during normal aging, yet the quantification and characterization of this process by MRI is limited. In this work we used the virtual.com framework to segment the SN's compartments and characterize their unique contrast finger-prints that facilitated quantitative comparison between young and elderly subjects.

Methods

Eight subjects aged below 30 and four subject aged above 65 years (both without any neurological disorders or diseases) 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 coils bias field was corrected using SPM. Next the midbrain was manually marked using its salient landmarks. The following step was to execute the virtual.com algorithm on the midbrain's ROI. The main steps of this algorithm are: 1. Basic contrast enhancement in order to exclude outlier pixels and thus to stretch the dynamic range of the images. This step also normalizes the different MRI methods to have the same value range (i.e. 0-1); 2. Dimensionality and noise reduction using Principle Component Analysis; 3. Executing the K-means clustering function with a growing number of clusters, until reaching a statistical difference criteria (measured by ANOVA) between the clusters.

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

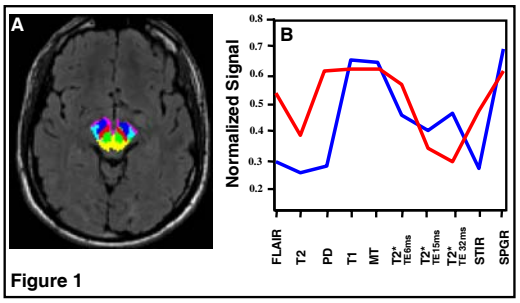

Figure 1

Results & Discussion

Using the virtual.com framework, we were able to segment the midbrain into six clusters (Figure 1), two of which were assigned, by visual comparison with an atlas, to the two parts of the SN (SNc and SNr - red and blue regions in Figure 1). Each of these regions presents a unique contrast finger-print (Figure 1B) that well suits the SN – i.e. low signal in FLAIR, T2 and especially T2*. Note the large difference between the two regions in the PD method indicating different tissue density between them. Similar segmentation was done for all twelve subjects revealing significant differences in the sizes and finger-print of the SNc and SNr between age groups. Three-dimensional analysis of the SNc and SNr structures demonstrates massive shrinkage of the SNc compared with the SNr in older subjects (Figure 2A) which is also manifested in the sizes of the two segments (Figure 2B, averaged over all subjects) and in the ratio between their volumes (Figure 2C). The finger-prints of the SNc and SNr (Figure 3) show that the SNr profile is very similar between the two age groups. By contrast, the SNc has different profiles with significant differences in the heavily weighted T2* contrast image (method #8) where old subjects have higher signal than young subjects. This implies longer T2* at this region for old subjects that might indicate of iron disposition in this region (i.e. lower iron content).

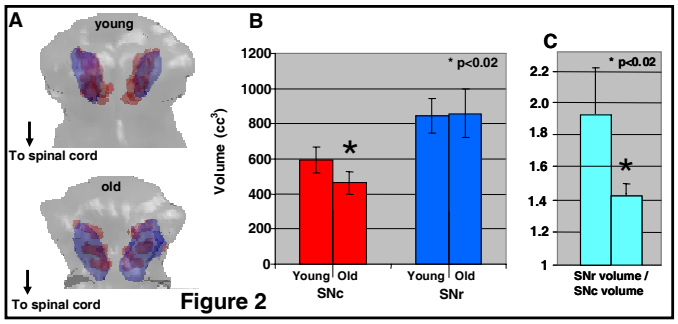

Figure 2

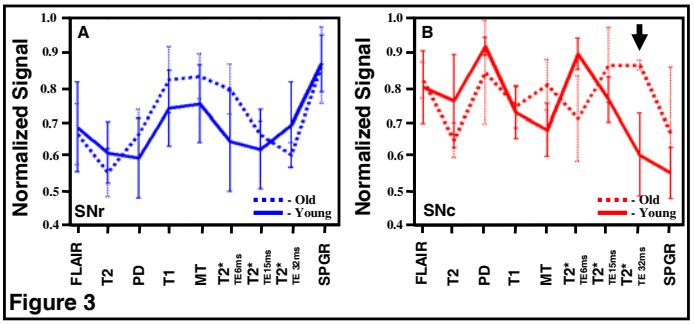

Figure 3

Conclusions

The virtual.com MR image analysis framework provides means to quantify MRI contrast changes between different methodologies, across subjects. Within the scope of this work, this algorithm enables characterization and follow-up of neurodegenerative processes in the SN. However, this methodology can be applied to the study of any brain-substructure or pathology.

References: 1. Y. Yovel, Y. Assaf. Virtual Definition of Tissue by Cluster Analysis of Multi-Parametric MRI, Neuroimage, In press.