# THREE-DIMENSIONAL VOLUMETRIC ANALYSIS OF SUBSTANTIA NIGRA IN PARKINSONS DISEASE AT 7.0T MRI

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**Introduction**

Parkinson's disease (PD) is a neurodegenerative disorder resulting from progressive loss of dopaminergic (DA) neurons in the substantia nigra (SN). Especially the degree of neuronal loss was significantly higher in the *nigrosomes* and the degree of loss of dopamine-containing neurons in the SN was related to the duration of the disease. [1] Therefore, change of the SN structure has been regarded to hold greatest potential for use in the diagnosis of PD. High resolution 7T MR image were able to show markedly improved images of the SN and the surrounding midbrain structures. Our previous study with 7T MRI indicated that 2D analysis of the shapes and boundaries of the SN. [2] In this study, we were directly investigated volume changes in the SN between the normal controls and PD patients by using 7.0T MRI.

**Method**

***Subject :*** We studied 18 subjects who were obtained on 9 patients and 9 age-matched controls. The control group included 9 subjects [age (mean ± S.D.) : 59.7 ± 5.1 years; 1 male and 8 females] without any known neurological deficits or abnormal findings on conventional 1.5T MR images. The PD group included 9 patients [age (mean ± S.D.) : 60 ± 7.2 years ; 3 males and 6 females]and Hoehn-Yahr score ranged from 1 to3. ***MRI acquisition :*** We used a 7 tesla research-prototype MRI scanner (Magnetom 7T, Siemens) using 7 Tesla-optimized 8-channel radiofrequency (RF) coil designed specifically for use in this study. 3D T2*-weighted gradient-echo sequence parameters were as follows : TR/TE = 50/25 ms, flip angle = 10°, total acquisition time = 8.23 min, bandwidth = 30 Hz/pixel and matrix size = 504x576, in-plane resolution was 0.35 mm iso-voxel. In addition, we obtained whole brain images using a T1-MPRAGE sequence for normalizing the SN due to variance of brain size in each subject. T1-MPRAGE image was scanned on a 1.5T clinical MRI scanner (Avanto, Siemens). The used T1-MPRAGE parameters were as follows: TR/TE = 1160/4.27 ms; flip angle = 15 and matrix size = 256 x 256. The in-plane iso-voxel resolution was 0.9 mm. ***Image tracing and 3D model reconstruction :***To make 3D SN and ICV model, we has been manually segmented using software of 3D Slicer (http://www.slicer.org). Segmentation of the SN was been processed from lower slices of caudal midbrain to upper slices. To identify clear boundary of SN, we used phase image. It distinguished SN from STN which were overlapped in some image slices. ICV was also segmented and determined following the protocol of Eritaia et al. [3] ***Volumetric analysis :***As brain size varies across subjects, it is necessary to normalize individual SN volumes with respect to ICV. Several morphological studies have used already ICV as useful normalizing factor. We were calculated 'normalized SN volume ratio' using the following formula.

$$\text{Normalized SN volume} = \frac{\text{Raw SN volume}}{\text{ICV of the same subject}} \times 1000\ (\text{mm}^3)$$

**Results**

Representative samples of 3D SN and ICV model images of the normal control and PD, namely normal control and PD patient with an H&Y2 are selected and compared. **Fig 1. (*top*)** shows 3D model of SN in the ventral and dorsal positions and differences in the intermediate and caudal levels between the two group (see red arrow). This pattern were closely mirror of similarity between our results and the subgroups of dopamine-containing neurons named *nigrosomes* in a histology study using immunostaining for calbindin $D_{28K}$. [1]. **Fig 1. (*bottom*)** is the 3D segmented results of ICV. The entire SN was divided into three parts on the rostral, intermediate, and caudal levels. **Fig 2. (A-C)** shows group difference which is calculated by normalized SN volume ratio of the individuals who participated in the experiment. The SN volume were averaged both (left and right) side in normal control. For PD patients, the values of SN volumes contralateral and ipsilateral were compared with normal controls. Quantitative measurements revealed that the normalized SN volume ratio in PD patients [n=9, 2.252] were larger than those of the age-matched normal controls [n=9, 1.843]. The comparison of normalized SN volume in each portion between controls and PD (contralateral , ipsilateral) were represented ; in rostral portion [0.8468, 0.8847, 0.9148], in intermediate portion [0.9154, 1.1293, 1.0826], in caudal portion [0.1466,0.1691, 0.1488], respectively. We have also measured UPDRS motor score dependent correlation and the result is shown in **Fig.2 (D)**. We found normalized SN volume ratio negatively correlated with the UPDRS motor score. ($r^2$=0.126, *P*=-0.023). As the UPDRS motor score increase, the normalized SN volume ratio was decreased.

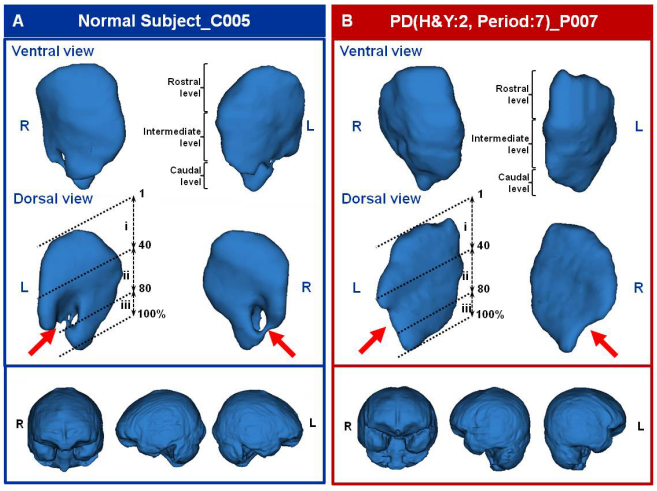


**Fig 1. 3D reconstruction of the SN (*top*) and ICV (*bottom*). 3D model of SN and ICV in normal control (A), 3D model of SN and ICV in Parkinson's disease patient (B). The entire SN was divided into three parts on the rostral, intermediate, and caudal levels. Red arrow indicates that inner structure of the SN change in PD.**

**Discussion**

This study demonstrates the potential of the 7.0T MRI for the quantification of volume changes in the SN. Especially, in the intermediate and caudal aspects, significant correlation was found subgroups of *nigrosomes*. This pattern of SN disappeared commonly in all the PD patients. The measured correlation analyses show that UPDRS motor score dependent correlation. These statistical results would obviously be useful in setting the criteria for diagnosis of digression of PD patients.

**Reference**

1] P. Damier, et al., *Brain* 122(Pt 8) (1999) [2] Z.H. Cho, et al., *Movement Disorders* 10-0301.R2 (2010) [3] J. Eritaia, et al., *Magnetic Resonance in Medicine* 44:973-977 (2000)

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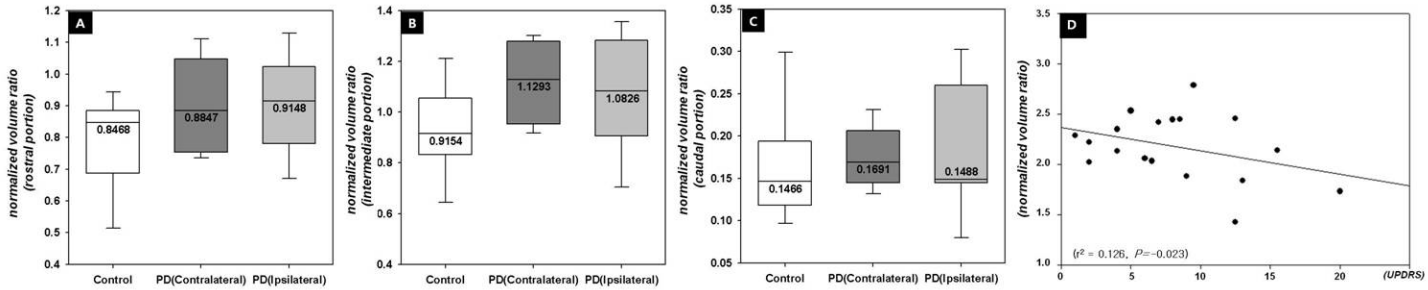


**Fig 2. Results of analysis in typical PD patients and normal controls (A-C). Correlation between normalized SN volume ratio and UPDRS motor score (D).**