Detecting Alterations in Caudal Portion of Substantia Nigra in Parkinson's Disease

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Target Audience Academic researchers, physicians and scholars who are interested in studying the alterations of substantia nigra (SN) in Parkinson's disease (PD)

Purpose Magnetic resonance imaging (MRI) can be used to measure the volume of SN [1, 2]. Previous studies have reported a volumetric change in the SN of PD patients when compared with healthy controls [2]. As histological studies suggest that the caudal portion of SN may be more significantly affected by PD [3], we hypothesized that similar alterations could also be detected with MRI in PD patients. This hypothesis was investigated in this study.

Methods Forty-one subjects (including 19 controls and 22 PD patients) participated in this study. MRI data were obtained on a 3.0 Tesla Siemens Magnetom TRIO scanner (Siemens Medical Solutions, Malvern, PA) using a 2D gradient echo (GRE) sequence with magnetization transfer contrast (MTC) preparation pulse: TR/TE = 335/2.68 ms, 15 slices, slice thickness = 3.0 mm, FOV = 200 × 162 mm^2, matrix size = 512 × 416, 7 measurements, FA = 40º, MTC pulses (FA = 300°, 1.2 kHz off-resonance, 10 ms duration), and bandwidth = 465 Hz/Pixel. Whole brain T_1 images were also acquired with a MPRAGE sequence: TE/TR/TI = 3.02/2600/800 ms, FA = 8°, voxel size = 1.0 × 1.0 × 1.0 mm^3. The scan slices of the above 2D GRE-MTC sequence were positioned based on the sagittal T_1 images (Fig 1a). Imaging data were analyzed with AFNI [4]. The SN was segmented by following the same procedure as in the previous study [1]. Volumes (# of voxels) and centers of mass (CM) were calculated for the left and right SN regions in all slices which showed detectable SN. Distances between the left and right CMs were also calculated (Fig 1b). Further statistical analysis was performed with SPSS.

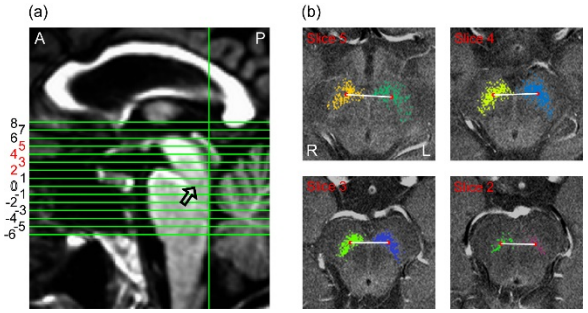

Fig 1. (a) Slice positioning. Slices were positioned perpendicular to the dorsal edge of the brain stem along the fourth ventricle with one slice running across the pons and midbrain junction (pointed by arrow). This slice was referred to as S0. The slices above and below were named as S1, S2, ... and -S1, -S2, ..., respectively. A: anterior, P: posterior. (b) CM of segmented SN. The SN could be segmented in S5, S4, S3, and for some subjects, in S2. Red dots: CMs. R: right, L: left.

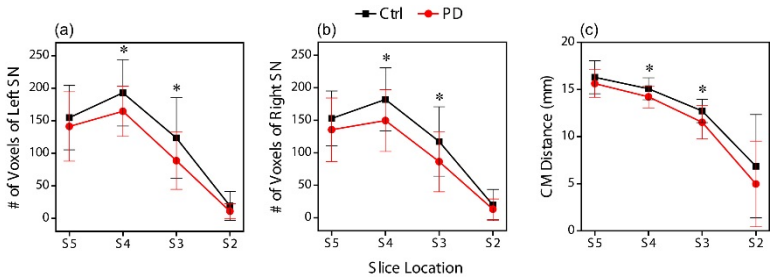

Fig 2. Group differences in SN volume (# of voxels, a and b) and CM distance (c). Ctrl: controls. * in (a) and (b): 1-tail t-test, $p < 0.05$. * in (c): 2-tail t-test, $p < 0.05$.

Results A 2 (group: control, PD) × 2 (side: left, right) × 4 (4 slice locations) ANOVA on the SN volume showed that the group, side and slice location effects were all significant ($p < 0.05$). One-tail t-test showed that the controls had larger SN volumes in S4 and S3 locations than the PD (Figs 2a and 2b, $p < 0.05$). A 2 (group: control, PD) × 4 (4 slice locations) ANOVA on the CM distance showed that the group and slice location effects were all significant ($p < 0.05$). Further 2-tail t-test showed significant ($p < 0.05$) difference in CM distance in S4 and S3 locations between the control and PD groups (Fig 2c).

Discussion These *in vivo* data measured with MRI also suggest that the caudal portion of SN is significantly affected by PD, which is consistent with the findings of histological studies on post mortem brains [2]. Moreover, we predicted that the PD induced neuronal loss could occur in the lateral parts of both left and right SNs, which could lead to a shift of the CMs of SNs toward the midline of brain stem. Therefore, the distance between the CMs of the left and right SNs could be shorter in PD patients. Our data support this hypothesis. The voxel count of SN for the most caudal slice location (S2) was much lower than those for the other locations (Figs 1b, 2a and 2b). For some subjects, including both controls and PD patients, the SNs were not detectable in this slice location. This result may be attributed to the neuronal loss in PD, or to the possibility that this slice location is beyond the anatomical range of SN in some subjects. For these subjects, zeros were set for the number of voxels and CM distance in the above ANOVA analysis. Future MRI studies with thinner slices may generate a more accurate estimation of PD effects on the SN in this brain location.

Conclusion PD induces significant alteration in the caudal portion of SN, which may be used as a biomarker in clinical diagnosis.

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