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Universality analysis of the existence of substantia nigra "swallow tail" appearance of non-Parkinson patients in 3T SWI

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Abstract. – OBJECTIVE: To use the 3.0T susceptibility-weighted imaging (SWI) for universality analysis of the "swallow tail" appearance in the substantia nigra of non-Parkinson disease and discuss its lack of the value of imaging diagnosis of Parkinson disease (PD).

PATIENTS AND METHODS: Take 3.0TMR SWI in 60 PD patients (Group PD) and non-PD volunteers (Group N-PD), on the map of range analyze morphology and number of "swallow tail" appearance in *substantia nigra* of N-PD group volunteers, and compare the performance image of the corresponding region of the patients in the PD group.

RESULTS: After, 15 patients with lesions in the brain stem and significant motion artifacts were excluded. Forty-nine cases of group N-PD (96.08%) had typical "swallow tail" appearance in the bilateral or unilateral substantia nigra compacta posterolateral. All 54 patients with group PD (100%) lacked the "drop" rear elliptical high signal.

CONCLUSIONS: On the 3.0T SWI range map, the "swallow tail" appearance is ubiquitous in the substantia nigra of patients with non-PD. The deficiency of the signs has high sensitivity and specificity for PD diagnosis.

Key Words:
Parkinson disease, Susceptibility weighted imaging, *Substantia nigra*.

Introduction

Parkinson's disease[1-3], (PD) is a common neurodegenerative disease. Although the etiology and pathogenesis of this disease are not clear, it is related to abnormal iron metabolism[4,5]. In 1999, Damier et al[6] through autopsy, pathology found a PD biomarker nigrosomes in the substantia nigra of healthy people while in the substantia nigra of patients with PD the marker was deleted. In nearly two years, researchers[8-11] tried to use the 7.0T and 3.0T scanner on healthy people and specimens of PD patients for susceptibility-weighted imaging (SWI)[7] and compared the results with pathological staining specimens. They found a wedge high signal in the normal middle at 1/3 substantia nigra, as the equivalent of the nigrosomes-1 pathological anatomical position. In April 2014, Schwarz et al[12] used 3.0T SWI to study *in living body*, and reached a similar conclusion. He named the black matter structure of low signal surrounding the healthy nigrosomes-1 zone as the "swallow tail" appearance. The purpose of this study is to investigate the universal "swallow tail" appearance existence in non-PD individuals, and analyze the sensitivity and specificity of the deficiency of the signs for PD diagnosis.

Patients and Methods

Clinical Data

All subjects consented to the examination content by signing the informed consent prior to the exam. A total of 60 PD patients (group PD) from the neural department internal medicine of the Xiangyang Hospital affiliated to Hubei College of Medicine from June 2012 to May 2014 were selected for this study. There were 37 male cases and 23 female cases. Their age was 48-79 years old, with an average of (66.21 ± 7.73) years old. The sick time was 3-12 years, with an average of (7.72 ± 3.51) years. Patients were all right-hand-

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ed. The patients were diagnosed by experts of Neural Extrapyramidal Disease Department of Internal Medicine. The diagnostic criteria referenced the clinical diagnostic criteria of the British Parkinson Disease Association and excluded other Parkinson syndrome (Parkinson plus syndrome, tremor, secondary Parkinson syndrome). All subjects underwent the Mini-mental state examination, MMSE, the Montreal cognitive assessment, and the MoCA for cognitive evaluation to exclude patients with dementia.

Sixty non-PD elderly people whose age, gender and handedness-matched as control (Non-Parkinson's, disease, N-PD) group were selected. These included 30 male cases and 30 female cases, aged 52-77 years old, with the average age of (65.37 ± 9.22). The subjects had no definite PD clinical symptoms and related history, and the conventional MRI examination of the brain was permitted for mild brain atrophy (47 cases), different degrees of cerebral infarction (34 cases), and a small amount of cerebral hemorrhage (8 cases) or tumors (4 cases) (Table I).

Scanning Method

The GE Company's Signa HDXt 3.0T superconduct MRI scanner was used to take eight channel high-resolution scans of the head-neck coil, with axial baseline parallel corpus callosum body direction. The scanning sequences included: axial SE T2WI (TR 8000 ms, TE 113 ms); T1WI Flair (TR 1814 ms, TE 23.8 ms, TI 860 ms); axial SWI: Oblic 3D Mode, FSPGR, TR/TE: 68.2 ms/6.06, 13.44, 20.81, 28.18, 35.55, 42.92, 50.30, 57.67 ms, flip angle 20°, the thickness of 2 mm, the layer distance of 0 mm, FOV = 24 mm, excitation frequency NEX = 1, matrix of 416 * 356, accept the bandwidth of 31.25. The original image was obtained on aw 4.6 workstation by Functool software with Magnitude imaging and Phase image map.

Image Analysis

All images were read by two senior radiologists. Each SWI amplitude diagram showed visible nigrosomes with high signal, and they analyzed its morphological features. The 120 cases were classified in the N-PD and PD group respectively for count, compared with the clinical gold standard, analyzed the lack of the signs used to determine the sensitivity and specificity of PD.

During the data image acquisition and determining measurement of the related features, in order to reduce the visual error, all images were measured by the same physician. For patients with typical wedge substantia nigra high signal, we measured its widest point of the lateral wedge at the high signal behind the dense zone (a). Then, we measured the vertical middle width of the long axis of the high signal in the substantia nigra and the wedge (b), and then divided them into ratio (a/b), in order to reduce the errors due to different patients with different brain capacity.

For patients whose "swallow tail" sign was not typical, but also with the strip of high signal in substantia nigra, we measured at the widest of its high signal strip (c), and obtained the corresponding ratio by the dividing the width of the middle level in the substantia nigra (c/b).

Statistical Analysis

We used the SPSS17.0 statistical software package (SPSS Inc., Chicago, IL, USA). Two groups of gender distribution were tested by the χ^2 test; age distribution was tested by the independent sample *t*-test. The average value of

Table I. General informations of the PD and N-PD groups.

General informations	PD group (60 cases)	N-PD group (60 cases)
Gender [M/F(cases)]	37/23	30/30
Age (years)	66.21 ± 7.73	65.37 ± 9.22
Right-handed (cases)	60	60
Brain atrophy (cases)	51	47
Cerebral infarction (cases)	40	34
Cerebral hemorrhage (cases)	6	8
Nuclei iron deposition (cases)	2	4
Brain tumors (cases)	0	4
Cerebral vascular malformations (cases)	1	2

The gender distribution of the two groups performed χ^2 test, $p = 0.270 > 0.05$; age distribution of the two groups performed independent samples *t*-test, $p = 0.590 > 0.05$, it showed no significant difference, comparable.

each group of data measured in the image and the corresponding ratio were calculated, represented by ($\bar{x} \pm s$). The result of the reclassification of physicians and clinical gold standard were contrasted. χ^2 test, specificity and sensitivity were calculated. $p < 0.05$ was considered statistically significant.

Results

The data of gender distribution tested by the χ^2 test was $p = 0.27 > 0.05$ and the data of age distribution tested by the χ^2 test was $p = 0.59 > 0.05$. So, gender and age of the two groups had no significant difference and could be compared (Table II).

N-PD group of 47 cases (including patients with a variety of other basic diseases) whose wedge or "drops" like high signal in the bilateral substantia nigra are visible (Figures 1-A,1-B,2). This consists of the anteromedial band fusion lateral oval structure. Among the 14 cases, a clear, bilateral substantia nigra trailing edge oval high signal and a less clear front strip is shown (Figure 1-C); two cases whose complete "drops" like high signal on one side of substantia nigra was visible. The high signal intensity on the other side was not clear. There are eight cases of non-clear high signal intensity in the bilateral substantia nigra. The original image was analyzed, and six cases of evident brain motion artifacts were found. Another two patients with brainstem area revealed an old infarction or hemorrhage. One case of local metal artifacts affected the observation. The "Drop" at the widest diameter line was a = 1.22-3.43 mm, with the average (2.06 ± 0.54) mm, corresponding to the width of the middle level of the substantia nigra vertical high signal band of about b = 4.88-7.95 mm, with the average (6.74 ± 0.89) mm, a/b = 0.21~0.43, and (0.31 ± 0.07) mm.

In the four cases of the N-PD group, the bilateral basal ganglia, red nucleus, *substantia nigra* and dentate nucleus signals decreased, but the bilateral "droplets" high signal was still clearly shown (Figure 2).

In 54 cases of the PD group, the "water drop," rear elliptical high signal structure showed deletion (Figure 1). Among which in the 35 cases "water" like high signal was completely absent. In the other 13 cases, the ferret-like high signal was still faintly visible on one side. In the six cases ferret-like, a high signal was visible in the bilateral. The maximum width of strip high signal was c = 1.13-1.32 mm, with the average (1.22 ± 0.05) mm. The middle width of substantia nigra of the corresponding level was b = 4.90-7.51 mm, with the average (6.69 ± 0.73) mm, c/b = 0.15-0.25, and (0.19 ± 0.03). The motion artifact of the other two cases was heavy, with a visible old infarct in the brain stem area of one case. Three cases of local metal artifacts affected the observation.

Two senior radiologists reclassified the control results on all patients in the PD group and N-PD group that suggested the deletion of nigrosomes-1 high signal for PD sensitivity. The determination was 100%, specificity was 96.08%. Amongst which, eight cases of heavy motion artifact, four cases of brain stem regions with metal artifacts, and three cases of old infarction or he-

Table II. Two physicians reclassified patients compared with clinical gold standard according to nigrosomes-1 high signal was visible or not in *substantia nigra*.

n = 105	Physician A		Physician B		Agreement	
	N-PD group	PD group	N-PD group	PD group	N-PD group	PD group
Unilateral or bilateral visible (cases)	47	0	50	1	49	0
Invisible (cases)	4	54	1	53	2	54
Clinical gold standard (cases)	51	54	51	54	51	54
Lack signs of sensitivity in the diagnosis of PD	100%		98.15%		100%	
Lack signs of specific in the diagnosis of PD	92.16%		98.04%		96.08%	

χ^2 test was used according to the signs of "yes", "no" classification. The result was $p = 0.00 < 0.05$ bilateral. The differences were statistically significant.

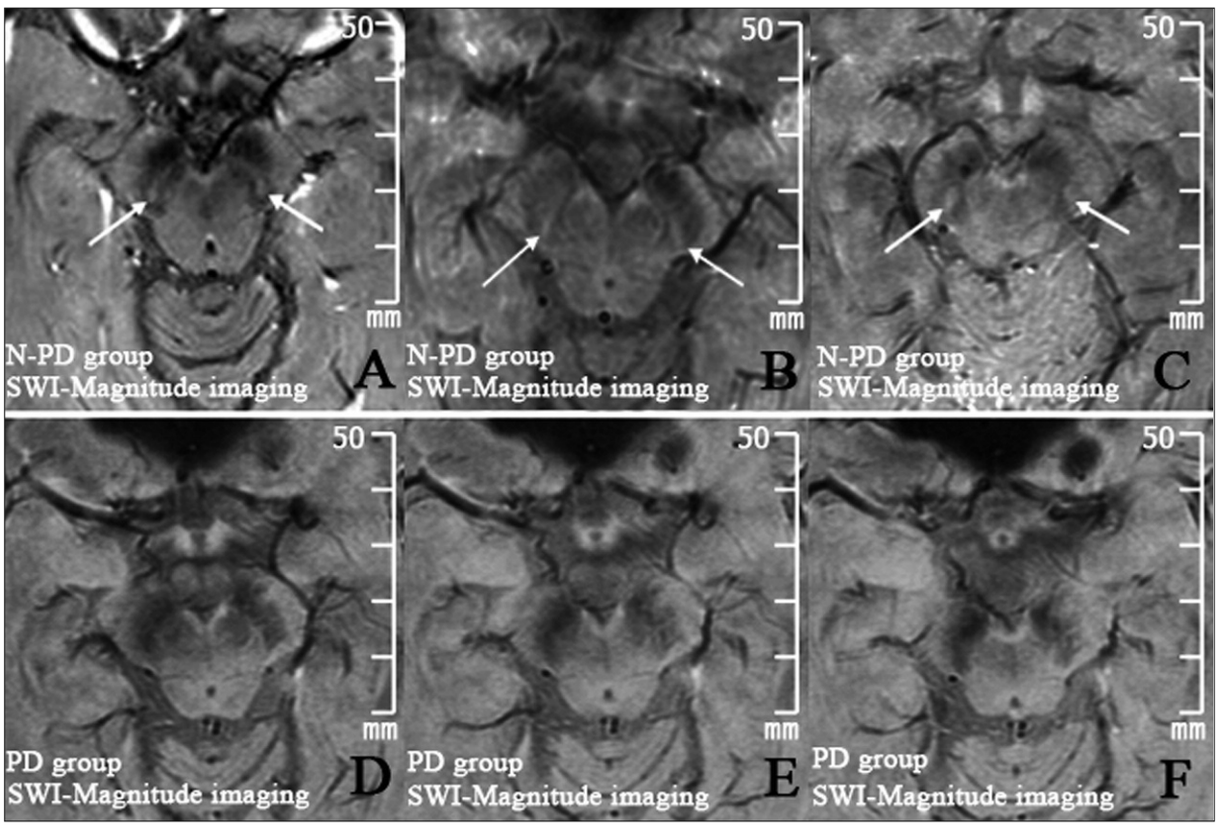

Figure 1. On 3T SWI amplitude diagram, the bottom level of substantia nigra of N-PD group compared with PD group; ***A,***-***B,*** SWI axial amplitude diagram of three non-PD volunteer: from top to bottom, just the end of the level of red nucleus can be displayed the substantia nigra rear nigrosomes-1 high signal (***A,*** "drop" shape; ***B,*** wedge; ***C,*** oval. *White arrow*), showing "dovetail syndrome"; ***D,***-***F,*** SWI axial amplitude diagram of PD patients: in three consecutive levels of the corresponding region, "dovetail" signs were missing.

morrhage in brain stem area. Since the local structure images were not clear, they were excluded in statistics.

Discussion

Parkinson's disease is a common neurodegenerative disease of the central nervous system[13-20]. The neuropathological based selective dopaminergic neurons degeneration in the substantia nigra, striatal dopamine content decreases significantly. The presence of Lewy bodies in the substantia nigra and the locus coeruleus result in the basal ganglia and cortical loop functioning abnormally[21-25]. Fearnley et al[26], found that, before the movement symptoms appear, PD patients have a 60-80% of the corresponding neuron loss[27].

In 1999, Damier et al[6] through an autopsy pathology found a PD biomarker, nigrosomes in the substantia nigra. It is a dopaminergic cell in the healthy substantia nigra, without coloration in the calcium antagonistic protein D_{28K} immune group. While patients with PD, the substantia nigra did not have the marker with visible coloration. Nigrosomes has a total of five groups, of which nigrosomes-1 is one of the largest groups, showed up to 98% of the dopaminergic cells depletion in the zone in patients with PD.

SWI is T2* pulse sequences technology developed by the local tissue or internal magnetic sensitive differences in the magnetic field to produce an enhanced of MRI contrast in MRI technology in recent years. The MRI images show a significant difference of fat, iron, and calcium. The deoxygenated hemoglobin and other substances in magnetic sensitivity from background cause the uneven distribution of the local magnetic field, in order to show the iron in the brain[28,29].

In 2013, Blazejewska et al[30] used 7.0T and 3.0T scanner on healthy individuals and patients with PD for SWI, and found an oval high signal

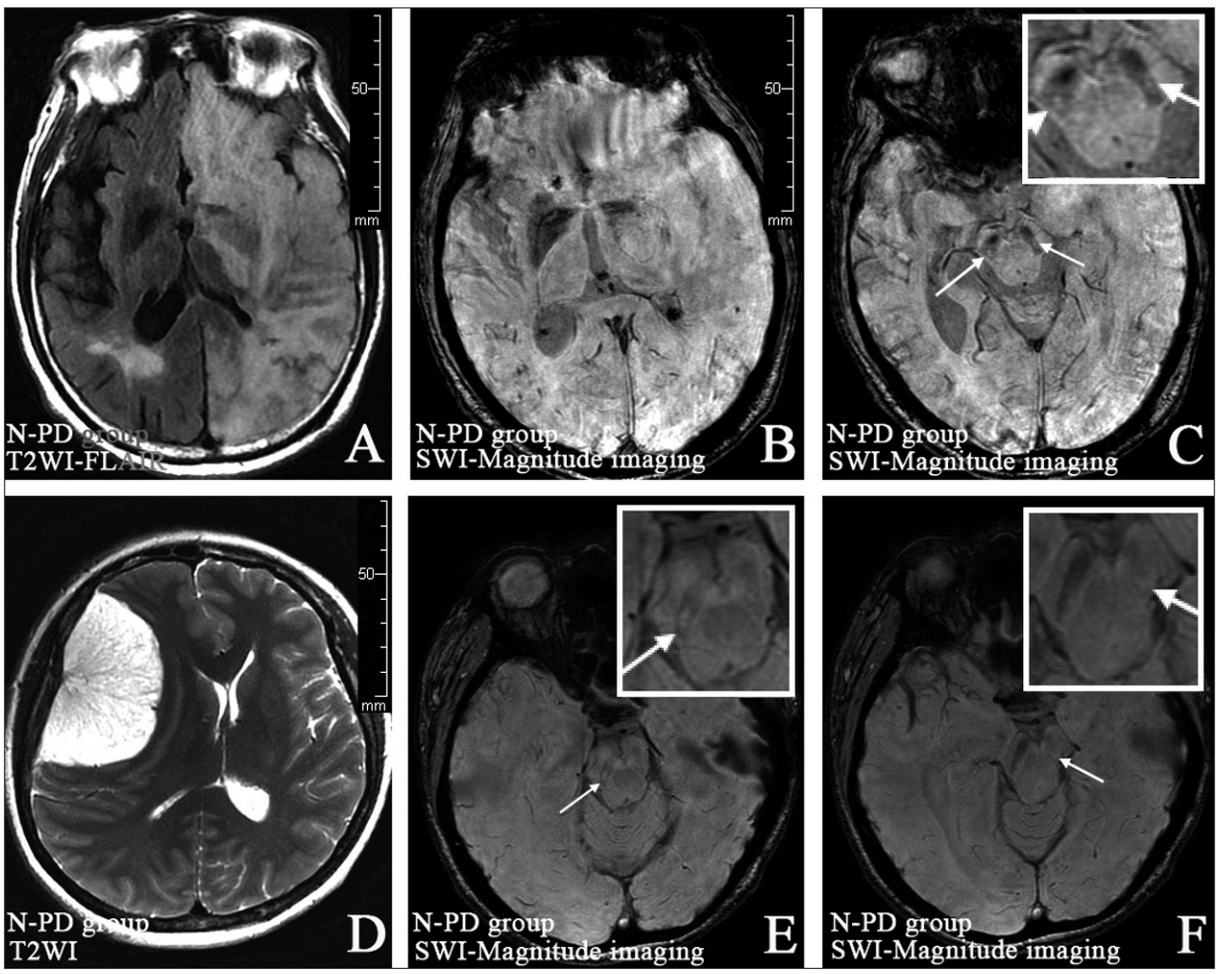

Figure 2. In the substantia nigra of patients with different basic disease of N-PD group, "dovetail syndrome" can be seen: ***A,-C,*** For patients with cerebral infarction: T2WI-FLAIR Axial showed cerebral infarction in left hemispheric large area (***A,*** corresponding levels of SWI transverse amplitude diagram confirmed the same patient ***(A)***; the bottom level of substantia nigra of SWI transverse amplitude diagram displays vaguely discernible "dovetail" sign in bilateral midbrain compression deformation (***C,*** partial enlarged drawing, *white arrow*). ***D,-F,*** For patients with brain tumors: T2WI transverse plane shows huge source meningeal tumors of right frontotemporal ***(D)***; on the bottom of the lower surface of the substantia nigra of SWI transverse amplitude diagram, there displays "dovetail syndrome" on each side (***E, F,*** partial enlarged drawing, *white arrow*).

in the substantia nigra pars compacta posterolateral in two kinds of scans, corresponding to the nigrosomes-1 immune group, while in the patients with PD the oval high signal was lost. In 2014, Cosottini et al[31] further found that the normal cerebral peduncle region structure in the 7.0T SWI images (including the substantia nigra and red nucleus) in the environment of 7T could clearly show the seven layers, wherein the C1 area in the C layer equivalent to nigrosomes-1 immunohistochemical staining could not be found. In April 2014, Schwarz et al[12] used 3.0T SWI to study *in living body*, and reached a similar conclusion. He named the black matter structure of the low signal surrounding healthy nigrosomes-1 zone as "swallow tail" appearance. However, in PD patients, the high signal was lost in C1 area, namely the "swallow tail" sign disappeared.

This study found that in the axial SWI amplitude in the baseline parallel corpus callosum body, wedge or "drops" like high signal in the bilateral substantia nigra consists of the anteromedial band fusion lateral oval structure (Figure 1), some can only display the posterolateral oval region (Figure 1). The elliptical high signal at its widest point was (2.06 ± 0.54) mm, corresponding to the average width of the middle level of the *substantia nigra* vertical high signal band (0.31 ± 0.07) mm.

This study takes non-PD rather than completely healthy elderly people as a control group, aiming to explore whether there are universal "swallow tail" appearance signs in non-PD patients. The results showed that after exclusion of the brainstem area artifacts and other lesions, in subjects of health elderly with non-PD and other various basic diseases, high signal intensities with corresponding characteristics showed in the substantia nigra pars compacta, showed a "swallow tail" appearance sign (Figure 2). The lack of PD sensitivity signs was 100%, specificity 96.08%. Brainstem motion and metal artifacts and other diseases have a remarkable effect on the signs. Therefore, the removal of the metal parts before and during the scanning process is crucial for improving the accuracy of the diagnosis.

The etiology and pathogenesis of PD are not clear. There have been a large number of studies showing that the iron deposition is significantly related to the substantia nigra[32-35]. The study found that in four cases of the N-PD group the gray nucleus (including the red nucleus, substantia nigra) signal in the brain decreased, prompting the related nuclei iron deposits. However, bilateral substantia nigra in the "droplets" high signal was displayed (Figure 3), with the appearance of the typical "swallow tail". To a certain extent, it meant that the iron deposition in the

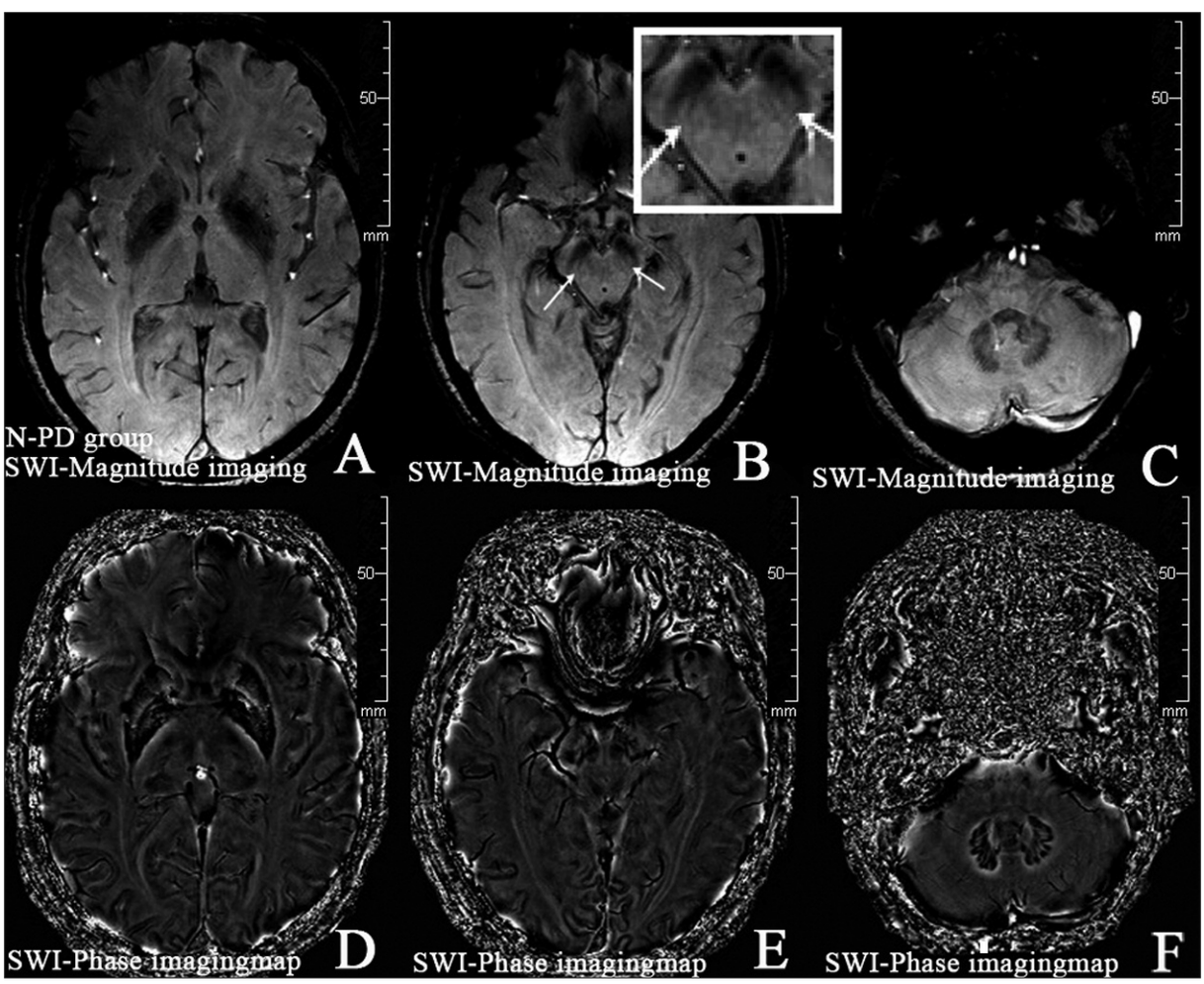

Figure 3. SWI cross section of patients with the nuclei common iron deposition: ***A,-C,*** are the range maps, display basal ganglia ***(A)***, substantial nigra ***(B)***, dentate body of cerebellum ***(C)***, Signal generally decreased, and the bilateral substantia nigra posterolateral "dovetail" sign was still clearly in display (***B,*** partial enlarged drawing, *white arrow*). ***D,-F,*** are the corresponding layer negative phase mask phase diagrams, showing the corresponding nuclei signal also generally reduced, proved to be iron deposition performance (rather than the nucleus calcification).

substantia nigra occurs in specific parts and leads to PD. After removing the brainstem area artifacts and other lesions, the "drop" rear elliptical high signal structure of the subjects in the PD group showed deletion (100%). The front strip high signal showed deletion (unilateral counting) (77%). The area was replaced by a low signal ferromagnetic material. Thus, this proves that the area is the specific location of the PD iron deposition. In conclusion, the "swallow tail" appearance performance is ubiquitous in the substantia nigra of non-PD on the 3.0T SWI range map. The lack of signs shows high sensitivity and specificity for PD diagnosis. A series of changes to the signs is of great value for the differential diagnosis of PD.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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