



# OPEN Susceptibility map-weighted MRI can distinguish tremor-dominant Parkinson's disease from essential tremor

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Distinguishing between Parkinson's disease (PD) and essential tremor (ET) can be challenging sometimes. Although positron emission tomography can confirm PD diagnosis, its application is limited by high cost and exposure to radioactive isotopes. Patients with PD exhibit loss of the dorsal nigral hyperintensity on brain magnetic resonance imaging (MRI). Novel MRI-based approaches, including susceptibility map-weighted imaging (SMWI), allow visualization of the dorsal nigral hyperintensity at an increased resolution. Herein, we investigated the diagnostic accuracy of dorsal nigral hyperintensity evaluation on SMWI for distinguishing tremor-dominant PD from ET. Consecutive patients with tremor who underwent SMWI and were diagnosed with tremor-dominant PD or ET between July 2021 and July 2022 were enrolled. The dorsal nigral hyperintensity loss on SMWI was compared between the PD and ET groups. All 143 patients (100%) with tremor-dominant PD showed unilateral or bilateral dorsal nigral hyperintensity loss. Among 136 patients with ET, 131 (96.3%) exhibited an intact dorsal nigral hyperintensity, while 5 (3.7%) showed unilateral/bilateral dorsal nigral hyperintensity loss. SMWI discriminated between tremor-dominant PD and ET with a sensitivity and specificity of 100% and 96.3%, respectively. <sup>18</sup>F-FP-CIT PET revealed normal findings in 4/5 patients with ET who had false-positive results on SMWI. These results indicate that dorsal nigral hyperintensity loss on SMWI could differentiate between tremor-dominant PD and ET with high accuracy.

**Keywords** Parkinson's disease, Essential tremor, Nigrosome-1, Dorsal nigral hyperintensity, Diagnostic accuracy

Parkinson's disease (PD) is the second most common neurodegenerative disease, with an estimated prevalence of 8.5 million cases globally<sup>1</sup>. Its clinical symptoms include resting tremor, rigidity, bradykinesia, and gait disturbance. Although resting tremor is characteristic of PD, they are also observed in 19% of patients with essential tremor (ET)<sup>2</sup>. Furthermore, postural or action tremor, which is more disabling than classic resting tremor<sup>2</sup>, are generally observed in patients with ET; however, they are also observed in more than 40% of PD cases<sup>3</sup>. This overlap in clinical symptoms between PD and ET can result in misdiagnosis, with one study showing that 37% of patients presumed to have ET were misdiagnosed<sup>4</sup>.

Early diagnosis of PD can facilitate symptom management, thereby improving quality of life and potentially slowing disease progression. The diagnosis of PD can be confirmed through 18 F-N-(3-fluoropropyl)-2β-carboxymethoxy-3β-(4-iodophenyl) nortropane (FP-CIT) positron emission tomography (PET)<sup>5,6</sup>; however, the use of this modality is limited by its high cost and the use of radioactive isotopes. The nigral hyperintensity of the nigrosome-1 regions on specific magnetic resonance imaging (MRI) sequences (including gradient echo [GRE] and susceptibility-weighted imaging [SWI] sequences) is significantly reduced in individuals with PD compared to healthy individuals<sup>7,8</sup>. A reduction in the dorsal nigral hyperintensity volume on high-resolution

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MRI in individuals with PD also shows a correlation between volume and disease severity<sup>9</sup>. However, most of the previous studies included small number of study population and only compared PD patients with healthy controls. We believe that a comparison between PD patients presenting primarily with tremor and patients with ET would be helpful because differentiating two groups are essential in clinical practice. Furthermore, the sensitivity and specificity of dorsal nigral hyperintensity imaging show variations across studies, with values ranging from 79 to 100% and 82–92%, respectively<sup>10–12</sup>.

Accordingly, the susceptibility map-weighted imaging (SMwI) technique has been developed to increase the resolution of dorsal nigral hyperintensity visualization<sup>13</sup>. This novel technology resolves the blooming artifacts observed in SWI, while providing better contrast-to-noise and signal-to-noise ratios than SWI<sup>13–16</sup>. However, information regarding the diagnostic accuracy of SMwI in discriminating between ET and tremor-dominant PD is limited. Therefore, this study investigated the diagnostic accuracy of dorsal nigral hyperintensity assessment on SMwI at distinguishing tremor-dominant PD from ET.

Results

Patient characteristics

This study assessed 281 patients newly diagnosed with tremor-dominant PD or ET between July 2021 and July 2022. After excluding those with symptomatic stroke ( $n=2$ ), a total of 279 consecutive patients (women: 169 [60.6%]) were included in the analysis, among whom 143 (51.3%) and 136 (48.7%) had tremor-dominant PD and ET, respectively. The mean patient age was 65.0 years (interquartile range [IQR], 56.0–72.0 years). Patients with ET had a lower age at symptom onset and a longer disease duration than those with PD (both  $p \leq 0.001$ ; Table 1). Compared to the PD group, the ET group also had a higher proportion of women (51.4% vs. 71.3%,  $p=0.001$ ). For the healthy control group, we enrolled 20 individuals (mean age  $\pm$  SD: 53.4  $\pm$  14.4, women: 50%).

Diagnostic accuracy

All 143 patients with tremor-dominant PD (100%) showed either unilateral or bilateral loss of the dorsal nigral hyperintensity (Table 1). Conversely, among the 136 patients with ET, 131 (96.3%) had an intact dorsal nigral hyperintensity bilaterally, while the remaining five patients (3.7%) showed bilateral loss of the dorsal nigral hyperintensity. The sensitivity and specificity of SMwI in distinguishing tremor-dominant PD from ET were 100.0% (143/143; 95% confidence interval [CI], 97.5–100.0%) and 96.3% (131/136; 95% CI, 91.6–98.8%), respectively; while the positive and negative predictive values were 96.6% (143/148; 95% CI, 92.3–98.5%) and 100.0% (131/131; 95% CI, 96.5–100.0%), respectively. Because PD medication could affect the dorsal nigral hyperintensity<sup>17</sup>, we investigated the use of PD medication. Among 143 PD patients, 21 (14.7%) patients were using levodopa or dopamine agonists, and the loss of dorsal nigral hyperintensity was observed in 100% of both the medicated and non-medicated groups. Additionally, there was no significant difference in the unilaterality of dorsal nigral hyperintensity between the two groups (19.0% vs. 9.0%,  $P=0.32$ ).

Subgroup analyses of patients who underwent <sup>18</sup>F-FP-CIT PET

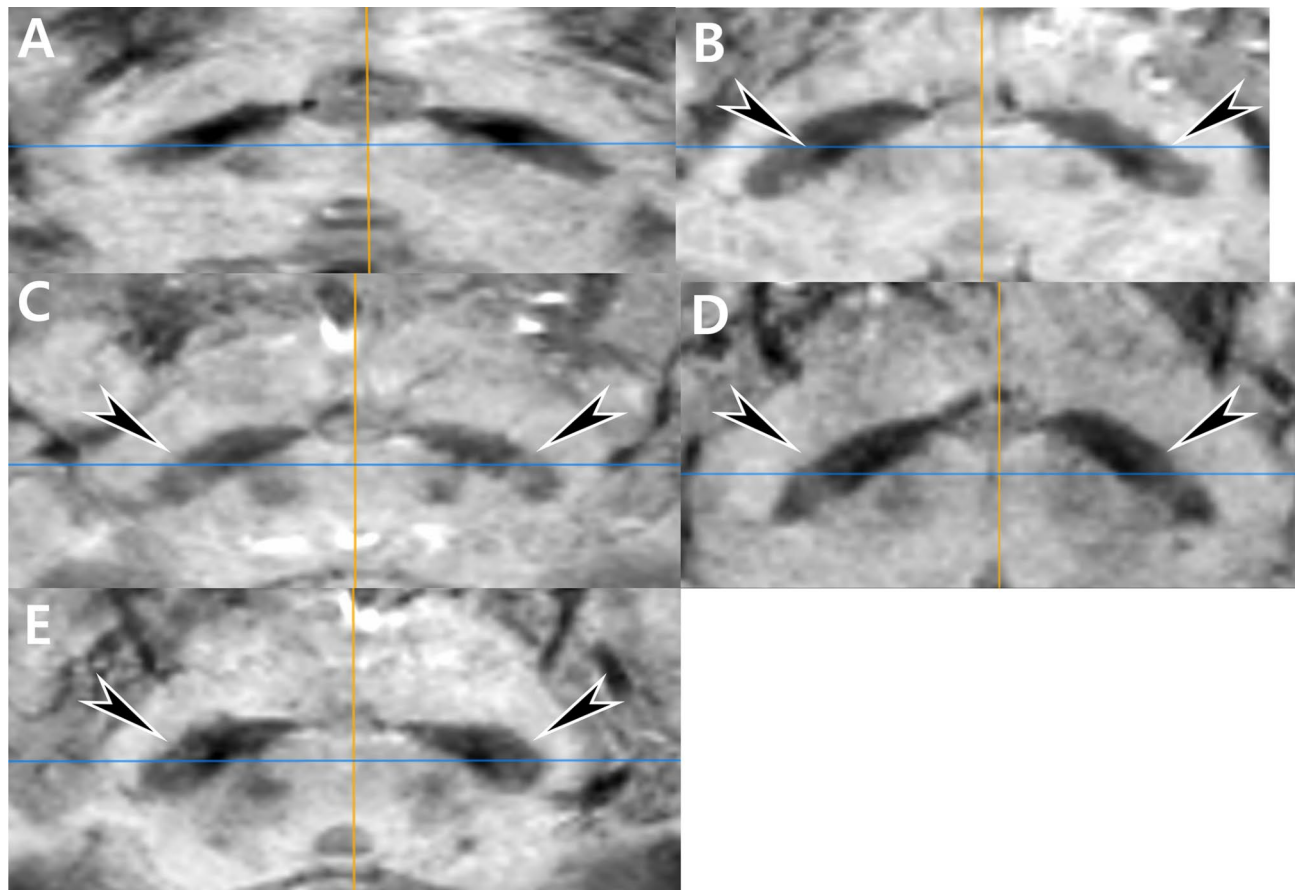
Out of all 279 patients, 245 (87.8%) underwent <sup>18</sup>F-FP-CIT PET, among whom 137 and 108 had tremor-dominant PD and ET, respectively. When only patients who underwent <sup>18</sup>F-FP-CIT PET were analyzed, the sensitivity and specificity of SMwI for distinguishing tremor-dominant PD from ET were 100% (137/137; 95%

|                                                   | ET ( $n=136$ )   | PD ( $n=143$ )   | $p$ value |
|---------------------------------------------------|------------------|------------------|-----------|
| Age at onset, years, median (IQR)                 | 62.5 (52.0–70.0) | 67.0 (59.5–73.0) | 0.001     |
| Age at MRI, years, median (IQR)                   | 67.5 (59.0–74.0) | 68.0 (61.5–74.0) | 0.32      |
| Women, $n$ (%)                                    | 97 (71.3%)       | 72 (51.4%)       | 0.001     |
| Hypertension, $n$ (%)                             | 38 (27.9%)       | 49 (34.3%)       | 0.31      |
| Diabetes mellitus, $n$ (%)                        | 27 (19.9%)       | 22 (15.4%)       | 0.41      |
| Hyperlipidemia, $n$ (%)                           | 13 (9.6%)        | 23 (16.1%)       | 0.15      |
| Disease duration of PD or ET, years, median (IQR) | 2.0 (1.0–6.0)    | 1.0 (1.0–2.0)    | <0.001    |
| Medication for PD, $n$ (%)                        | 0 (0%)           | 21 (14.7%)       | <0.001    |
| Hoehn and Yahr stage                              |                  |                  |           |
| 1                                                 | –                | 14 (10.0%)       |           |
| 2                                                 | –                | 89 (63.6%)       |           |
| 2.5                                               | –                | 24 (17.1%)       |           |
| 3                                                 | –                | 12 (8.6%)        |           |
| 4                                                 | –                | 1 (0.7%)         |           |
| Dorsal nigral hyperintensity on either side       |                  |                  | <0.001    |
| Negative                                          | 131 (96.3%)      | 0 (0.0%)         |           |
| Positive                                          | 5 (3.7%)         | 143 (100.0%)     |           |

**Table 1.** Baseline demographic characteristics of patients with ET and PD. *ET* essential tremor, *IQR* interquartile range, *MRI* magnetic resonance image, *PD* Parkinson’s disease, Medications for PD include levodopa and dopamine agonist.

|                                             | ET ( <i>n</i> = 108) | PD ( <i>n</i> = 137) | <i>p</i> value |
|---------------------------------------------|----------------------|----------------------|----------------|
| Dorsal nigral hyperintensity on either side |                      |                      | <0.001         |
| Negative                                    | 104 (96.3%)          | 0 (0.0%)             |                |
| Positive                                    | 4 (3.7%)             | 137 (100.0%)         |                |

**Table 2.** Diagnostic accuracy of dorsal nigral hyperintensity imaging on SMwI in patients with ET and PD in subgroup analyses of patients who underwent  $^{18}\text{F}$ -FP-CIT PET. *ET* essential tremor, *PD* Parkinson's disease, *SMwI* susceptibility map-weighted imaging.



**Fig. 1.** Images of the dorsal nigral hyperintensity in patients with essential tremor (ET) whose tests were false-positive. Loss of the bilateral dorsal nigral hyperintensity in a (A) 61-year-old man, (B) 73-year-old man, (C) 78-year-old man, (D) 60-year-old man, and (E) 79-year-old man.

CI, 97.3–100.0%) and 96.3% (104/108; 95% CI, 90.8–99.0%), respectively (Table 2). Further, the positive and negative predictive values were 97.2% (137/141; 95% CI, 92.9–98.9%) and 100.0% (104/104; 95% CI, 96.5–100.0%), respectively.

In the 137 patients with PD,  $^{18}\text{F}$ -FP-CIT PET revealed bilateral and unilateral losses of the presynaptic dopaminergic neurons in 132 (96.4%) and 5 (3.6%) patients, respectively. Further, 4/5 (80.0%) PD patients with unilateral loss of presynaptic dopaminergic neurons in  $^{18}\text{F}$ -FP-CIT PET also showed unilateral loss of the dorsal nigral hyperintensity on SMwI, while one patient showed bilateral loss. In the 108 patients with ET,  $^{18}\text{F}$ -FP-CIT PET revealed normal presynaptic dopaminergic neurons.

#### False-positive cases

No false-negative cases were observed. However, among the 136 patients with ET, five (3.7%) showed a definitely abnormal dorsal nigral hyperintensity on SMwI (false-positive cases; age:  $\geq 60$  years [range, 60–79]). Images from each of these abnormal cases are presented in Fig. 1. Among these patients, four underwent  $^{18}\text{F}$ -FP-CIT PET, which revealed normal findings: three patients (cases 1–3; Table 3) showed bilateral loss of the dorsal nigral hyperintensity, while  $^{18}\text{F}$ -FP-CIT PET findings were normal for both sides. The remaining patient (case 4; Table 3) presented with unilateral loss of the dorsal nigral hyperintensity on the right side, with inconclusive findings on the left side, and normal  $^{18}\text{F}$ -FP-CIT PET.

| Participant | Age | Sex | SMwI                |                     |             | <sup>18</sup> F-FP-CIT-PET |             |             |
|-------------|-----|-----|---------------------|---------------------|-------------|----------------------------|-------------|-------------|
|             |     |     | Right               | Left                | Per patient | Right                      | Left        | Per patient |
| 1           | 78  | M   | Definitely abnormal | Definitely abnormal | Abnormal    | Normal                     | Normal      | Normal      |
| 2           | 81  | M   | Definitely abnormal | Definitely abnormal | Abnormal    | Normal                     | Normal      | Normal      |
| 3           | 61  | M   | Definitely abnormal | Definitely abnormal | Abnormal    | Normal                     | Normal      | Normal      |
| 4           | 73  | M   | Definitely abnormal | Inconclusive        | Abnormal    | Normal                     | Normal      | Normal      |
| 5           | 62  | M   | Definitely abnormal | Definitely abnormal | Abnormal    | Unavailable                | Unavailable | Unavailable |

**Table 3.** Comparison of SMwI and <sup>18</sup>F-FP-CIT-PET images in patients with ET presenting with loss of dorsal nigral hyperintensity. *ET* essential tremor, <sup>18</sup>FFP-CIT-PET 18 F-N-(3-fluoropropyl)-2β-carboxymethoxy-3β-(4-iodophenyl) nortropane positron emission tomography, *M* male, *SMwI* susceptibility map-weighted imaging.

Discussion

In this study, we investigated the diagnostic accuracy of dorsal nigral hyperintensity assessment on SMwI in differentiating between tremor-dominant PD and ET. Overall, normal dorsal nigral hyperintensity findings were suggestive of ET, allowing exclusion of PD with a negative predictive value of 100.0%. Most patients with PD exhibited a loss of dorsal nigral hyperintensity, while only 3.7% of those with ET exhibited this finding. These patients with false-positive results were all over 60 years old, indicating that aging may affect the loss of the dorsal nigral hyperintensity.

In this study, the sensitivity of dorsal nigral hyperintensity observation on SMwI was 100%. This was higher than that reported in prior studies comparing dorsal nigral hyperintensity findings between PD and ET<sup>10–12</sup>. In two studies by Bienz et al.<sup>10</sup> and Jin et al.<sup>11</sup>, GRE sequences were used, revealing similar or lower sensitivities of 100% and 79.4%, respectively. Conversely, Perez et al.<sup>12</sup> used SWI and reported a sensitivity of 93.8%. Furthermore, in the present study, the specificity of dorsal nigral hyperintensity assessment from SMwI was 96.3%, which was higher than that reported in the aforementioned studies<sup>10–12</sup>. Perez et al.<sup>12</sup> (who used SWI) also reported a specificity of 87.5%, whereas Bienz et al.<sup>10</sup> and Jin et al.<sup>11</sup> (who used GRE) reported specificities of 82% and 92.0%, respectively. SMwI improved the quality of dorsal nigral hyperintensity images by improving the contrast-to-noise and signal-to-noise ratios of the phase image, and by avoiding artifacts through application of a weighting factor with quantitative susceptibility mapping<sup>13–16</sup>. SMwI has a good capacity for visual evaluation, which is particularly useful in quick interpretations. Moreover, the collection process for SMwI is quicker than that for other modalities, such as neuromelanin-sensitive imaging<sup>8</sup>.

Patients with PD typically exhibit resting tremor, whereas those with ET exhibit kinetic tremor<sup>18</sup>. However, some patients with PD may also exhibit postural or kinetic tremor; consequently, the clinical symptoms between tremor-dominant PD and ET show some overlap. One-third of patients with ET were misdiagnosed with another disease, including PD<sup>4</sup>. The U.S. Food and Drug Administration and the European Medicines Agency have both stated that dopamine transporter scanning can help to distinguish between ET and PD<sup>19,20</sup>. However, this scan is expensive, and requires the use of radiopharmaceuticals, which not only confer side effects, but also have reduced accessibility; in comparison, MRI has fewer side effects and better accessibility. MRI is not often required in patients with typical clinical features of ET; however, structural brain imaging (mostly brain MRI) is commonly conducted in patients with ET who show difficulties with tandem gait, mild cognitive impairment, and resting tremor<sup>21</sup>. Consequently, dorsal nigral hyperintensity imaging using SMwI, in addition to structural MRI, could serve as an optimal screening test with no false-negative results. The use of MRI as a screening tool can allow more rapid detection of patients, while reducing unnecessary testing.

In the present study, 5/136 (3.7%) patients with ET showed loss of the dorsal nigral hyperintensity. Similar false-positive findings have also been reported by Bienz et al.,<sup>10</sup> Jin et al.,<sup>11</sup> and Perez et al.,<sup>12</sup> in 2/11 (18.2%), 2/25 (8.0%), and 2/16 (12.5%) patients, respectively. Another study revealed false-positive results in patients with ET and drug-induced Parkinsonism, and normal controls<sup>22</sup>. False-positive results have also been attributed to the misdiagnosis of ET among patients with pre-symptomatic PD<sup>23</sup>, poor image quality<sup>24</sup>, lower signal-to-noise, and contrast-to-noise ratios achievable at a magnetic field strength of 3 T, within a routinely reasonable scan time<sup>25</sup>, and a possibility of individual anatomic variation<sup>25</sup>. In our study, 4/5 patients with ET who had false-positive results on SMwI showed normal presynaptic dopaminergic neurons on <sup>18</sup>F-FP-CIT PET. Because <sup>18</sup>F-FP-CIT PET findings are abnormal in the prodromal stage of PD, the possibility of pre-symptomatic idiopathic PD could be excluded. Furthermore, we obtained the images using a voxel size of 0.5×0.5×1 mm<sup>2</sup>; therefore, the possibility of the false-positive results having arisen as a consequence of a poor image quality was deemed to be low. We found that all patients with false-positive results were over 60 years of age; thus, we speculated that dorsal nigral hyperintensity loss on SMwI could be affected by aging-related dopaminergic loss<sup>26</sup>. However, further studies on the age-based pathological changes in the calbindin-poor zone in the substantia nigra, which is a nigrosome, are required to better distinguish the effects of aging from PD pathology. Furthermore, considering that increasing the contrast-to-noise and signal-to-noise ratios improved the sensitivity and specificity of SMwI, technological improvements in MRI could also reduce the false-positive results.

The primary strength of our study is that we included a relatively large sample size of 279 consecutively-enrolled patients, enhancing the generalizability of our findings. Furthermore, we compared patients with tremor-dominant PD and ET, meaning that our findings could be directly applied to clinical settings. Also, our subgroup analysis involved patients who underwent <sup>18</sup>F-FP-CIT PET, further validating our findings.

Our study also had several limitations. First, this was a retrospective, single-center study; to overcome limitations inherent to this study design, we enrolled consecutive patients who presented with tremor. Second, the false positive-cases observed in the ET group, although detected at a rate lower than in previous studies, nevertheless raises concerns regarding the specificity of SMwI, particularly among older patients. Further studies are required to reduce this false positive rate.

In conclusion, we found that dorsal nigral hyperintensity evaluation using SMwI helped to differentiate between patients with tremor-dominant PD and ET, with a high sensitivity and specificity. With a sensitivity of 100%, our findings suggest that a normal appearance of dorsal nigral hyperintensity may help to rule out PD entirely. Thus, this parameter could contribute to the early and accurate diagnosis of both PD and ET.

## Methods

### Patient inclusion

This retrospective, observational, single-institution study enrolled consecutive patients who met the following eligibility criteria: (1) patients who visited movement disorder clinics with complaints of tremor and underwent brain MRI (including SMwI) between July 2021 and July 2022, (2) patients with a final diagnosis of tremor-dominant PD or ET, and (3) patients with images of a readable quality. Patients with a final diagnosis of diseases other than tremor-dominant PD and ET, as well as those with symptomatic stroke were excluded. In addition, healthy individuals who underwent brain MRI (including SMwI) between September 2024 and October 2024 also included. This study was approved by the Asan Medical Center Institutional Review Board (2022–0138). The requirement for informed consent was waived by the ethical committee of this center, because the study posed minimal risk to participants since it involved no new data collection or interventions that might affect them. This study was performed and reported in accordance with Standards for Reporting Diagnostic accuracy studies (STARD) 2015<sup>19</sup>.

### Clinical diagnoses of the patients

Two neurologists (S.-J. C. and S.-Y. J.) diagnosed patients with PD based on the diagnostic criteria established by the International Parkinson and Movement Disorder Society (2015)<sup>20</sup>, and ET using the WHIGET criteria<sup>27,28</sup>. We defined tremor-dominant PD as the presence of a tremor at rest in either the head-neck region or in at least 1 upper or lower extremity that was given a score of 2 from the motor examination section of the Unified Parkinson's Disease Rating Scale (UPDRS)<sup>29</sup>. Patient data were collected from electronic medical records.

### Image acquisition

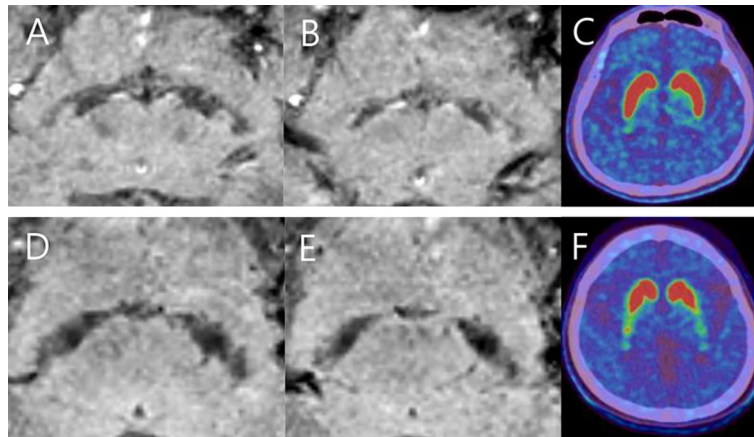
For all patients, brain MRI was performed using a 3 T MRI scanner (Ingenia CX; Philips Healthcare, Best, Netherlands) with a 32-channel SENSE head coil. SWI was performed with the shortest repetition time (TR) and three echoes. Additional parameters were as follows: shortest TR; a total of three echoes; first time to echo, 14 msec; echo interval, 13 msec; flip angle, 20°; FOV, 192 × 192 mm<sup>2</sup>; voxel size, 0.5 × 0.5 × 1 mm<sup>3</sup>; and slice number, 32. Following SWI acquisition, SMwI images were generated to enhance the visibility of the dorsal nigral hyperintensity. These images were subsequently subjected to post-processing and reconstruction using the method reported by Nam et al.<sup>13</sup> Oblique coronal planes were obtained as a parallel plane from the posterior commissure to the anterosuperior border of the pons, approximately perpendicular to the midbrain<sup>8</sup>. All reconstructed SMwI images were resliced in increments of 0.5 mm using Syngovia (Siemens Healthineers, Germany), after repositioning the images as symmetrically as possible at the level of the inferior pole of the red nuclei<sup>30</sup>.

<sup>18</sup>F-FP-CIT PET shows the dopamine transporter of presynaptic dopaminergic neurons, and the cardinal motor features of PD become evident after some 60–80% of nigral dopaminergic neurons are lost<sup>31</sup>. In pathologically confirmed PD, 100% (47/47) showed abnormalities on <sup>18</sup>F-FP-CIT PET<sup>5</sup>. In one meta-analysis, excluding one patient whose diagnosis was unclear, the sensitivity of dopamine transporter SPECT, which is similar to <sup>18</sup>F-FP-CIT PET, for detecting PD was 100%<sup>6</sup>. In contrast, 100% (27/27) of patients with essential tremor (ET) had normal <sup>18</sup>F-FP-CIT PET results<sup>32</sup>. Recently, the biological definition of PD suggests performing <sup>18</sup>F-FP-CIT PET or dopamine transporter SPECT to confirm neurodegeneration. Therefore, CIT-PET was often used to confirm decreased dopamine transporter binding in patients with PD, while for ET cases with tremor and suspicious bradykinesia, <sup>18</sup>F-FP-CIT-PET was performed to differentiate Parkinsonism. Accordingly, 245/279 patients (87.8%) underwent <sup>18</sup>F-FP-CIT PET imaging with a PET/CT scanner after receiving a 5 mCi (185 MBq) injection of <sup>18</sup>F-FP-CIT.

### Image analysis

All SMwI images were reviewed in consensus by two neuroradiologists (S.J.K. [35 years of experience] and C.H.S. [12 years of experience]), who independently evaluated the nigral hyperintensity status on the bilateral substantia nigra of eligible patients. The evaluators were blinded to the clinical diagnoses and <sup>18</sup>F-FP-CIT PET findings. The dorsal nigral hyperintensity region was defined as a hyperintense area of the posteroinferior aspect of the hypointense substantia nigra on five consecutive images, immediately below the inferior pole of the red nucleus on oblique coronal imaging<sup>8</sup>. The two sides of the substantia nigra were assessed separately. SMwI images were classified as “definitely normal” only when the bilateral dorsal nigral hyperintensity regions were conclusively determined as normal. Abnormalities were reported when a hypointense area obliterated the differentiation among the inner, middle, and outer hypointense layers; such SMwI images were classified as “definitely abnormal”<sup>22</sup>. SMwI not meeting either of these criteria were classified as “inconclusive”. “Definitely normal” was considered normal and “inconclusive” and “definitely abnormal” were considered abnormal.

For inter-rater reliability between two readers, we obtained a weighted kappa of 0.89 (95% CI, 0.84–0.93) for the right side and 0.85 (95% CI, 0.80–0.90) for the left side. For intra-rater reliability, the weighted kappa was



**Fig. 2.** Representative dorsal nigral hyperintensity and  $^{18}\text{F}$ -FP-CIT PET images of patients with essential tremor (ET) and Parkinson's disease (PD). (A–C) Intact dorsal nigral hyperintensity and  $^{18}\text{F}$ -FP-CIT PET images of a 63-year-old man with ET. (D–F) Loss of the dorsal nigral hyperintensity and  $^{18}\text{F}$ -FP-CIT PET findings in a 50-year-old woman with PD.

0.87 (95% CI, 0.80–0.94) for the right side and 0.88 (95% CI, 0.82–0.94) for the left side. For the healthy control group, all healthy controls showed normal dorsolateral nigral hyperintensity on SMwI.

The striatal dopamine transporter activity on  $^{18}\text{F}$ -FP-CIT PET was visually assessed according to previously-published criteria<sup>33</sup>. Each side of the basal ganglia was evaluated separately, and the presence or absence of an abnormality on each side was recorded. Participants with abnormalities on  $^{18}\text{F}$ -FP-CIT PET had nigrostriatal degeneration. Figure 2 presents representative images of the dorsal nigral hyperintensity and an  $^{18}\text{F}$ -FP-CIT imaging.

### Statistical analysis

The Mann-Whitney U test was used to compare the continuous variables between the ET and PD groups. Categorical variables were compared using the Chi-square test. The primary outcome of this study was the diagnostic accuracy of SMwI in distinguishing tremor-dominant PD from ET. The diagnostic performance of SMwI was evaluated using per-patient analysis. Patients with abnormalities on either side of dorsal nigral hyperintensity on SMwI were classified as having abnormalities. Statistical significance was set at  $p < 0.05$ . All analyses were performed using R software (version 4.2.1). To evaluate inter-rate and intra-rate reliability, weight kappa was obtained.

### Data availability

The data supporting the study findings have not been deposited in a public repository to safeguard participant privacy but are available from the corresponding author upon reasonable request.

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Study concept and design: SJ, CHS, WHS, SJK, EYK, EYK, SJC. Data acquisition: SJ, CHS, SL, JH, HH, SJC. Data analysis: SJ, CHS, SL, JH, MY, HH. Draft the manuscript: SJ, CHS, MY, WHS, SJK, EYK, SJC.

## Declarations

## Competing interests

The authors declare no competing interests.

## Ethical approval

This study was approved by the Asan Medical Center Institutional Review Board (2022-0138).

## Consent to participate/publish

The requirement for informed consent was waived by the ethical committee of the Asan Medical Center due to the retrospective design and low risk to participants.

## Additional information

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