Does the pattern of striatal dopamine depletion contribute to non-motor symptoms in Parkinson's disease?

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Does the pattern of striatal dopamine depletion contribute to non-motor symptoms in Parkinson's disease?

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ABSTRACT

Does the pattern of striatal dopamine depletion contribute to non-motor symptoms in Parkinson's disease?

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Background : Non-motor symptoms (NMS) has been recognized as a key determinant factor for quality of life in Parkinson's disease (PD), but the mechanism underlying NMS in PD has not yet been elucidated well. To investigate whether the pattern of striatal dopamine depletion contributes to NMS in PD, we hypothesized that PD patients with greater NMS might have a different pattern of striatal dopamine depletion, particularly the areas other than the posterior putamen, compared to those with less NMS.

Methods : We conducted a survey of the degree of NMS (using non-motor symptoms scale, NMSS) in 151 PD patients who had been initially diagnosed at our hospital by dopamine transporter (DAT) scanning, using a [^{18}F] N-(3-Fluoropropyl)-2β-carbon ethoxy-3β-(4-iodophenyl) nortropane (FP-CIT) PET scan (from March 2009 to June 2013).

Results : Patients with a high NMSS score (above the median) had an older age of PD onset (64.9 ± 9.1 vs 61.5 ± 10.1 years, $p = 0.034$), a higher initial part III

of the Unified Parkinson Disease rating scale (UPDRS-motor, assessed in drug-naïve state) (26.9 ± 11.7 vs 20.9 ± 10.3, p = 0.003), a higher levodopa-equivalent dose (636.3 ± 293.0 vs 524.4 ± 196.2, p = 0.007), and a greater Beck Depression Inventory (BDI) score (14.7 ± 8.1 vs 11.5 ± 7.5, p = 0.013), compared to those with a low NMSS score. A general linear model showed that patients with a high NMSS score had significantly higher UPDRS-motor score than those with a low score after controlling for onset age, gender, symptom duration, BDI score, and DAT activity in the posterior putamen (p = 0.034). However, DAT activities in 6 striatal subregions and inter-subregional ratios (ISRs) were comparable between the two groups. There were no correlations between subregional DAT activities and NMSS scores (either total or each domain scores), except for the mood/cognition domain score, which was negatively correlated to the anterior putamen/posterior putamen ISR (r = -0.175, p = 0.032).

Conclusion : This study demonstrates that the pattern of striatal dopamine depletion does not contribute to the degree of NMS in early PD, although some clinical features are different between the patients with greater NMS and those with less NMS. This study also suggests that patients with less NMS may have a benign course of motor symptom progression, compared to those with more NMS. NMS in PD may be more likely associated with extra-striatal lesions accompanied in PD than striatal dopaminergic deficits.

Key words : non-motor symptoms; parkinson's disease; striatal dopamine depletion

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I. INTRODUCTION

Parkinson's disease (PD) is a chronic degenerative disorder of the central nervous system, resulting in motor disability such as bradykinesia, rigidity, resting tremor, and postural instability. Besides motor symptoms, PD is also accompanied by variety of non-motor symptoms (NMS) involving sleep, mood, cognition, attention, and autonomic functions. NMS can occur across all stage of PD, and has been recognized as a key determinant factor for quality of life in PD patients. Some NMS such as olfactory deficit, constipation, rapid eye movement sleep behavior disorder (RBD), and depression may precede the motor symptoms by many years.[1] In contrast to the motor symptoms, NMS may be easily misdiagnosed, and may have inappropriate medical interventions.[2] Although the importance of NMS in PD has been widely recognized in recent years, the mechanism underlying NMS has not yet been elucidated well.

The motor symptoms of PD result mainly from the loss of dopaminergic

neurons in the substantia nigra, but PD pathology also involves widespread brainstem and cortical lesions with alterations of several neurotransmitters other than dopamine, such as serotonin, norepinephrine, and acetylcholine.[3] Similar to motor symptom fluctuation, the presence of NMS fluctuation in advanced PD patients has been well recognized. Some NMSs are exacerbated during the off-period, suggesting a potential dopaminergic contribution. The importance of the dopaminergic contribution to NMS in PD was highlighted by a recent positron emission tomography (PET) study, in which dopaminergic depletion in the hypothalamus is associated with the development of sleep, endocrine, and autonomic dysfunctions.[4] A number of clinical trials have demonstrated a beneficial effect of specific dopaminergic drugs on some NMSs, such as RBD, pain, restless leg syndrome, and depression.[5] However, a majority of NMSs may seldom respond to PD medications, and some of them can even be exacerbated by dopaminergic treatments. Thus, the pathophysiological mechanism underlying NMS in PD is still unclear, and appears to be more heterogeneous than pure dopaminergic deficits.[6]

Dopamine transporter (DAT) activity, since it represents the integrity of presynaptic dopaminergic neurons in the striatum, has been widely used as an imaging biomarker for the diagnosis of PD. Accordingly, various techniques using different radioligands have been developed for this purpose, and used in clinical practice. Among them, [^{18}F] N-(3-Fluoropropyl)-2β-carbon ethoxy-3β-(4-iodophenyl) nortropane (FP-CIT) PET has been available in Korea as well as in our hospital since 2008.[7] Compared to DAT single photon emission computed tomography (SPECT), ^{18}F-FP-CIT PET has better spatial

resolution and more sophisticated attenuation correction, and can be used to evaluate subregional changes in the striatal DAT.[8] Compared to healthy people, DAT activity is significantly reduced in all areas of the striatum in PD patients, but the degree of reduction is different among the striatal subregions. In PD patients, DAT reduction in the posterior putamen is much greater than that in other striatal subregions.[9,10] In addition, inter-subregional ratios (ISRs) are also different among various parkinsonism, suggesting the diverse patterns of striatal dopaminergic depletion specific to different parkinsonism syndromes.[10]

Therefore, we performed this study to investigate whether the pattern of striatal dopamine depletion contributes to NMS accompanied in PD. We hypothesized that PD patients with greater NMS might have a different pattern of striatal dopamine depletion, particularly the striatal subregions other than the posterior putamen, compared to those with less NMS. Secondly, in this study, we also investigated whether early PD patients with greater NMS have different clinical features compared to those with less NMS.

II. MATERIALS AND METHODS

1. Subjects

We conducted a survey of the degree of NMS (using Korean version of the non-motor symptoms scale, NMSS) in PD patients who had been initially diagnosed at our hospital by DAT scanning, using a ^{18}F-FP-CIT PET scan (from March 2009 to June 2013). PD in these patients was diagnosed according to the clinical criteria of the UK PD Brain Bank,[8] the presence of appropriate DAT defects on ^{18}F-FP-CIT PET scans,[10] and the presence of PD drug response

during follow-up (≥ 18 months). The interpretation of ^{18}F-FP-CIT-PET scans was performed by nuclear medicine physicians who were blind to the clinical status of each patient. For this study, we excluded the patients with having focal lesions or lacunar infarctions in the basal ganglia, those with atypical parkinsonism or secondary parkinsonism, those having severe medial illness which could affect NMS, and those were taking dopaminergic medication in other hospital already. The part III of the Unified Parkinson Disease rating scale (UPDRS-motor) and modified Hoehn and Yahr stage (HYS) were used to assess PD motor severity at the time of the diagnosis. Mini-mental State Examination (MMSE), Beck Depression Inventory (BDI), and Cross Cultural Smell Identification Test (CCSIT)[11] were performed as a routine diagnostic work-up. Parkinsonian medications prescribed at the time of NMSS assessment were checked, and levodopa-equivalent dose (LED) was calculated on the basis of previously described methodology.[12] We received approval from the Ethics committee of our hospital for experiments using human participants.

2. Assessment of non-motor symptoms

The original NMSS was developed for NMS assessment in PD patients by the International Parkinson's Disease Non-Motor Group,[13] and has been widely used in clinical studies of PD. The Korean version of the NMSS has been developed and validated.[14] The NMSS is composed of thirty items that are grouped to the nine domains: cardiovascular including falls (2 items), sleep/fatigue (4 items), mood/cognition (6 items), perceptual problems/hallucinations (3 items), attention/memory (3 items), gastrointestinal

tract (3 items), urinary (3 items), sexual function (2 items), and miscellaneous (4 items; pain, taste or smell, weight change, and excessive sweating). Score for each item is based on a multiple of severity (from 0 to 3) and frequency scores (from 1 to 4). The total NMSS score ranged from 0 to 360, in which higher score represents more severe NMS. The NMSS was rated by a neurologist, and obtained through interviews of the patients and their caregivers.

3. PET-CT image acquisition

^{18}F-FP-CIT PET scans were used with a GE Discovery STe (DSTE) PET-CT scanner (GE Healthcare Technologies, Milwaukee, WI). DAT images were obtained with 3D resolution, and performed a post hoc 3D Gaussian smoothing with 2.3 mm full width at half maximum. After fasting for at least 6 hours before PET scanning, 5 mCi (185 MBq) of ^{18}F-FP-CIT was injected intravenously. Images were taken in a 3D mode at 120 KVp and 380 mAs during a 20- minute session that came about 90 minutes after injection.

4. Quantitative analysis of ^{18}F-FP-CIT PET data

Quantitative analyses of ^{18}F-FP-CIT PET data were fulfilled through a previously described procedure.[10] Image processing was performed using SPM8 (Wellcome Department of Imaging Neuroscience, Institute of Neurology, UCL, London, UK) under MATLAB 2013a for Windows (MathWorks, Natick, MA). Quantitative analyses were based on volumes of interests (VOIs), which were defined based on a template in standard space. All reconstructed PET images were spatially normalized to Montreal Neurology Institute (MNI) template

space using a standard ^{18}F-FP-CIT PET template, which was made using ^{18}F-FP-CIT PET and T1 MRI of 13 normal controls to remove inter-subject anatomical variability. Twelve VOIs of bilateral striatal subregions and one occipital VOI were drawn on a co-registered spatially normalized single T1 MRI and ^{18}F-FP-CIT PET template image on MRIcro version 1.37 (Chris Rorden, Columbia, SC), based on previous study (Figure 1).[10] These VOIs were adjusted by a minor translation in our in-house VOI editing software called ANTIQUE.[15] Using DAT activity concentration in each VOI, we estimated the surrogate of nondisplaceable binding potential (BP_{ND}), defined as follows: (mean standardized uptake value [SUV] of the striatal subregions VOI - mean SUV of the occipital VOI)/mean SUV of the occipital VOI.[16] We used mean BP_{ND} for each bilateral striatal subregions. The ISR was defined as the ratio of DAT activity of one striatal subregion to that of another striatal subregion. Posterior putamen was used to the common denominator, and 5 ISRs were calculated.

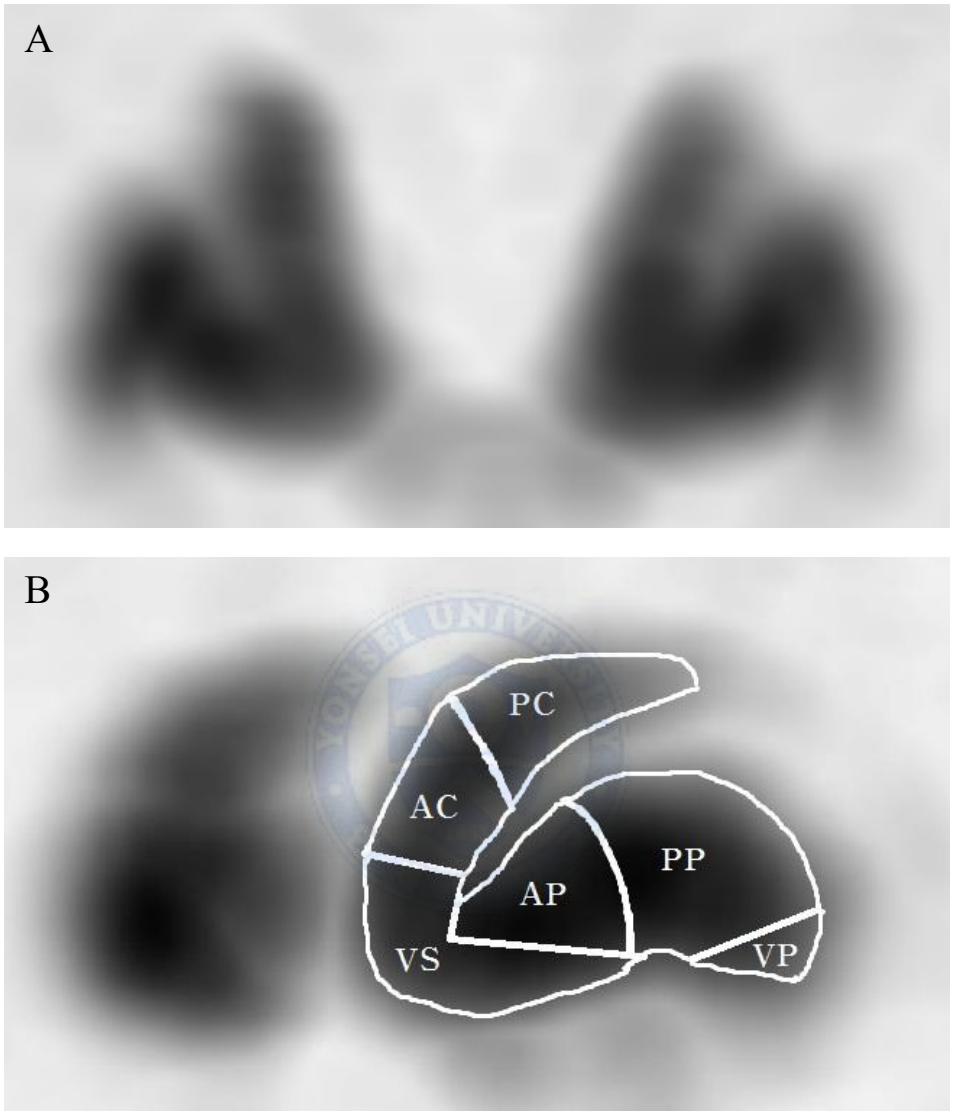

Figure 1. Images of ^{18}F-FP-CIT uptakes at the level of striatum. A healthy control (A), and diagram of 6 striatal subregions (B).

VS: ventral striatum, AC: anterior caudate, PC: posterior caudate, AP: anterior putamen, PP: posterior putamen, VP: ventral putamen.

5. Statistical analysis

Data were expressed as means ± SDs. We divided the patients into two groups according to their total NMSS scores (above the median and the median or less). An independent *t* test was used to compare numeric variables, and χ^2 test was used to compare categorical variables between the patients with greater NMS and those with less NMS. A general linear model was used to compare the difference of UPDRS-motor score between the two groups after controlling for onset age, gender, duration of motor symptoms, BDI score, and DAT activity in the posterior putamen. A partial correlation analysis was conducted to evaluate the relationship between striatal subregional DAT activity and the NMSS scores (total and each domain scores), after controlling for the follow-up duration (intervals from DAT scan to the NMSS). SPSS Statistics 20 (IBM SPSS, Armonk, NY, USA) was used to perform all statistical analyses. *P*–values <0.05 were regarded as significant.

III. RESULTS

One hundred and fifty-one patients (mean age, 67.9 ± 9.6 years; range, 41 – 88 years; 67 men) were included in this study. Total NMSS score in each patient ranged from 0 to 169 (mean, 45.5 ± 34.0; median, 37). Seventy-six (50.3%) patients belonged to the low NMSS group (total NMSS ≤ 37), while seventy-five (49.7%) patients were in the high NMSS group (total NMSS > 37). Clinical characteristics of the two patient groups are shown in Table 1. High NMSS patients were older PD onset age (64.9 ± 9.1 vs 61.5 ± 10.1 years, p = 0.034), had a higher initial UPDRS-motor score (26.9 ± 11.7 vs 20.9 ± 10.3, p =

0.003), more severe initial HYS (p = 0.017), a higher LED at follow-up (636 ± 293 vs 524 ± 196, p = 0.007), and a higher BDI score (14.7 ± 8.1 vs 11.5 ± 7.5, p = 0.013), compared to low NMSS patients. A general linear model showed that high NMSS patients had significantly higher UPDRS-motor score than low NMSS patients after controlling for onset age, gender, duration of motor symptoms, BDI score, and DAT activity in the posterior putamen (p = 0.034) (Figure 2). However, DAT activities in 6 striatal subregions and ISRs were comparable between the two groups (Table 2).

Table 1. Clinical characteristics of the two patient groups

	Low NMSS score (n=76)	High NMSS score (n=75)	*p*-value
Onset age (years)	61.5 ± 10.1	64.9 ± 9.1	0.034
Gender (% man)	44.7	44.0	0.927
Education (years)	10.0 ± 4.7	8.9 ± 5.9	0.248
Duration of motor symptoms (years)	1.2 ± 0.9	1.5 ± 1.3	0.058
Follow-up duration (years)	3.3 ± 1.2	3.5 ± 1.3	0.297
Initial UPDRS-motor score	20.9 ± 10.3	26.9 ± 11.7	0.003
Initial Hoehn and Yahr stage (%)			0.017
1.0/1.5	34.8	20.0	
2.0/2.5	62.1	64.6	
3.0/4.0	3.0	15.4	
Levodopa-equivalent dose (mg)	524.4 ± 196.2	636.3 ± 293	0.007
MMSE score	25.9 ± 2.9	25.6 ± 3.6	0.631
BDI score	11.5 ± 7.5	14.7 ± 8.1	0.013
CCSIT score	6.9 ± 2.5	6.9 ± 2.6	0.847

Data are means ± SDs.

UPDRS: Unified Parkinson's Disease rating scale, MMSE: Mini-Mental State Examination, BDI: Beck Depression Inventory, CCSIT: Cross Cultural Smell Identification Test.

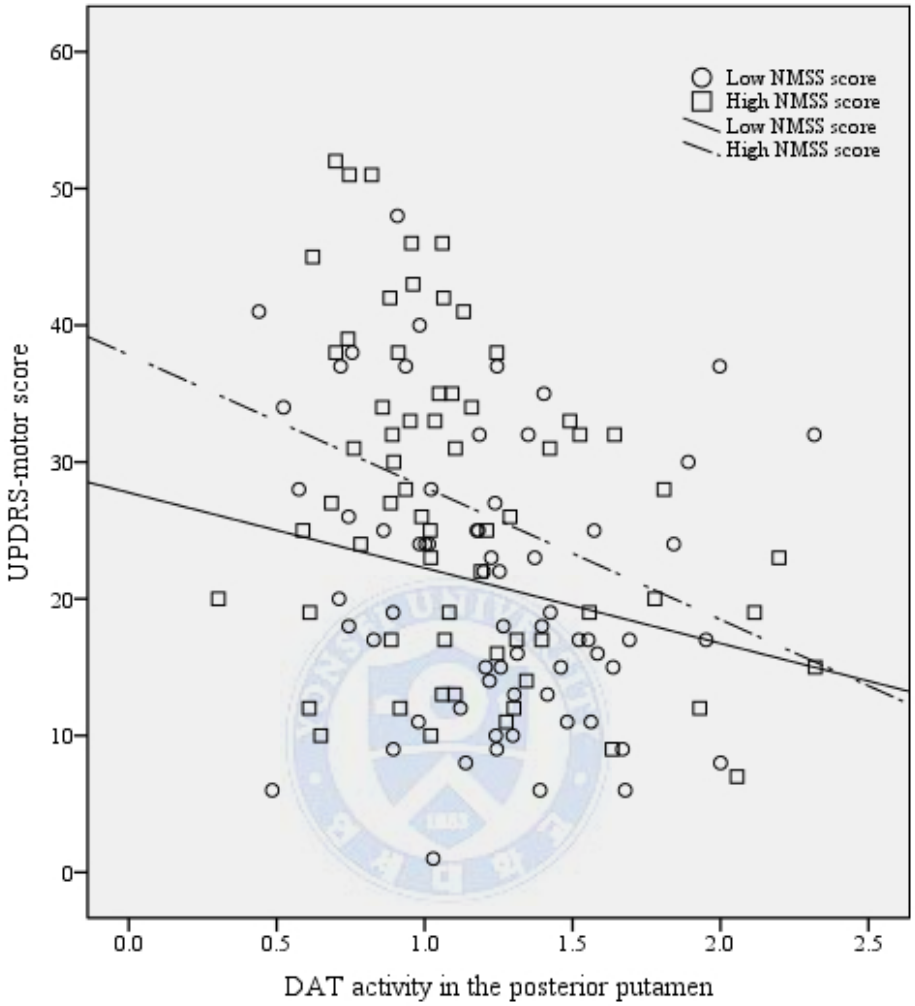

Figure 2. A scatterplot showing the relationship between DAT activity in the posterior putamen and UPDRS-motor score in each patient. Low NMSS score patients (circle) represent significantly lower UPDRS-motor score at same DAT activity in the posterior putamen than high NMSS score patients (rectangle).

Table 2. ^{18}F-FP-CIT uptakes of striatal subregions and inter-subregional ratios between the two patient groups

	Low NMSS score (n=76)	High NMSS score (n=75)	*p*-value
Striatal subregions			
VS	2.38 ± 0.57	2.32 ± 0.66	0.578
AC	2.09 ± 0.67	2.11 ± 0.83	0.873
PC	1.30 ± 0.47	1.32 ± 0.56	0.811
AP	2.13 ± 0.60	2.06 ± 0.68	0.510
PP	1.21 ± 0.39	1.19 ± 0.44	0.690
VP	1.40 ± 0.37	1.34 ± 0.40	0.367
Inter-subregional ratios			
AP/PP	1.82 ± 0.41	1.81 ± 0.42	0.919
AC/PP	1.78 ± 0.53	1.85 ± 0.58	0.443
VP/PP	1.19 ± 0.19	1.18 ± 0.23	0.877
VS/PP	2.09 ± 0.69	2.12 ± 0.70	0.797
PC/PP	1.09 ± 0.31	1.16 ± 0.40	0.282

Data are means ± SDs.

VS: ventral striatum, AC: anterior caudate, PC: posterior caudate, AP: anterior putamen, PP: posterior putamen, VP: ventral putamen.

The correlations between subregional DAT activities and the each domain score of the NMSS after controlling for follow-up duration are shown in Table 3. The mood/cognition domain score significantly and negatively correlated to the anterior putamen/posterior putamen ISR (r = -0.175, p = 0.032) (Figure 3). In contrast, the cardiovascular and sleep/fatigue domain scores positively correlated with the anterior caudate/posterior putamen ISR. The other NMSS domain scores and total NMSS score did not correlate to subregional DAT activities.

Table 3. Correlation between ^{18}F-FP-CIT uptakes and the each domain score of the NMSS

	Cardio-vascular	Sleep/ Fatigue	Mood/ Cognition	Perceptual/ Hallucina-tions	Attention/ Memory	Gastro-intestinal	Urinary	Sexual function	Miscella-neous	Total
Inter-subregional ratios										
AP/PP	0.091	0.067	-0.175*	-0.011	-0.067	0.042	-0.068	0.060	-0.134	-0.079
AC/PP	0.184*	0.176*	-0.117	0.087	0.029	0.030	-0.095	0.034	-0.034	-0.004
VP/PP	0.108	0.016	-0.063	-0.015	-0.061	0.079	-0.124	-0.014	-0.036	-0.053
VS/PP	0.159	0.047	-0.116	0.054	-0.037	0.133	-0.043	0.013	-0.079	-0.020
PC/PP	0.156	0.157	-0.081	0.086	0.041	0.069	-0.089	0.083	0.034	0.034

Significant difference across groups, *p < 0.05.

VS: ventral striatum, AC: anterior caudate, PC: posterior caudate, AP: anterior putamen, PP: posterior putamen, VP: ventral putamen.

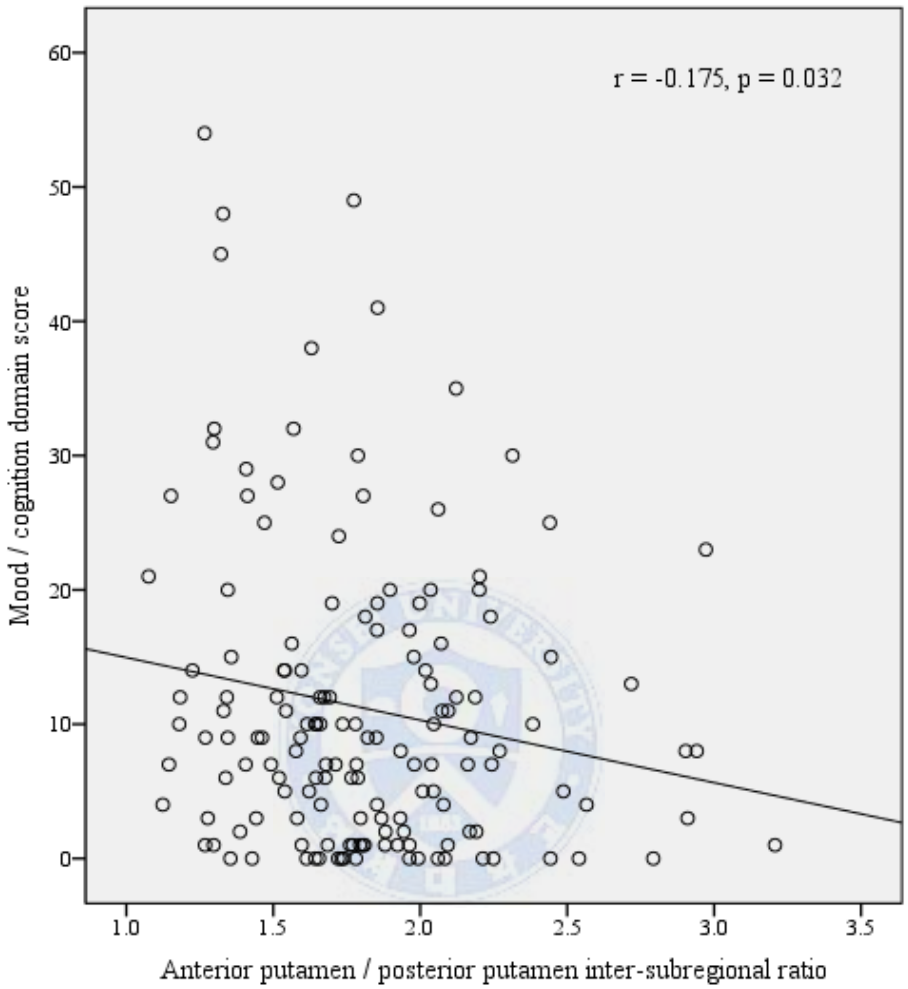

Figure 3. A scatterplot showing anterior putamen/posterior putamen inter-subregional ratio and the mood/cognition domain score of the NMSS in each patient. There is significant negative correlation after adjustment for follow-up duration.

IV. DISCUSSION

This study demonstrated that high NMSS patients showed different clinical characteristics, such as an older onset age, more severe motor symptoms, and more severe depression, when compared to low NMSS patients. DAT activities in the striatal subregions and ISRs in high NMSS patients were similar to those in low NMSS patients. After controlling DAT activity in the posterior putamen as well as onset age, gender, motor symptom duration and BDI score in each patient, UPDRS-motor scores were still higher in high NMSS patients than low NMSS patients. This result suggests that low NMSS patients shows either a more benign course or a greater reserve compensating for the pathological processes when compared to high NMSS patients. Less LED in low NMSS patients when compared to that in high NMSS patients after similar follow-up duration support this assumption. Although the total NMSS score did not correlated to ISRs, the mood/cognition domain score correlated inversely and significantly with the anterior putamen/posterior putamen ISR, and the cardiovascular and sleep/fatigue domain scores correlated positively and significantly to the anterior caudate/posterior putamen ISR. The inverse relationship between mood/cognition and the anterior putamen/posterior putamen ISR suggests that patients with greater DAT defects in the anterior putamen relative to those in posterior putamen shows greater deficits in mood/cognition function. However, the meaning of the positive relationship between cardiovascular, sleep/fatigue and the anterior caudate/posterior putamen ISR is uncertain and might be incidental, because it is hard to explain how greater DAT defects in the anterior caudate is associated with less

cardiovascular and sleep/fatigue dysfunction.

The mean NMSS score in our patients was relatively lower than that in the original study,[13] presumably because we enrolled early stage PD patients. The association between NMS and PD progression has been well documented in a number of studies, in which a number of NMS increases along with PD duration, HYS, and UPDRS scores.[13,17] In this study, high NMSS patients also showed a higher UPDRS-motor score than low NMSS patients, which is compatible to the previous studies. Because depression is a main component of the mood/cognition domain of the NMSS, and could be an important factor influencing other NMS such as sleep/fatigue, attention/memory, and so on, it is fully expected that high NMSS patients had a higher BDI score, i.e., a greater depression, than low NMSS patients. In this study, high NMSS patients were older at PD symptom onset than low NMSS patients. Because many of NMSs can be associated with aging in healthy people, this result is also predictable like as previous study.[18]

PD symptoms do not develop until 50 - 60% of the dopaminergic neurons in the substantia nigra are lost,[19] suggesting the presence of a mechanism for compensation in the motor system. The ability of the brain to show no functional impairment until the damage reaches a critical threshold, which is called compensatory ability, may reflect an individual's neuronal reserve.[20] Similarly, in the present study, the low NMSS patients showed less motor deficits when compared to the high NMSS patients, despite a similar degree of striatal dopamine reduction in the posterior putamen. Therefore, PD patients with less NMS represent either a more benign course or a greater reserve

compensating for the pathological process when compared to those with greater NMS.

The mood/cognition domain of the NMSS contains apathy, anxiety, fear, depression, and dysthymia. Depression, anxiety, and apathy belong to the most common hypodopaminergic behavioral syndrome in PD patients.[21] Previous research that used [^{11}C]RTI-32 PET (an in vivo marker of both dopamine and noradrenaline transporter binding) detected decreased binding in the locus coeruleus and in several regions of the limbic system including the anterior cingulate cortex, thalamus, amygdala and ventral striatum in PD patients with depression and anxiety. In addition, apathy was inversely correlated with [^{11}C]RTI-32 binding in the ventral striatum, not in the caudate or the putamen.[22] A previous study performed in PD patients has shown an association between depression and altered putamen metabolism.[23] Among the studies using DAT SPECT, one showed that anxiety and depression were associated with reduced DAT activity in the left anterior putamen,[24] while the other demonstrated that anxiety severity was related with reduced DAT activity in the right caudate.[25] Thus, previous studies suggest a potential connection between affective symptoms in PD and striatal DAT reduction, although this assumption is still controversial. The present result showing an association between the degree of NMS and DAT reduction in the anterior putamen may provide an additional evidence to support the above assumption.

Recent studies have demonstrated that excessive daytime sleepiness and RBD in early PD patients are correlated with decreased striatal DAT binding.[26] [27] Another study has also shown that fatigue in PD is related to reduced

dopaminergic function in the caudate and the insula.[28] In this study, the anterior caudate/posterior putamen ISR was positively correlated with the sleep/fatigue domain score, which is quite opposite to the results shown in the above studies. In addition, the anterior caudate/posterior putamen ISR was also positively correlated with the cardiovascular domain score. Dopamine has a complex role in the sleep-wake cycle, and, in PD, sleep-related problems might be dopamine sensitive.[29] Also, the sleep/fatigue domain contains diverse symptoms of sleep, such as hypersomnia and insomnia, while the cardiovascular domain is only composed of two questions. These factors could have effect on distinct result from previous studies. Thus, it is hard to explain how greater DAT reduction is associated with less NMS, these results appear to be an incidental rather than a clinically relevant finding.

In this study, other NMSS domain scores were not correlated to striatal subregional ISRs. Previous studies have shown that reduced DAT uptakes in the caudate, ventral striatum, and anterior cingulate cortex are associated with cognitive impairment in PD,[30,31] while another study using ^{18}F-Dopa PET have demonstrated no significant correlation between cognitive abilities of non-demented PD and striatal dopaminergic depletion.[32]

Selection of de novo PD patients in this study minimized the influence of any PD medication on the assessments of striatal dopamine depletion and motor deficits. A programmed measure of striatal dopamine activities could minimize the inter- and intra-rater variability. However, a longitudinal follow-up study is warranted to assess whether PD patients with less NMS show more benign course of PD progression.

V. CONCLUSION

This study demonstrates that the pattern of striatal dopamine depletion does not contribute to the degree of NMS in early PD, although some clinical features are different between the patients with greater NMS and those with less NMS. Our research also suggests that patients with less NMS may have a more benign course of motor symptom progression or a greater reserve compensating for the pathological process, compared to those with more NMS. NMS in PD may be more likely associated with extra-striatal lesions accompanied in PD than striatal dopaminergic deficits. Further functional imaging study that handle pathogenesis underlying NMS in PD should be necessary, and it will be able to contribute to develop future therapeutic targets. A prospective and long term follow-up study is required to investigate striatal dopaminergic system associated with NMS.

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ABSTRACT(IN KOREAN)

파킨슨병 환자에서 선조체의 도파민 감소가 비운동 증상에 기여하는가?

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정 수 진

목적 : 파킨슨병의 비운동 증상은 삶의 질에 영향을 미치는 주요한 요인으로 알려져 있으나, 이에 대한 정확한 병태생리는 정립된 바가 없다. 선조체 도파민의 감소 양상이 파킨슨병의 비운동 증상에 영향을 미치는지 알아보기 위하여, 본 연구는 비운동 증상이 심한 파킨슨병 환자일수록 뒤쪽 조가비핵보다 오히려 다른 부위의 선조체에 도파민 신경세포의 감소율이 심할 것이라고 가정하였다.

방법 : 본원에서 2009년 3월부터 2013년 6월까지 파킨슨병을 처음 진단받았고, 진단 당시에 [^{18}F] N-(3-Fluoropropyl)-2β-carbon ethoxy-3β-(4-iodophenyl) nortropane (FP-CIT) 양전자 방출 단층촬영을 시행한 151명의 환자를 대상으로 비운동 증상 평가 척도(NMSS)를 작성하였다.

결과 : 비운동 증상 평가 척도의 점수가 높은 (중앙값 이상) 환자들이

점수가 낮은 환자들에 비하여 발병연령이 높았고 (64.9 ± 9.1 vs 61.5 ± 10.1 years, p = 0.034), 초기의 통합파킨슨병척도운동점수(UPDRS-motor)가 높았으며 (26.9 ± 11.7 vs 20.9 ± 10.3, p = 0.003), 레보도파 일용량이 높았고 (636.3 ± 293.0 vs 524.4 ± 196.2, p = 0.007), 벡 우울척도 (BDI) 점수가 높았다 (14.7 ± 8.1 vs 11.5 ± 7.5, p = 0.013). 발병연령, 성별, 이환기간, 벡 우울척도 점수 및 뒤쪽 조가비핵의 도파민 활성도를 보정한 후의 일반선형모형에서는 비운동 증상 평가 척도의 점수가 높은 환자들의 통합파킨슨병척도운동점수가 의미있게 높았다. 그러나 선조체 6구역과 소구역간의 비 (ISRs)는 두 군간에 차이가 없었다. 비운동 증상 평가 척도의 기분/인지 영역의 점수는 앞쪽 조가비핵/뒤쪽 조가비핵의 도파민 활성도 소구역간의 비와 음의 상관관계를 보였으나 (r = -0.175, p = 0.032), 총 점수 및 다른 영역의 점수와 선조체 소구역의 도파민 활성도 간에는 의미있는 상관관계가 없었다.

결론 : 본 연구는 선조체 도파민의 감소 양상이 초기 파킨슨병의 비운동 증상에 영향을 미치지는 않지만, 비운동 증상이 심한 환자와 경한 환자 사이에 임상 양상의 차이가 난다는 점을 나타낸다. 또한 비운동 증상이 경한 환자들은 운동 증상의 진행이 더디다는 것을 시사한다. 파킨슨병의 비운동 증상은 선조체의 도파민 감소보다는 파킨슨병과 연관된 선조체 외의 병변으로 인하여 초래될 것이다.

핵심되는 말 : 비운동 증상; 파킨슨병; 선조체 도파민 감소