Comparison of ^{18}F -DOPA and ^{18}F -DTBZ for PET/CT Imaging of Idiopathic Parkinson's Disease

Xinchong Shi

Sun Yat-sen University First Affiliated Hospital

Yang Yang

Sun Yat-sen University First Affiliated Hospital

LuLu Jiang

Sun Yat-sen University First Affiliated Hospital

Jinhua Chen

Sun Yat-sen University First Affiliated Hospital

Chang Yi

Sun Yat-sen University First Affiliated Hospital

Ganhua Luo

Sun Yat-sen University First Affiliated Hospital

Lei Wu

Sun Yat-sen University First Affiliated Hospital

Jianmin Chu

Sun Yat-sen University First Affiliated Hospital

Jian Wang

Huashan Hospital Fudan University

Xiangsong Zhang (✉ zhxiangs@mail.sysu.edu.cn)

Sun Yat-sen University First Affiliated Hospital <https://orcid.org/0000-0002-1730-9923>

Ling Chen

Sun Yat-sen University First Affiliated Hospital

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Abstract

Objective: To compare the two imaging tracers ^{18}F -DOPA and ^{18}F -DTBZ for PET/CT imaging in idiopathic Parkinson's Disease (PD).

Methods: 32 patients with final diagnosis of idiopathic PD and 12 healthy controls were recruited in our study. The clinical symptoms of PD patients were evaluated by using the UPDRS-III and modified H-Y stage. All subjects underwent both ^{18}F -DOPA and ^{18}F -DTBZ PET/CT, and the results were interpreted by visual analysis and semi-quantitative analysis. Semi-quantitative analysis was performed to calculate the specific uptake ratios (SURs) in the subregions of striatum with the occipital cortex as reference area. A one-way ANOVA test was used to compare the clinical data and the SURs among the patients at different stages. Regression analysis was performed to analyze the correlation between the SURs and the clinical data. A kappa test was used to evaluate the consistency of the visual inspection results.

Results: Among the PD patients, there were 7 patients in H-Y stage I, 14 patients in stage II, and 11 patients in stage III. No statistical difference in age or gender was found among the three groups ($p > 0.05$). The semi-quantitative analysis of ^{18}F -DOPA and ^{18}F -DTBZ PET images showed that PD patients in different stages had significantly lower SURs in the striatum than the healthy controls ($p < 0.05$), and the SURs generally decreased with the progression of PD staging ($p < 0.05$). An exponential correlation was found between the SURs of each tracer in the putamen with the UPDR-III score ($p < 0.05$), and a linear correlation was found in striatum SURs between two tracers ($p < 0.05$). By visual analysis, ^{18}F -DOPA detected 29 cases with bilateral uptake decrease and the other 3 stage I cases with unilateral uptake decrease, while ^{18}F -DTBZ detected 26 cases with bilateral uptake decrease and 6 cases with unilateral uptake decrease. The overall consistency of visual analysis between these two tracers was 90.63% (Kappa=0.62, $p < 0.001$).

Conclusion: Both ^{18}F -DTBZ and ^{18}F -DOPA are reliable imaging tracers for PET/CT imaging in PD patients with good consistency, and they have the same level of striatal SURs decline percent for PD patients in early stages.

Introduction

Parkinson's disease (PD) as a clinically common neurodegenerative disorder is characterized by loss of dopaminergic neurons in the substantia nigra and the formation of Lewy Bodies (LBs), leading to a decrease in dopamine neurotransmitters in the brain and a series of motor and non-motor symptoms[1–3].

Owing to no obvious change in brain morphology in PD patients, it is difficult to diagnose and evaluate PD using conventional examinations, such as computed tomography (CT), magnetic resonance imaging (MRI) and Doppler ultrasound. Thanks to the development of molecular probes, positron emission tomography (PET) imaging as a noninvasive medical imaging tool can observe the metabolic and

biochemical processes in the brain, as well as the distribution of macromolecular proteins, thus playing an important role in the diagnosis, differential diagnosis, progression monitoring, and treatment evaluations of PD[4]. At present, the molecular probes commonly used in the clinic target pre- and post-synaptic dopaminergic system and glucose metabolism. Among them, the presynaptic dopaminergic imaging is recognized as effectively reflecting the apoptosis in neurons of the substantia nigra and thus it plays an irreplaceable role in the research and clinical diagnosis of PD[5]. Currently, the commonly used molecular probes for presynaptic dopaminergic imaging mainly include three types: L-6-[¹⁸F]fluoro-3,4-dihydroxyphenylalanine (¹⁸F-DOPA), which targets the dopamine synthesis capacity in substantia nigra neurons, [¹¹C] dihydrotetrabenazine(¹¹C-DTBZ)/ 9-[¹⁸F]fluoropropyl-(+)-dihydrotetrabenazine (¹⁸F-DTBZ, ¹⁸F-AV133), which targets vesicular monoamine transporter type 2 (VMAT2) in substantia nigra neurons, and ¹¹C-CIT([¹¹C] 2 beta-carbomethoxy-3 beta-(4-iodophenyl)tropane)/¹¹C-CFT([¹¹C] 2-β-carbomethoxy-3-β-(4-fluorophenyl)tropane)/ ¹⁸F-FECNT(2β-carbomethoxy-3β-(4-chlorophenyl)-8-(2-[¹⁸F]-fluoroethyl)-nortropane), which targets the presynaptic dopamine transporter (DAT)[6]. These tracers are biomarkers for PET imaging in mapping integrity of dopamine neurons, especially for patients with neurodegenerative diseases. In animal models, these tracers have been proven reliable in detecting the apoptosis of substantia nigra neurons even when movement symptoms have not occurred yet[7, 8]. Clinical evidence has proven that both VMAT2- and DAT-targeted imaging have good sensitivity to distinguish PD from diseases without the damage of dopamine system, but they cannot differentiate idiopathic PD from other parkinsonism[9].

So far, there are still problems in the popularization of these three tracers in clinical practice. To be specific, imaging using ¹¹C-DTBZ, ¹¹C-CFT and ¹¹C-CIT is difficult to achieve large-scale application because of its relatively short half-life of ¹¹C, which is only used in medical centers with cyclotron on site. Meanwhile, ¹⁸F-DTBZ and 2β-carbomethoxy-3β-(4-chlorophenyl)-8-(2-[¹⁸F]-fluoroethyl)-nortropane(¹⁸F-FECNT) are still under clinical trials, so they cannot be applied and popularized now.[10] In contrast, due to the popularization of the automatic synthesis module and the optimization of synthetic process, the application of ¹⁸F-DOPA is available in many medical clinics now.[11, 12] However, the clinical application of ¹⁸F-DOPA is still controversial. Some studies have pointed out that ¹⁸F-DOPA imaging displayed false-negative results in early PD patients, and failed to detect the progression of motor symptoms[13, 14].

In this study, we directly compared ¹⁸F-DOPA with ¹⁸F-DTBZ in PD patients to better evaluate the application value of these two tracers in IPD.

Methods

Subjects

Between 2017 and 2019, we prospectively recruited 38 patients with a 'probable' or 'established' diagnosis of idiopathic PD according to the Clinical Diagnostic Criteria for Parkinson's disease (MDS-PD Criteria) from International Parkinson and Movement Disorder Society (MDS)[15]. 12 healthy controls

were recruited by advertisement in the community in Guangzhou, China. All subjects underwent a magnetic resonance imaging (MRI) examination (3T Siemens Magnetom TIM Trio scanner), and their T1- and T2-weighted images were obtained to exclude the subjects with cerebral lesions. All patients received neurologic examination by two experts in movement disorders at the drug-off state. The motor symptoms and clinical stages were evaluated using the Unified Parkinson's Disease Rating Scale, part III (UPDRS-III) and the Hoehn and Yahr (H-Y) staging scale, respectively.

All subjects received ^{18}F -DOPA and ^{18}F -DTBZ PET/CT imaging, and then we followed up the patients for at least two years. Finally, the diagnosis of clinically established PD was made in 32 patients and the other 6 patients were excluded from the diagnosis of PD.

This study was approved by the Ethics Committee of the First Affiliated Hospital of Sun Yat-Sen University. We explained to all subjects the purpose of this study and the PET examination procedures. All the subjects enrolled in this study signed the written informed consent form.

Radiochemistry

The two imaging tracers used in this study were synthesized in our center. The synthesis of ^{18}F -DTBZ was performed by the Key Laboratory of Radiopharmaceuticals (Beijing Normal University) in accordance with the procedures described in a previous study.[16] The synthesis of ^{18}F -DOPA was accomplished using the Trasis AllinOne® Module (Belgium).

Data Acquisition

The examinations for the participants were performed using a Philips Gemini GXL 16 PET/CT scanner. All subjects stopped taking any anti-parkinsonian medications for at least 12 hours before ^{18}F -DTBZ and ^{18}F -DOPA imaging. The time interval between these two imaging was at least 24 hours but no more than two weeks. The subjects were injected with ^{18}F -DOPA (370MBq, 10 MCi) after taking 200mg entacapone for two hours, or ^{18}F -DTBZ (370MBq, 10 MCi) and had quiet rest for 90 minutes before the PET/CT imaging.

A brain specific scanning program was selected for the PET/CT imaging. Low-dose CT scanning was performed for attenuation correction before 10-minute PET acquisition. Finally, PET images were reconstructed with the resolution of $2 \times 2 \times 2 \text{ mm}^3$. In order to ensure the PET imaging quality, the reconstructed PET images were evaluated preliminarily by nuclear medicine physicians to determine whether the subjects had excessive head movement during the PET acquisition, and repeated PET/CT acquisition was performed if necessary.

Image Preprocessing

Image preprocessing and semi-quantitative analysis were conducted using MIPAV software (version 7.4.0, US Department of Health and Human Service) and statistical parametric mapping (SPM) software (Wellcome Trust Centre for Neuroimaging, London, UK). For each subject, the reconstructed ^{18}F -DOPA

image and the ^{18}F -DTBZ image were initially co-registered with the MRI T1-weighted image. Next, the MRI T1-weighted images were normalized into Montreal Neurological Institute (MNI) standard brain template, and then the transform parameters were applied to the co-registered ^{18}F -DOPA and ^{18}F -DTBZ images.

Semi-quantitative analysis

The volume of interests (VOIs) in areas of caudate nuclei and anterior/posterior putamen were included for the current study. The specific uptake ratio (SUR) of the VOIs was calculated using occipital cortex as reference region ($\text{SUR} = (\text{VOI uptake}/\text{reference uptake}) - 1$). And then, the whole-brain SUR images were obtained using the uptake of occipital cortex as reference. In order to investigate the relationship between the SUR of the two tracers and the motor symptoms, the SUR of the striatum was compared among the different groups, and its correlation with UPDRS-III was also analyzed. In this study, the striatum on the ipsilateral side of the initially affected limb was defined as the ipsilateral side, and the opposite side was defined as the contralateral side.

Visual analysis

Visual analysis, blinded to the clinical information of all subjects, was performed by three experienced nuclear medicine physicians. A significant decrease of radioactivity uptake in the putamen at least one side was considered positive. At first, we calculated the average SUR ($\text{SUR}_{\bar{}}$) of the putamen for the two tracers in healthy controls, and then the upper limit of SUR images was set to $\text{SUR}_{\bar{}}$. When the imaging result was positive, re-evaluation should be performed to confirm if it was decreased unilaterally or bilaterally. If the results of the three physicians were inconsistent, they discussed the case and achieved a consensus.

Statistical analysis

Statistical analysis was conducted using SPSS (IBM SPSS Statistics 19, USA). The SUR of striatum sub-regions in the healthy controls and PD patients at different stages were compared by the non-parameter Kruskal-Wallis test. The visual inspection consistency between two tracers was tested by kappa test. The correlation between the SUR and the clinical motor symptoms was tested by exponential regression analysis, and the correlation between the SUR of the two tracers was evaluated by Spearman's rank correlation coefficient.

Results

Clinical data of the subjects

The clinical data of the 32 PD patients is shown in Table 1. PD patients and health controls were demographically well matched as no significant group differences were found in age and gender ($p > 0.05$). The PD patients at different H-Y stages were significantly different from each other in motor symptom scores (UPDRS-III) ($p = 0.004$).

Semi-quantitative analysis results

The SUR of the striatum sub-regions were shown in Table 2. In healthy controls, the striatal SURs was significantly higher in ^{18}F -DOPA than that in ^{18}F -DTBZ ($p < 0.001$). Compared with the healthy controls, the PD patients in the different stages had lower SUR in both ^{18}F -DOPA and ^{18}F -DTBZ PET/CT imaging ($p < 0.05$). And the SUR decreased significantly among the PD groups in both ^{18}F -DOPA and ^{18}F -DTBZ imaging.

In the H-Y I and II PD group, the decline percent of SUR in striatum showed no difference between ^{18}F -DOPA and ^{18}F -DTBZ imaging (paired t-test, $p > 0.05$). In the H-Y III PD group, the SUR decline percent in bilateral putamen was significantly higher in ^{18}F -DTBZ images than that in ^{18}F -DOPA. (paired t-test, $p < 0.05$). (Fig. 1)

The SUR of the bilateral putamen and caudate nucleus in the ^{18}F -DOPA and ^{18}F -DTBZ PET images was exponentially correlated with the UPDRS-III scores ($p < 0.05$). The SUR of each subregion for the two tracers was linearly correlated ($p < 0.05$). (Fig. 2)

Visual analysis

In healthy controls, the average SUR of putamen was 2.67 for ^{18}F -DOPA (95% CI: 2.42-2.92) and 1.56 for ^{18}F -DTBZ (95% CI: 1.41-1.71). After setting the upper limit of the SUR images according to the SUR of the putamen in the healthy controls (^{18}F -DOPA: 2.42, ^{18}F -DTBZ: 1.41), all the PD patients showed decreased uptake in striatum area in ^{18}F -DOPA and ^{18}F -DTBZ images, while healthy controls had normal radioactivity uptake. (Fig. 3) These two tracers both had the 100% sensitivity for detecting PD.

^{18}F -DOPA PET/CT imaging identified 29 patients with decreased radioactivity uptake in bilateral striatum and 3 stage I cases in unilateral striatum. Meanwhile, ^{18}F -DTBZ PET/CT imaging detected 26 patients with decreased radioactivity uptake in bilateral striatum and 6 cases in unilateral striatum, among whom 5 cases were in stage I and 1 case was in stage II. Moreover, the 3 PD patients with unilateral uptake decrease identified by ^{18}F -DOPA PET/CT imaging were also confirmed by ^{18}F -DTBZ PET/CT imaging. Finally, the two imaging agents had a coincidence rate of 90.63% on visual analysis (Kappa = 0.62, $p < 0.001$).

Discussion

In the area of molecular imaging for PD, presynaptic tracers play an irreplaceable role in the evaluation of neuron degeneration in substantia nigra. Among those tracers, PET imaging targeting the dopamine active transporter (DAT) and the vesicular monoamine transporter 2 (VMAT2) has been reported to have good sensitivity and that its results are closely related to the motor and non-motor symptoms.[17] By contrast, although ^{18}F -DOPA is more convenient for clinical application and can reflect the capability of substantia nigra neurons to synthesize dopamine, its application is still limited due to the report of false-negative results and the factors affecting the imaging results.[13, 14] In this study, we directly compared

the PET/CT imaging results of ^{18}F -DTBZ and ^{18}F -DOPA in PD patients. In ^{18}F -DOPA PET/CT imaging, entacapone was administered to inhibit the absorption of the imaging agent in peripheral tissues and thereby improved its imaging quality and consistency. Besides, the visual inspection was assisted by the uptake of putamen in healthy controls. Eventually, both ^{18}F -DOPA and ^{18}F -DTBZ imaging presented no false-negative results. These findings proved that these two tracers are both reliable in PET/CT imaging for PD patients.

^{18}F -DTBZ as a specific imaging agent can specifically bind with VMAT2 in the terminals of substantia nigra neurons to reflect the density of vesicular monoamine in the striatum, so it is recognized as having relatively few interfering factors.[18–20] In previous studies, ^{18}F -DTBZ was considered to have no false-negative results, and the radioactivity uptake of the striatum is related to the clinical stage and the motor and non-motor symptom scores, which can be used to evaluate the apoptosis of substantia nigra neurons. The finding of this study is consistent with the above results and confirmed the reliability of ^{18}F -DTBZ in PET imaging for PD patients.

^{18}F -DOPA as a metabolic imaging agent can be transformed into ^{18}F -dopamine under the action of aromatic amino acid decarboxylase (AADC) and then transported to the striatum.[21] Because ^{18}F -DOPA is a metabolic agent, it can also be absorbed by peripheral tissues for anabolism. Therefore, carbidopa is usually administered to patients to inhibit AADC activity in peripheral tissues, so as to increase the radioactive concentration in the intracranial blood and better reflect the capability of dopamine synthesis in substantia nigra neurons. Apart from carbidopa, entacapone can also inhibit the uptake of ^{18}F -DOPA in peripheral tissues by inhibiting the activity of catechol-O-methyl transferase, and thereby improve the intracranial concentration of the radioactive tracer and its uptake by striatum.[22, 23] In the current study, we used entacapone instead of carbidopa and also obtained images of good quality.

Previous studies reported that the sensitivity of ^{18}F -DOPA PET/CT imaging to PD diagnosis is 90%-100% and the false negative result can be seen among patients at early stage.[24] However, there is no convincing explanation for the false negative result. Some researchers assumed that the ability of substantia nigra neurons to synthesize dopamine was enhanced under the condition of the insufficient dopamine supply, which leads to false negative results of radioactivity uptake in the striatum.[25] However, this explanation is not consistent with the results of animal experiments. For example, even when a monkey had decreased substantia nigra neurons without motor symptoms, the dopamine concentration in the striatum already decreased significantly, and the SUR in the striatum of ^{18}F -DOPA also decreased. [26, 27]

Studies on animals have proven that the motor symptoms only occur when more than 60% of the substantia nigra neurons are damaged and the concentration of dopamine in striatum decreased significantly.[28–31] In this study, the SUR of the contralateral putamen in PD patients at stage I was about 40% of that in the healthy controls (^{18}F -DTBZ, 38.46%; ^{18}F -DOPA, 40.07%), which is in consistency with the results of animal studies and suggested that both ^{18}F -DOPA and ^{18}F -DTBZ PET/CT imaging can

reliably reflect the damage of the substantia nigra neurons.[26] With the progression of PD disease, the radioactivity uptake of the two tracers in the striatum decreased significantly in different rate. The radioactivity uptake of ^{18}F -DTBZ in the striatum decreased more significantly with the progression of PD, indicating the synthetic regulation of substantia nigra neurons.

Conclusions

Both ^{18}F -DTBZ and ^{18}F -DOPA are reliable imaging tracers for PET/CT imaging in PD patients with good consistency, and they have the same level of striatal SURs decline percent for PD patients in early stages.

Abbreviations

PD, Parkinson's disease

UPDRS-III, Unified Parkinson's Disease Rating Scale part III

H-Y, Hoehn and Yahr

SURs, specific uptake ratios

^{18}F -DOPA, L-6- ^{18}F fluoro-3,4-dihydroxyphenylalanine

^{11}C -DTBZ, [^{11}C] dihydrotetrabenazine

^{18}F -DTBZ, 9- ^{18}F fluoropropyl-(+)-dihydrotetrabenazine

VMAT2, vesicular monoamine transporter type 2

^{11}C -CIT, [^{11}C] 2 beta-carbomethoxy-3 beta-(4-iodophenyl)tropane

^{11}C -CFT, [^{11}C] 2-β-carbomethoxy-3-β-(4-fluorophenyl)tropane

^{18}F -FECNT, 2β-carbomethoxy-3β-(4-chlorophenyl)-8-(2- ^{18}F -fluoroethyl)-nortropane

DAT, dopamine transporter

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the First Affiliated Hospital of Sun Yat-Sen University. All the subjects enrolled in this study signed the written informed consent form.

The authors extend our thanks to the patients and their families and physicians for their trust and contribution to this study.

Consent to publication

Consent for publication had been obtained from the subjects whose imaging results were displayed in this article.

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Competing interests

The authors declare that they have no Competing interests.

Authors' contributions

1) Research project:

Ling Chen and Xiangsong Zhang designed and organized this study.

Jian Wang reviewed the study design and gave valuable suggestions.

2) Research execution and statistical analysis:

Yang Yang, Lulu Jiang, Jinhua Chen, Jianmin Chu and Lei Wu selected the PD patients, assessed their motor symptoms and made the follow-up.

Ganhua Luo and Chang Yi prepared the radio-tracers ¹⁸F-DOPA/¹⁸F-DTBZ.

Xinchong Shi and Chang Yi were responsible for PET/CT imaging and data analysis.

3) Manuscript writing:

Finally, Xinchong Shi, Yang Yang and Lulu Jiang completed the initial writing, and then Ling Chen and Xiangsong Zhang reviewed and revised the manuscript.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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Tables

Table 1. Demographic and clinical profiles of all participants.

Group	Age	Sex	UPDRS-III	Disease Duration(y)
HC (n=12)	59.39±9.48	6F/6M		
PD H-Y I(n=7)	60.56±10.07	5F/2M	15.60±4.97*	1.04±0.52*
PD H-Y II(n=14)	65.5±8.55	5F/9M	27.62±7.91	1.93±0.61
PD H-Y III(n=11)	66.81±9.44	5F/6M	38.72±5.85	4.51±2.26

HC, Healthy Control. PD, Parkinson Disease. UPDRS-III, part III of Unified Parkinson's Disease Rating Scale. H-Y, Hoehn and Yahr stage.

*Significance from comparison of different PD groups.

Table 2. Regional SURs and percentage decline rate for two tracers.

Group	SUR of 18F-DTBZ								SUR of 18F-DOPA							
	Con-APu (Decline, %)	Con-PPu (Decline, %)	Con-Pu (Decline, %)	Con-Cau (Decline, %)	Ip-APu (Decline, %)	Ip-PPu (Decline, %)	Ip-Pu (Decline, %)	Ip-Cau (Decline, %)	Con-APu (Decline, %)	Con-PPu (Decline, %)	Con-Pu (Decline, %)	Con-Cau (Decline, %)	Ip-APu (Decline, %)	Ip-PPu (Decline, %)	Ip-Pu (Decline, %)	Ip-Cau (Decline, %)
HC (n=12)	1.68±0.22 (-)	1.43±0.29 (-)	1.56±0.23 (-)	1.17±0.16 (-)	1.68±0.22 (-)	1.43±0.29 (-)	1.56±0.23 (-)	1.17±0.16 (-)	2.72±0.58 (-)	2.62±0.56 (-)	2.67±0.56 (-)	1.97±0.41 (-)	2.72±0.58 (-)	2.62±0.56 (-)	2.67±0.56 (-)	1.97±0.41 (-)
PD H-Y I(n=7)	0.83±0.22 ^{a,b} (50.60)	0.35±0.12 (75.52)	0.60±0.15 ^{a,b} (61.54)	0.72±0.27 ^{a,b} (38.46)	1.10±0.25 (34.52)	0.69±0.19 (51.75)	0.90±0.18 ^{a,b} (42.31)	0.83±0.28 ^b (29.06)	1.38±0.34 ^{a,b} (49.26)	0.74±0.32 (71.76)	1.07±0.18 ^{a,b} (59.93)	1.08±0.28 ^{a,b} (45.18)	1.66±0.41 (38.97)	1.15±0.43 (56.11)	1.41±0.41 ^{a,b} (47.19)	1.20±0.27 ^b (39.09)
PD H-Y II(n=14)	0.57±0.23 ^{a,b} (66.07)	0.25±0.13 (82.52)	0.41±0.17 ^{a,b} (73.72)	0.53±0.20 ^{a,b} (54.70)	0.74±0.31 (55.95)	0.41±0.18 (71.33)	0.58±0.15 ^{a,b} (62.82)	0.61±0.27 ^{a,b} (47.86)	1.07±0.18 ^{a,b} (60.66)	0.59±0.13 (77.48)	0.84±0.13 ^{a,b} (68.53)	0.87±0.15 ^{a,b} (55.84)	1.23±0.26 (54.78)	0.75±0.23 (71.37)	1.00±0.23 ^{a,b} (62.55)	0.93±0.16 ^{a,b} (52.79)
PD H-Y III(n=11)	0.35±0.16 ^{a,b} (79.17)	0.14±0.08 (90.20)	0.25±0.12 ^{a,b} (83.97)	0.32±0.17 ^{a,b} (72.65)	0.51±0.20 (69.64)	0.26±0.13 (81.82)	0.39±0.16 ^{a,b} (75.00)	0.44±0.18 ^{a,b} (62.39)	0.84±0.20 ^{a,b} (69.12)	0.43±0.11 (83.59)	0.64±0.14 ^{a,b} (76.03)	0.78±0.20 ^{a,b} (60.41)	1.02±0.25 (62.50)	0.66±0.26 (74.81)	0.85±0.24 ^{a,b} (68.16)	0.81±0.18 ^{a,b} (58.88)

HC, healthy control. PD, Parkinson disease. SUR, specific uptake ratio. H-Y, Hoehn and Yahr stage. Con-Pu, Putamen on the contralateral side of the initially affected limb. Ip-Pu, Putamen on the ipsilateral side of the initially affected limb. Con-Cau, Caudate nucleus on the contralateral side of the initially affected limb. Ip-Cau, Caudate nucleus on the ipsilateral side of the initially affected limb.

^a Significance from comparison with HC.

^b Significance from comparison among PD groups.

Figures

Figure 1

The regional SURs of striatum in PD patients compared with that in healthy controls (HC). H-Y, Hoehn and Yahr stage. SUR, specific uptake ratio. Con-Pu, Putamen on the contralateral side of the initially affected limb. Ip-Pu, Putamen on the ipsilateral side of the initially affected limb. Con-Cau, Caudate nucleus on the contralateral side of the initially affected limb. Ip-Cau, Caudate nucleus on the ipsilateral side of the initially affected limb. *significance was observed between two tracers ($p < 0.05$).

Figure 2

An exponential correlation was found between the SURs in the putamen on both sides with the UPDR-III scores ($p < 0.05$), and a linear correlation was found between the SURs of 18F-DOPA and 18F-DTBZ in the subregions of the striatum ($p < 0.05$). SUR, specific uptake ratio. Con-Pu, Putamen on the contralateral side of the initially affected limb. Ip-Pu, Putamen on the ipsilateral side of the initially affected limb. UPDRS-III, part III of Unified Parkinson's Disease Rating Scale.

Figure 3

SUR images of a healthy control and three PD patients in different H-Y stages. In comparison with healthy control, PD patient in H-Y I stage showed unilateral decrease for both tracers, while patients in stage II and III showed bilateral decrease for both tracers. H-Y, Hoehn and Yahr stage.