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Semiquantitative Analysis of Dopamine Transporter Scans in Patients With Parkinson Disease

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Abstract

Purpose: Dopamine transporter (DaT) imaging is an adjunct diagnostic tool in parkinsonian disorders. Interpretation of DaT scans is based on visual reads. SBRquant is an automated method that measures the striatal binding ratio (SBR) in DaT scans, but has yet to be optimized. We aimed to (1) optimize SBRquant parameters to distinguish between patients with Parkinson disease (PD) and healthy controls using the Parkinson's Progression Markers Initiative (PPMI) database and (2) test the validity of these parameters in an outpatient cohort.

Methods: For optimization, 336 DaT scans (215 PD patients and 121 healthy controls) from the PPMI database were used. Striatal binding ratio was calculated varying the number of summed transverse slices (N) and positions of the striatal regions of interest (*d*). The resulting SBRs were evaluated using area under the receiver operating characteristic curve. The optimized parameters were then applied to 77 test patients (35 PD and 42 non-PD patients). Striatal binding ratios were also correlated with clinical measures in the PPMI-PD group.

Results: The optimal parameters discriminated the training groups in the PPMI cohort with 95.8% sensitivity and 98.3% specificity (lowest putamen SBR threshold, 1.037). The same parameters discriminated the groups in the test cohort with 97.1% sensitivity and 100% specificity (lowest putamen SBR threshold, 0.875). A significant negative correlation ($r = -0.24$, $P = 0.0004$) was found between putamen SBRs and motor severity in the PPMI-PD group.

Conclusions: SBRquant discriminates DaT scans with high sensitivity and specificity. It has a high potential for use as a quantitative diagnostic aid in clinical and research settings.

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Keywords

caudate; parkinsonism; putamen; SPECT imaging; striatal binding ratio

The substantia nigra pars compacta in the midbrain contains dopaminergic neurons projecting to the striatum. The nigrostriatal terminals express the dopamine transporter (DaT) protein that is responsible for the uptake of dopamine from the synaptic cleft back inside the presynaptic terminal. Loss of nigrostriatal terminals leads to parkinsonism, and idiopathic Parkinson disease (PD) is the proto-typical neurodegenerative disease of the nigrostriatal pathway. The clinical diagnosis of PD in most cases is straightforward; however, atypical or early presentations and concomitant medical conditions can complicate the diagnosis. Therefore, single-photon emission computed tomography (SPECT) imaging of DaT with ^{123}I-ioflupane (^{123}I-FP-CIT) has gained acceptance as an adjunct diagnostic tool in the evaluation of adult patients with suspected parkinsonian syndromes.[1–3]

^{123}I-ioflupane is a DaT radioligand. In vivo SPECT imaging of striatal ^{123}I-ioflupane uptake is a measure of DaT sites and reflects the nigrostriatal terminal integrity. Reduced striatal uptake is observed in PD as well as other Parkinson-plus syndromes; thus, DaT imaging cannot distinguish these conditions. However, it can distinguish PD and Parkinson-plus syndromes from other parkinsonian presentations without striatal dopaminergic deficit (eg, essential and dystonic tremors, vascular parkinsonism, drug-induced parkinsonism, psychogenic parkinsonism, dopa-responsive dystonia, X-linked dystonia-parkinsonism, and pallidal atrophies and toxins).[4]

^{123}I-ioflupane gained regulatory approval on the basis of visual reads.[5] The associated reader study trials showed that in patients with early signs and/or symptoms of a parkinsonian syndrome the positive percent agreement among 3 readers was 77% to 79%, and the negative percent agreement was 96.8%.[6] In order to aid the clinician with assessing the quantitative loss of DaT sites in patients, several image processing methods have been developed.[7–17] Computer-aided analysis can provide critical adjunct information, a “second read,” which may be particularly useful for challenging cases[18,19]; however, a criterion standard for testing the validity of automated methods is desirable.

In recent years, our group has developed an automated software program for semiquantitative analysis of striatal ^{123}I-ioflupane uptake. We have demonstrated good correlation between expert reads and semiquantitative analysis of the images,[18,19] yet the analysis needs to be optimized and validated.

The Parkinson’s Progression Markers Initiative (PPMI) offers an unprecedented opportunity for testing the validity of an automated analysis software for quantitating ^{123}I-ioflupane DaT SPECT scans (from here on “DaT scans”). The PPMI is a large, international multicenter clinical study to identify a variety of biomarkers for progression of de novo PD. Dopamine transporter imaging with ^{123}I-ioflupane is an important biomarker under study in this trial. The imaging is conducted at numerous sites in Australia, Europe, and the United States. The PPMI database contains a large number of DaT scans and extensive clinical evaluations for each subject. A tool for quantitating the DaT scans that has been tested on this extensive

database can be very valuable in aiding in the clinical diagnosis of PD and monitoring disease progression.

Our main purpose was 2-fold: (1) to determine the discriminatory power of our analysis tool in a large, well-characterized cohort of PD patients and control subjects, using a set of DaT scans from the PPMI database to test and optimize the analysis parameters, and (2) to test the validity of these parameters in an independent outpatient-based cohort, which is a more realistic representative of diagnostic challenges the clinician faces. To do this, we applied the optimized parameters to an outpatient cohort of patients with parkinsonian features who had DaT scans at the Yale New Haven Hospital (YNHH) for diagnostic purposes. In addition, we examined the relationship between the striatal ^{123}I-ioflupane uptake ratios and clinical measures of disease severity in the PPMI-PD group.

METHODS

Subjects

PPMI Cohort—Subjects with PD were male or female 30 years or older at time of PD diagnosis. The eligibility criteria for inclusion in the PPMI study were as follows: (1) exhibited at least 2 of the following: resting tremor, bradykinesia, rigidity (must have either resting tremor or bradykinesia); or either asymmetric resting tremor or asymmetric bradykinesia; (2) received a diagnosis of PD within 2 years or less at screening; (3) had a Hoehn and Yahr (H&Y) stage 1 or 2 status at baseline; (4) received confirmation from the imaging core that screening DaT scan is consistent with DaT deficit; and (5) were not expected to require PD medication within at least 6 months from baseline. Healthy controls (HCs) were male or female 30 years or older at screening, with the following exclusion criteria: (1) current or active clinically significant neurological disorder; (2) a first-degree relative with idiopathic PD (parent, sibling, child); (3) a Montreal Cognitive Assessment score of 26 or less; and (4) had received any of the following drugs that might interfere with DaT SPECT imaging: neuroleptics, metoclopramide, α-methyldopa, methylphenidate, reserpine, or amphetamine derivative, within 6 months of screening.

Dopamine transporter scans of 224 PD patients and 134 HCs obtained between July 2010 and May 2012 met the inclusion criteria. Six PD patients and 6 HCs either withdrew from the study or did not consent to further analysis for research purposes and therefore were excluded. Three PD and 7 HC scans were excluded because image quality was too poor because of artifacts for reliable analysis. We included the scans from 215 PD patients and 121 HCs in our final optimization analysis. We also obtained the H&Y and Movement Disorders Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III motor examination scores of 215 PD patients.

YNHH Cohort—Upon study approval by the Yale University Institutional Review Board, we obtained the medical record numbers of all patients who underwent a DaT scan on an outpatient basis in the Department of Nuclear Medicine at the YNHH between January 1, 2013, and June 1, 2016, for a total of 135 patients. Demographic and clinical information was gathered from provider notes. The DaT scan results were obtained from radiologists' reports based on visual reads. Forty-eight patients were excluded from the analysis because

of lack of sufficient clinical follow-up data or because they had positive reads by the radiologist that were for conditions other than PD (eg, Parkinson-plus syndrome, Lewy body dementia). In addition, 10 patients were excluded because the DaT scan quality was too poor because of artifacts for reliable analysis. A total of 77 patients were included in the final analysis. In 35 of these patients, the reason for DaT scan referral was to confirm high clinical suspicion of idiopathic PD, which was corroborated by the radiologist's positive DaT scan read. In the remaining 42, conditions other than idiopathic PD (eg, essential tremor, drug-induced parkinsonism, psychogenic movement disorder, and vascular parkinsonism) were considered highly likely on the differential diagnosis, and idiopathic PD was ruled out by the clinician with support from the radiologist's negative DaT scan read.

Imaging

The PPMI scans were downloaded and reconstructed from the site-specific projection data using the site-specific attenuation correction value. The DaT scans of the outpatient cohort were collected in a Siemens Symbia T SPECT-CT scanner (Siemens Medical Solutions USA, Inc, Malvern, PA) at the Yale Nuclear Medicine Department. ^{123}I-ioflupane unit doses were supplied by GE Healthcare (Chicago, IL) for routine clinical scans. The dose activity was verified as per clinical protocol. Image reconstruction was performed on a Siemens Syngo workstation. Patient and radiopharmaceutical preparation, camera settings, and reconstruction parameters were followed as outlined in the guidelines published by the Society of Nuclear Medicine.[20] The clinical images were reconstructed using the default Siemens Symbia brain SPECT protocol, which applies an attenuation correction based on the low-dose CT scan associated with each acquisition.

Automated Image Processing Steps Using SBRquant

First, each brain volume was spatially normalized to a standard geometry. The fully automated, SBRquant software package builds on the algorithms described in previous developments.[15,21–25] The analysis scripts were developed using MATLAB version 2012a (MathWorks, Natick, MA), resulting in a fully automated Windows 7 executable program that carries out the following image processing steps:

Locating the Central Slice—The central plane through the subject's striatum is found by locating the maximum value in the top-to-bottom profile in the summed sagittal view of the reconstructed images.

Summing the Central Striatal Slices—A parameter N describes the number of slices that are summed to place the 2-dimensional regions of interest (ROIs). In order to maintain symmetry, the same number of slices is added above and below the central slice through the striatum; hence, the total number of slices summed for semiquantitative analysis is always an odd number N, as shown in Figure 1A.

Locating the Individual Striata—Within the 2-dimensional transverse summed slice, by looking for maxima in the subject's left-to-right profiles, the intensity centroids of the left and right caudate are located.

ROI Placement—A crescent-shaped ROI is automatically placed on the occipital area of the brain (occ-ROI) (Fig. 1B) using the method described by Zubal et al.[15] The occ-ROI is used to calculate the background count density. A caudate ROI (green circle) is moved automatically within the vicinity of each located striatum until the SBRquant locates a maximum count value representing the initial location of each caudate. The smaller caudate ROI (white circle) is then placed by the software in its center and is used for the caudate's count density measurement.

Locating the Left and Right Putamen—The putamen ROI (white circle) is automatically determined in relation to the caudate (white circle) using the parameter *d* in units of pixels (Fig. 1B). The SBRquant software allows the selection of different values for *d* from its default settings, thereby allowing the angular placement of the putamen ROI to be varied around the caudate systematically for all subjects in the group being analyzed until a maximum value is found for extracting the putamen's count density.

Calculating the Specific Striatal Binding Ratio—The striatal binding ratio (SBR) in each scan is calculated using the following formula:

$$\text{SBR} = (\text{caudate or putamen ROI count density} - \text{occ-ROI count density})/\text{occ-ROI count density}.$$

A final report is generated with all quantitative values written directly into the image containing the ROI placements for the report hard copy.

Optimizing the Parameters for the PPMI Cohort

Using SBRquant, we calculated the SBRs separately for the left and right caudate and putamen while varying the number of summed transverse slices (N) and the separation of the ROIs (*d*) for determining the optimum threshold cutoff between HCs and PD patients. That is, all 336 scans were reanalyzed 98 times using the values of $3 \leq N \leq 15$ and $1 \leq d \leq 14$. For each reanalyzed data set, the lower of the 2 (i.e., left or right) putamen SBRs for each subject's scan was evaluated via an area under the receiver operating characteristic curve (AUC) using the tools available in MedCalc (www.medcalc.org). This analysis generated a binary classification of the PD and HC data at varying SBRs with a range of sensitivity and specificity values.

Applying the Optimized Parameters to the YNHH Cohort

Once the optimal parameters N and *d* were determined using the PPMI data set (based on the highest AUC obtained after varying N and *d*), the same SBRquant analysis was applied to the YNHH cohort of 77 patients. The lowest putamen SBR was again chosen as the quantitative variable, and the receiver operating characteristic curve analysis was performed, where the finalized neurological diagnosis (PD vs non-PD) for each patient was used as the patient classifier. A binary classification of the PD and non-PD data with a range of sensitivity and specificity values was obtained.

Correlations Between SBR Values and Clinical Data

Laterality Comparison Between the SBR Values and Clinical Data—To determine the most affected hemisphere, the percent difference in SBR between the left and right putamen was calculated for PD subjects in both cohorts. The hemispheric lateralization was then compared with the clinical lateralization. In the PPMI cohort, the more affected body side was determined by the MDS-UPDRS Part III limb scores in rigidity, bradykinesia, and tremor assessments. In the YNHH cohort, the symptom-onset side and/or the side that exhibited more rigidity, bradykinesia, and tremor on examination were accepted as the more affected body side.

Correlations Between the SBR Values and Disease Severity in the PPMI Cohort—We examined whether the lowest putamen SBR values were significantly different between PD patients with H&Y score 1 versus 2 in the PPMI cohort (2 patients with H&Y 3 were excluded). We also investigated the correlation between the lowest putamen SBR values and MDS-UPDRS Part III motor examination scores of PD patients in the PPMI cohort.

RESULTS

Subjects

Demographic and clinical data of the PPMI and YNHH cohorts are summarized in Tables 1 and 2, respectively.

Striatal Binding Ratio

The SBR values for all ROIs and cohorts are listed in Table 3.

PPMI Cohort

Among all combinations of the parameters N and d, N = 9 and $d = 8$ yielded an optimal AUC of 0.989 (95% confidence interval [CI], 0.971–0.997; $z = 92.5$, $P < 0.0001$) for the lowest putamen SBR cutoff of 1.037 (Figure 2A). The full statistical analysis showed an associated sensitivity = 95.8% (95% CI, 92.8–98.1) and specificity = 98.3% (95% CI, 94.2–99.8).

YNHH Cohort

Using the same parameters N = 9 and $d = 8$, we found an AUC = 0.998 (95% CI, 0.949–1.000; $z = 212.6$, $P < 0.0001$) for the lowest putamen SBR cutoff of 0.875 with an associated sensitivity of 97.1% (95% CI, 85.1–99.9) and specificity of 100% (95% CI, 91.6–100.0). Figure 2B shows the PD and non-PD clusters.

Laterality

PPMI Cohort—The lowest putamen SBR values were in the left hemisphere (mean % difference = 25.4 ± 15.2, left < right) in 115 and in the right hemisphere (mean % difference = 24.0 ± 14.1, right < left) in 100 PD patients. Clinically, the more affected side was right in

128 and left in 87 PD patients. In other words, there was a mismatch in laterality between clinical assessment and SBR values in 13 of 215 PD patients (6% error).

The lowest putamen SBR values were in the left hemisphere (mean % difference = 7.7 ± 6.1 in SBR, left < right) in 66 and in the right hemisphere (mean % difference = 8.5 ± 6.1 in SBR, right < left) in 55 HCs.

YNHH Cohort—The lowest putamen SBR was in the left hemisphere (mean % difference = 29.7 ± 20.9, left < right) in 16 PD patients and in the right hemisphere (mean % difference = 37.5 ± 21.9, right < left) in 19 PD patients.

The lowest putamen SBR was in the left hemisphere (mean % difference = 16.1 ± 10.4, left < right) in 21 non-PD patients and in the right hemisphere (mean % difference = 12.9 ± 11.6, right < left) in 21 non-PD patients.

The SBR laterality findings in the PD group were consistent with the clinically more affected side in all but 3 of 32 patients (10% error), whereas the visual reads accurately predicted the more affected side in all 32.

Correlations Between the SBR Values and Disease Severity in the PPMI Cohort—There were 93 PD patients with H&Y 1 (mean lowest putamen SBR = 0.67 ± 0.27) and 120 with H&Y 2 (mean lowest putamen SBR = 0.61 ± 0.21). The difference in the lowest putamen SBR between the 2 groups reached a strong trend toward significance (t = 1.96, P = 0.052, unequal variances assumed).

The lowest putamen SBR values also showed a significant negative correlation with the MDS-UPDRS Part III motor examination scores of 215 PD patients (r = −0.24, P = 0.0004).

DISCUSSION

Discriminatory Power of SBRquant

Using the well-defined PPMI database, we showed that the semiquantitative analysis of DaT scans with SBRquant can discriminate between PD and HC subjects with high sensitivity (95.8%) and specificity (98.3%). Moreover, semiquantitative analysis of DaT scans in an independent outpatient-based cohort using the same parameters as in the PPMI analysis also yielded high sensitivity (97.1%) and specificity (100%) in discriminating PD from non-PD patients with negative DaT scan reads. Relying on these discrimination characteristics, one could consider this semiquantitative analysis to serve as a possible “second reader” tool. Such a computer-assisted evaluation could be helpful for readers without extensive experience in interpreting DaT scans.[18,19]

The lowest putamen SBR cutoff values that yielded the highest specificity and sensitivity in discriminating the PPMI and YNHH cohorts were 1.037 and 0.875, respectively. These values are close to the previously reported cutoff of 1.08 (with 95% sensitivity and 89% specificity) obtained from a patient cohort with 94 DaT scans using the same quantification method.[18] Despite the differences between these cohorts in several demographic aspects including size, age, and disease characteristics, the proximity of the cutoff values is

noteworthy. It implicates convergence toward a common lowest putamen SBR range for reliable discrimination. Determination of this range in future prospective studies with large patient cohorts from various centers would be invaluable to improve diagnostic certainty and clinical management.

Clinical Implications

SBRquant analysis revealed hemispheric putamen SBR differences that were larger and more variable in the YNHH compared with the PPMI cohort, possibly due to the smaller size and higher heterogeneity of the YNHH cohort. A hemispheric difference of 6% to 10% is considered nonlateralizing because this is the generally accepted error range for quantification in DaT imaging.[26,27] In line with this, the hemispheric laterality of the lowest putamen SBR values was highly consistent with the clinically more affected side in PD groups of the PPMI and YNHH cohorts with 6% and 10% error rates, respectively. In some scans, especially those with relatively high noise or without robust asymmetry in SBR, comparing the entire left or right striatum by visual inspection as opposed to the lowest putamen values, which are obtained from a rather small region, may yield more accurate readings regarding lateralization. Another factor contributing to the lateralization error might be the heterogeneity of the cases in clinical practice. Dopamine transporter imaging is used as a confirmatory tool by the clinician when there are diagnostic uncertainties or confounding factors suggesting that the body lateralization of the motor signs may not always be distinct. Finally, prior knowledge of body lateralization obtained from clinical reports may also potentially bias the visual reads.

We also found that the lowest putamen SBR values showed a significant negative correlation with the MDS-UPDRS Part III motor examination scores and a strong trend toward a significant correlation with disease stage in PD patients in the PPMI cohort.

Proper enrollment into clinical trials requires reliable diagnosis. Taken together, our results indicate that the SBRquant provides quantitative and clinically meaningful data and therefore can be an important adjunct tool in enrollment and stratification based on disease stage and motor severity in clinical trials. Beyond diagnosis, DaT imaging has tremendous potential as an objective biomarker in monitoring disease progression and response to disease-modifying therapies. SBRquant has the potential for use in longitudinal studies to reproducibly analyze the DaT imaging data.

Technical Advantages

An advantage of analyzing the DaT scans using the methods described here is that the accuracy and reproducibility of the quantitative measures do not rely on the registration of the individual subject’s scan to the normalizing template. The normalization of each individual scan to a standard geometry template is used primarily to align all the scans into a consistent orientation, resulting in a uniform size and number of slices for each scan. The placement of the caudate and putamen ROI is independent of the registration accuracy to the template. The placement of the ROIs relies primarily on algorithms that locate the structures in the brain and place the ROIs according to predetermined local characteristics of the target structures. This method of ROI placement contributes to the high reproducibility of the data

analysis, because it effectively excludes the requirements of starting with an accurately registered subject scan.

Because no operator intervention is required, the reproducibility of reanalyzed data exhibits no operator variability when using SBRquant. The fully automated nature of the program and the processing time of approximately 40 seconds per scan would ease implementation of the analysis into daily clinical workflow of the technologist or physician. Moreover, our optimization results based on the PPMI database that includes scans from numerous sites and countries suggest that this software has the robustness to accommodate different imaging techniques from a spectrum of imaging centers and gamma cameras.

Similar to our analysis, other semiquantitative analysis methods also rely on calculating uptake ratios between the striatal structures and the occipital cortex. The programs known as DaTQUANT[28,29] and BRASS[30,31] have been used clinically and rely on an initial accurate registration of the subject's DaT scan to a reference template, which reorients the original SPECT scan to a different geometry and does not affect the original SBR. After registration, these analysis programs pause the processing to allow for manual adjustment of the striatal and occipital regions. One might argue that human intervention would position the ROIs more accurately for the calculation of the SBR; however, this approach does not permit large numbers of scans to be noninteractively and reliably (re)analyzed. In contrast, once the analysis parameters N and *d* are set for an optimal determination of region position and/or size, the SBRquant will always place the ROIs in the exact same position over the striatal structures in any scan, ensuring reliability and reproducibility of the analyses.

Limitations

Regardless of the semiquantitative analysis program used, there is no single best method for calculating SBR in that the ROI placements on the caudate and especially the putamen strongly influence the calculated SBR. The SBRquant method is also not immune to this problem because it calculates the lowest SBR in the putamen ROI, which is determined in relation to the caudate. One could argue that either averaging the uptake over the complete anatomical structure of the putamen or selecting the highest remaining uptake in either the anterior or posterior region of the putamen could be the best measure for quantitating the SBR. Each of these 3 samples of the putamen will return different measures of uptake. The optimum quantification method will need to be determined by comparative studies using large cohorts. In addition, the background reference region used to normalize the SBR values is usually placed on the occipital lobe, which exhibits relatively noisy uptake values. Furthermore, biological and technical sources of noise compromise the image quality and contribute significantly to the between-subject variability of the DaT signal. This variability poses a particular challenge in the reliable analysis of serial DaT imaging data, which usually reveal relatively small (4%–11%) annual changes.[32] Signal size and variability are also important factors in determining the cohort sizes in clinical trials and need to be addressed in future prospective studies.

Various manufacturers' camera designs and models, as well as variable imaging and reconstruction parameters, could influence the image quality and quantitation of DaT scans. For this reason, the Society of Nuclear Medicine issued a set of guidelines[20] that should be

followed to ensure that the resulting DaT scans are as reproducible and consistent as possible using current state-of-the-art nuclear medicine imaging equipment. Major manufacturers of SPECT imaging cameras include standard imaging and reconstruction protocols with their cameras, which abide by these accepted guidelines. Although the PPMI and YNHH data sets may not have been identical in camera model and acquisition or reconstruction parameters, all of the data sets abided by the guidelines referenced here.[20] When comparing the results presented here to other studies in other imaging centers, attention should be paid to following these guidelines so as to make the analyses as reproducible and consistent as possible.

In conclusion, we have demonstrated that the fully automated SBRquant software is a robust tool in the semiquantitative analysis of DaT scans with a strong potential to be used as a diagnostic aid in clinical settings and a research tool in clinical trials.

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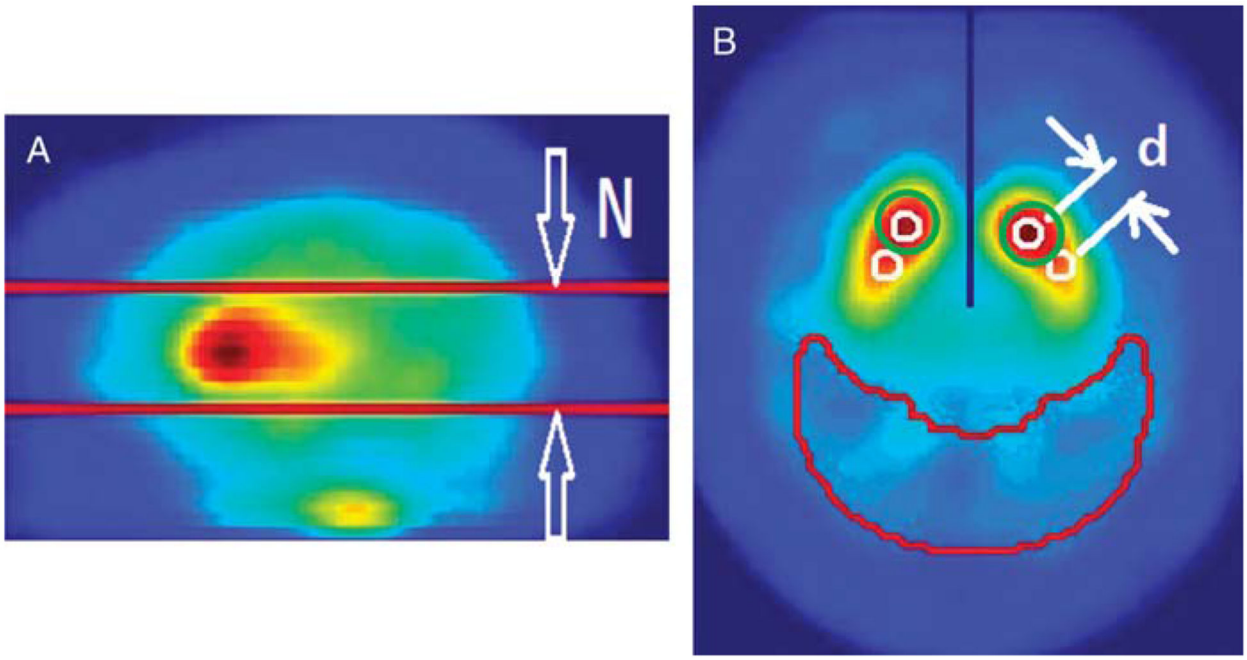

FIGURE 1.

Sagittal and axial planes of a reconstructed DaT scan. N is the number of summed slices surrounding the central striatal slice (**A**). Regions of interest: crescent-shaped occipital area and caudate and putamen (white circles) that are separated by distance *d* in units of pixels (**B**).

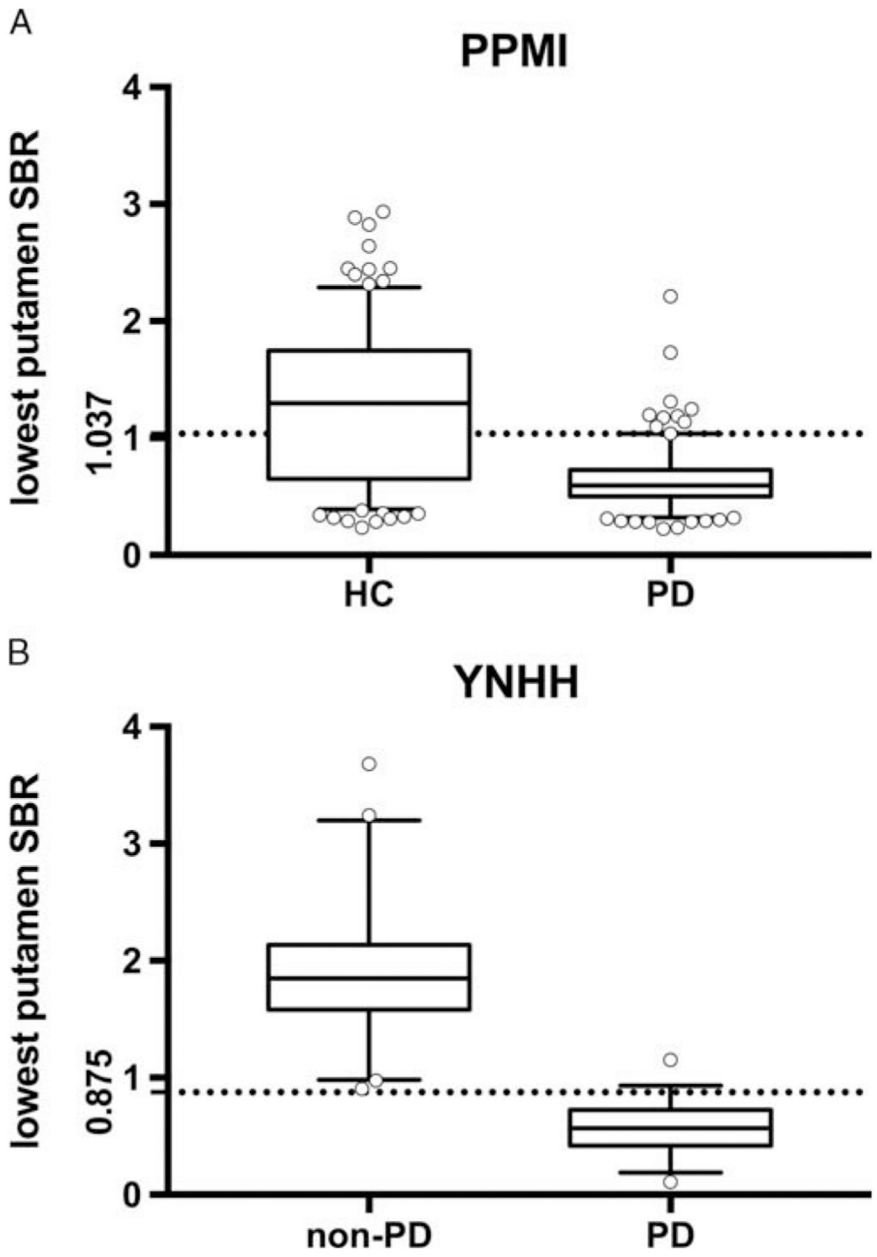

FIGURE 2.

Box plots of the lowest putamen SBR of the HC and PD groups in the PPMI cohort (**A**) and of the non-PD and PD groups in the YNHH cohort (**B**). Whiskers span 5th to 95th percentile. The dotted lines represent the SBR cutoff values 1.037 and 0.875 for the PPMI and YNHH cohorts, respectively.

TABLE 1.

Demographic and Clinical Data of the PPMI Cohort

	PD (n = 215)	HC (n = 121)
Female:male	66:149	47:74
Age at DaT scan, *y	61.9 ± 9.6	58.2 ± 12.3
More affected side right:left	128:87	—
H&Y	1.6 ± 0.5	—
MDS-UPDRS III	21.1 ± 9.0	—

H&Y score was 1 in 93, 2 in 120, and 3 in 2 subjects.

*Age at scan was significantly different between the PD and HC groups (2-sample *t* test, $t = 2.83$, $P = 0.005$, unequal variances assumed).

TABLE 2.

Demographic and Clinical Data of the YNHH Cohort

	PD (n = 35)	Non-PD (n = 42)
Female:male	14:21	20:22
Age at DaT scan, * y	62.5 ± 11.7	65.9 ± 10.5
Onset/more affected side	10 R, 22 L, 3 unknown	—
Tremor	23 (66%)	21 (50%)
Bradykinesia	19 (54%)	13 (31%)
Rigidity	23 (66%)	16 (38%)
Response to dopaminergic medication		0/2 (0%)
Yes	25 (78%)	
No	3 (9%)	
Unknown	4 (13%)	

Three PD patients were not started on medication because of mild symptoms. The nonresponders were only started on monoamine oxidase B inhibitors and/or dopamine receptor agonists. Response in the remaining cases was not documented in provider notes.

* Age at scan was not significantly different between the PD and non-PD groups (two-sample t-test, $t = 1.33$, $P = 0.19$, unequal variances assumed).

L indicates left; non-PD, patients without PD and with negative DaT scans; R, right.

TABLE 3.

SBR Values

	PPMI Cohort		YNHH Cohort	
	PD	**HC**	**PD**	**Non-PD**
Right caudate	1.54 ± 0.50	2.43 ± 0.56	1.35 ± 0.63	2.67 ± 0.78
Right putamen	0.76 ± 0.30	1.79 ± 0.43	0.72 ± 0.37	2.11 ± 0.68
Left caudate	1.53 ± 0.49	2.49 ± 0.56	1.36 ± 0.57	2.65 ± 0.65
Left putamen	0.73 ± 0.29	1.78 ± 0.43	0.77 ± 0.32	2.07 ± 0.63

Non-PD indicates patients without PD and with negative DaT scans.