Striatal Dopaminergic Depletion Pattern Reflects Pathological Brain Perfusion Changes in Lewy Body Diseases

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Abstract

Purpose In Lewy body diseases (LBD), various symptoms occur depending on the distribution of Lewy body in the brain, and the findings of brain perfusion and dopamine transporter single-photon emission computed tomography (DAT-SPECT) also change accordingly. We aimed to evaluate the correlation between brain perfusion SPECT and quantitative indices calculated from DAT-SPECT in patients with LBD.

Procedures We retrospectively enrolled 35 patients with LBD who underwent brain perfusion SPECT with N-isopropyl-p-[123I] iodoamphetamine and DAT-SPECT with 123I-ioflupane. Mini-mental state examination (MMSE) data were also collected from 19 patients. Quantitative indices (specific binding ratio [SBR], putamen-to-caudate ratio [PCR], and caudate-to-putamen ratio [CPR]) were calculated using DAT-SPECT. These data were analysed by the statistical parametric mapping procedure.

Results In patients with LBD, decreased PCR index correlated with hypoperfusion in the brainstem (medulla oblongata and midbrain) (uncorrected $p < 0.001$, $k > 100$), while decreased CPR index correlated with hypoperfusion in the right temporoparietal cortex (family-wise error corrected $p < 0.05$), right precuneus (uncorrected $p < 0.001$, $k > 100$), and bilateral temporal cortex (uncorrected $p < 0.001$, $k > 100$). However, there was no significant correlation between decreased SBR index and brain perfusion. Additionally, the MMSE score was correlated with hypoperfusion in the left temporoparietal cortex (uncorrected $p < 0.001$).

Conclusions This study suggests that regional changes in striatal 123I-ioflupane accumulation on DAT-SPECT are related to brain perfusion changes in patients with LBD.

Key words $\alpha$-synuclein · $\alpha$-synucleinopathy · 123I-FP-CIT · SPM · Parkinsonian syndrome · Parkinsonism

Abbreviations

CPR Caudate-to-putamen ratio
DAT Dopamine transporter
DLB Dementia with Lewy bodies
FEW Family-wise error
LB Lewy body
LBD Lewy body diseases
MMSE Mini-mental state examination
PCR Putamen-to-caudate ratio
PD Parkinson’s disease
PDD Parkinson’s disease with dementia
SBR Specific binding ratio
SPECT Single-photon emission computed tomography
SPM Statistical parametric mapping
3D-SSP Three-dimensional stereotactic surface projection
VOI Volume of interest
Introduction

Lewy body diseases (LBD), which are sequential neurodegenerative disorders, are considered subtypes of an α-synuclein-associated disease spectrum from incidental LBD and non-demented Parkinson’s disease (PD) to PD with dementia (PDD) and dementia with Lewy bodies (DLB). Although the nosologic relationship among these disorders is frequently being debated, it is currently difficult to classify them explicitly. Based on the conventional international consensus, DLB is diagnosed when cognitive impairment precedes parkinsonian motor symptoms or begins 1 year after the onset of parkinsonian; in contrast, in PDD, cognitive impairment develops in the setting of well-established PD [1]. Therefore, the diagnosis of LBD depends on the presence and timing of onset of cognitive impairment. Braak et al. proposed that LB pathology spreads via the olfactory bulb or gastrointestinal system from the peripheral to central nervous systems, and LB travels from the brainstem to the cortex [2]. The distribution and degree of LB pathology in the brain affect clinical symptoms in patients with LBD, including movement disorder, psychotic state, visual hallucination, and cognitive impairment, in patients with LBD.

Nuclear medicine imaging is useful in diagnosing LBD. Brain perfusion single-photon emission computed tomography (SPECT) shows changes in brain perfusion in this patient group. Notably, patients with PDD and DLB show parietal, temporal, or occipital hypoperfusion, while those with PD show no remarkable deterioration in brain perfusion compared with those with PDD or DLB [3]. These changes are related to cognitive impairment in these patients [4]. In addition, dopamine transporter (DAT)-SPECT is another useful nuclear medicine imaging approach to assess the function of the presynaptic nigrostriatal dopaminergic system. Quantitative indices calculated from DAT-SPECT are also useful in interpreting and assessing images [5, 6]. In patients with LBD, striatal tracer accumulation deteriorates as the disease condition progresses [7, 8]. The specific binding ratio (SBR), representing the strength of striatal tracer accumulation, is the most frequently used quantitative index in DAT-SPECT. Although the SBR index is useful because it correlates with the severity of motor dysfunction in patients with PD [9], it is not enough to differentiate between patients with PD and DLB [10]. On the other hand, the putamen-to-caudate (PCR) and caudate-to-putamen (CPR) ratios are different types of quantitative indices of DAT-SPECT that represent changes in the shape and distribution of striatal tracer accumulation. Accumulating studies have demonstrated that the PCR/CPR indices can differentiate patients with PD and DLB [10–12]. It is speculated that the anterior part of striatal uptake, especially caudate uptake, correlates with psychotic state or cognitive impairment, while the posterior part of striatal uptake correlates with movement disorders in patients with LBD.

We hypothesised that changes in striatal tracer accumulation on DAT-SPECT would correlate with brain perfusion in patients with LBD and that these changes would reflect their symptoms, such as movement disorder or cognitive impairment, caused by differential distributions of LB pathology in the brain. Accordingly, this study aimed to assess the correlation between brain perfusion and quantitative indices (SBR, PCR, and CPR indices) of DAT-SPECT using the statistical parametric mapping (SPM) analysis and to compare these quantitative indices among patients with LBD, including PD, PDD, and DLB.

Materials and Methods

Patients

A total of 231 consecutive patients who underwent brain perfusion SPECT with N-isopropyl-p-[123I] iodoamphetamine (IMP) and DAT-SPECT with 123I-ioflupane from February 2014 to January 2019 were included in this retrospective study. The interval between the two examinations was less than 1 year. Patients with a disease that affects the image quality of DAT and brain perfusion SPECT (e.g., extensive cerebral haemorrhage and infarction) were excluded. Enrolled patients were diagnosed based on the clinical diagnostic criteria of the UK Parkinson’s Disease Society Brain Bank [13] or established diagnostic criteria [1, 14]. Patients who were clinically undiagnosed with LBD were also excluded. General cognitive function was assessed in some of the participants using the mini-mental state examination (MMSE). Of the total 231 patients, 135 overlapped with those in our previous studies [10, 15].

The institutional review board of Keio University School of Medicine granted permission for this retrospective review of clinical data and imaging and waived the requirement for obtaining informed consent from the patients (approval number: 20211068).

Image Acquisition and Reconstruction

Fifteen minutes after injection of 222 MBq of 123I-IMP, brain perfusion SPECT were obtained on Discovery NM 630 or Discovery NM/CT 670 (GE Healthcare, Milwaukee, WI) equipped with an extended low-energy general-purpose collimator. Projection data were acquired for 30 min. Imaging parameters were as follows: matrix size, 128 × 128; pixel size, 2.9 mm; slice thickness, 2.9 mm; and energy window,
159 keV ± 10%. Data were reconstructed by the filtered back-projection method with a Butterworth filter (critical frequency, 0.45; power, 10.0). Attenuation correction was used, while scatter correction was not.

Three hours after injection of 185 MBq 123I-ioflupane, DAT-SPECT were obtained on the Discovery NM 630 or Discovery NM/CT 670 (GE Healthcare, Milwaukee, WI) equipped with a FAN beam collimator. Projection data were acquired for 30 min. Imaging parameters were as follows: matrix size, 128×128; pixel size, 4.4 mm; slice thickness, 4.4 mm; and energy window, 159 keV ± 10%. Data were reconstructed by the ordered-subset expectation–maximisation method (iterations, 3; subset, 10) with a Butterworth filter (critical frequency, 0.5; power, 10.0). Neither attenuation method (iterations, 3; subset, 10) with a Butterworth filter (critical frequency, 0.45; power, 10.0). Attenuation correction was performed. The Pearson’s chi-square test was used to compare sex between these groups. These tests were performed using SPSS software (version 27; SPSS Inc., Chicago, IL).

Brain perfusion imaging data were preprocessed and analysed with statistical parametric mapping (SPM) software (https://www.fil.ion.ucl.ac.uk/spm/software/spm12/), running on the Matlab R2020a software environment (Math-Works, Natick, MA). Brain perfusion SPECT data were first aligned and anatomically standardised to match each scan to the Montreal Neurological Institute (MNI) atlas based template (McGill University, Montreal, Canada) using a 12-parameter affine transformation, followed by non-linear transformations [19, 20]. SPECT images were then smoothed with an 8×8×8 mm Gaussian filter. Normalisation of global brain counts to a value of 50 was performed with proportional scaling to remove differences in global activity in and between subjects. Proportional scaling was performed by dividing each voxel value by the average value of the whole parenchyma [21, 22]. Linear regression analyses after adjusting for age were conducted to determine the correlations between brain perfusion and quantitative indices calculated from DAT-SPECT and between brain perfusion and MMSE scores.

The initial voxel threshold was set to 0.001 uncorrected for multiple comparisons. Clusters were considered significant when falling below a cluster-corrected \( p \) (family-wise error [FWE]) = 0.05. If statistical significance was not reached, the threshold at the voxel level was explored at \( p < 0.001 \) uncorrected.

**Results**

Of the included 231 consecutive patients, four were excluded from the study due to insufficient image quality because of extensive cerebral haemorrhage and infarction, along with 192 who were clinically undiagnosed with LBD. The remaining 35 patients (median age, 76.0 years; range, 58–91 years; men/women, 13/22), including eight with PD, three with PDD, and 24 with DLB, were included in this analysis. Figure 1 depicts the flow diagram of study participants.

Table 1 shows the characteristics of included patients. The means and standard deviations of the SBR, PCR, and CPR indices and MMSE scores are also shown. Significant differences were observed in age, and the PCR and CPR indices between the PD and DLB groups.

Figure 2 shows representative images of DAT-SPECT and brain perfusion (data not shown). Decreased PCR index correlated with hypoperfusion in the right temporoparietal cortex (FWE corrected < 0.001 uncorrected).

**Statistical Model**

The Kruskal–Wallis test was used to compare age, quantitative indices (SBR, PCR, and CPR), and the MMSE between the LBD (PD, PDD, and DLB) groups. If there were significant differences, post hoc analysis with Bonferroni correction was performed. The Pearson’s chi-square test was used to compare sex between these groups. These tests were performed using SPSS software (version 27; SPSS Inc., Chicago, IL).

Brain perfusion imaging data were preprocessed and analysed with statistical parametric mapping (SPM) software (https://www.fil.ion.ucl.ac.uk/spm/software/spm12/), running on the Matlab R2020a software environment (Math-Works, Natick, MA). Brain perfusion SPECT data were first aligned and anatomically standardised to match each scan to the Montreal Neurological Institute (MNI) atlas based template (McGill University, Montreal, Canada) using a 12-parameter affine transformation, followed by non-linear transformations [19, 20]. SPECT images were then smoothed with an 8×8×8 mm Gaussian filter. Normalisation of global brain counts to a value of 50 was performed with proportional scaling to remove differences in global activity in and between subjects. Proportional scaling was performed by dividing each voxel value by the average value of the whole parenchyma [21, 22]. Linear regression analyses after adjusting for age were conducted to determine the correlations between brain perfusion and quantitative indices calculated from DAT-SPECT and between brain perfusion and MMSE scores.

The initial voxel threshold was set to 0.001 uncorrected for multiple comparisons. Clusters were considered significant when falling below a cluster-corrected \( p \) (family-wise error [FWE]) = 0.05. If statistical significance was not reached, the threshold at the voxel level was explored at \( p < 0.001 \) uncorrected.
Discussion

This study showed that decreased putaminal uptake of $^{123}$I-ioflupane in DAT-SPECT significantly correlated with hypoperfusion in the brainstem; this correlation may reflect movement disorders in patients with LBD. Hacker et al. also demonstrated that midbrain-striatum functional connectivity was reduced in patients with PD, and in their study, striatal functional connectivity with the brainstem was graded as follows: posterior putamen > anterior putamen > caudate [23]. In addition, previous studies have shown more severe substantia nigra cell loss in PDD than in DLB, which consequently leads to more advanced parkinsonism [24]. The Hoehn and Yahr stage or Unified PD rating scale (motor part only) score has been reported to correlate with putaminal uptake of $^{123}$I-ioflupane in patients with PD [12]. These findings indicate that the midbrain-putamen dopaminergic connectivity contributes to motor dysfunction in patients with LBD. Thus, these findings represent a possibility that decreased PCR index could indicate enhanced severity of movement disorders caused by dysfunction of the putamen dopaminergic system connected from the brainstem.

We also demonstrated that decreased caudate uptake of $^{123}$I-ioflupane in DAT-SPECT was significantly correlated with hypoperfusion in the right temporoparietal cortex, right precuneus, and bilateral temporal lobes. Consistently, previous studies have shown that glucose hypometabolism in the temporoparietal areas correlates with dementia severity in LBD [25, 26] and that the caudate uptake of $^{123}$I-ioflupane correlates with cognitive impairment [25–30]. Our results and these previous findings indicate that the correlation between decreased CPR index and hypoperfusion in the right temporoparietal cortex may reflect cognitive impairment in patients with LBD. In particular, a remarkable correlation (FWE corrected $p < 0.05$) was observed between decreased CPR index and hypoperfusion in the right temporoparietal region in patients with LBD. Patients with PD and DLB are more likely to have visuospatial dysfunction than those with Alzheimer’s disease [31, 32], and previous studies have reported that visuospatial dysfunction presents as right-dominant hypoperfusion or hypometabolism in the brain [33–35]. In addition, Marquie et al. demonstrated that reduced caudate DAT concentration was associated with worse visuospatial ability in patients with DLB [36]. These findings indicate that significant hypoperfusion in the right temporoparietal region may be indicative of the visuospatial dysfunction observed in patients with LBD. Our results also showed that hypoperfusion in the precuneus is correlated with decreased caudal uptake of $^{123}$I-ioflupane on DAT-SPECT; however, the posterior cingulate was spared from this hypoperfusion.

Table 1: Patient characteristics

| Characteristics               | PD  | PDD | DLB |
|------------------------------|-----|-----|-----|
| n                            | 8   | 3   | 24  |
| Age (years, mean ± SD)       | 67.1 ± 5.9* | 80.3 ± 1.5 | 78.5 ± 6.6* |
| Sex (male/female)            | 2/6 | 1/2 | 10/14 |
| Quantitative indices from DAT-SPECT |     |     |     |
| SBR                          | 1.18 ± 0.50 | 1.07 ± 0.86 | 1.09 ± 0.44 |
| PCR                          | 0.73 ± 0.08* | 0.89 ± 0.16 | 0.89 ± 0.12* |
| CPR                          | 1.38 ± 0.14* | 1.15 ± 0.22 | 1.15 ± 0.16* |
| MMSE ($n$)                   | 27.0 ± 2.8 (2) | 24.0 ± 1.0 (3) | 21.8 ± 5.5 (14) |

CPR, caudate-to-putamen ratio; DAT, dopamine transporter; DLB, dementia with Lewy body; MMSE, mini-mental state examination; PCR, putamen-to-caudate ratio; PD, Parkinson’s disease; PDD, Parkinson’s disease with dementia; SBR, specific binding ratio; SD, standard deviation; SPECT, single-photon emission computed tomography

*p < 0.05 PD vs. DLB

Fig. 1 Flow diagram of patient inclusion. DLB, dementia with Lewy body; PD, Parkinson’s disease; PDD, Parkinson’s disease with dementia
This finding represents a characteristic sign, known as the "cingulate island sign," observed on the brain perfusion SPECT of patients with DLB [37]. Early caudate dopaminergic dysfunction is reportedly also a predictor of future cognitive impairment [38–40]. Cognitive decline and related symptoms are not a consequence of α-synuclein-induced neurodegeneration alone because amyloid β and tau pathologies also contribute to overall deficits [41–45]. These pathological changes may synergistically influence clinical features, including a shorter duration or a more malignant course [46, 47]. Therefore, we speculate that the CPR index has the potential to indicate the severity of cognitive impairment and clinical course in patients with LBD.

This study found that the SBR index had no significant correlation with brain perfusion. This result suggests that, unlike the PCR/CPR indices, the SBR index, which represents the magnitude of striatal uptake of 123I-ioflupane, has little advantage for assessing the symptoms of motor/cognitive dysfunctions in patients with LBD.

We demonstrated that global cognitive impairment measured using the MMSE correlated with left temporoparietal cortex hypoperfusion in patients with LBD. Moreover, left-sided lateralisation has been observed between brain

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**Fig. 2** DAT-SPECT and brain perfusion SPECT images of representative cases of PD and DLB. A commercially available software package DaTQUANT was used for VOI-based analysis. The brain perfusion image was visualised with 3D-SSP. a A representative case of PD (aged 66 years, female) shows striatal uptake deterioration, especially in the posterior part. b A representative case of DLB (aged 76 years, male) shows diffuse striatal uptake deterioration and remarkable hypoperfusion in the temporoparietal lobe. DAT, dopamine transporter; DLB, dementia with Lewy body; PD, Parkinson’s disease; SPECT, single-photon emission computed tomography; VOI, volume of interest; 3D-SSP, three-dimensional stereotactic surface projection.

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**Fig. 3** Correlations between brain perfusion SPECT and the PCR index. The PCR index correlated with brain hypoperfusion in the brain stem (medulla oblongata and midbrain) (uncorrected $p < 0.001$, $k > 100$ voxels). Regression lines at notable regions are shown. PCR, putamen-to-caudate ratio; SPECT, single-photon emission computed tomography.
perfusion and the MMSE score in patients with Alzheimer’s disease [48, 49], probably because most of the items of the MMSE questionnaire rely on left hemispheric cognitive processing.

Some patients included in this study overlapped with those included in our previous studies [10, 15]. In our previous studies, we assessed the combined diagnostic utility of the quantitative indices of DAT-SPECT or iodine-131-meta-iodobenzylguanidine scintigraphy for PD and atypical parkinsonian syndromes; however, we did not use brain perfusion SPECT or assess the correlation between brain perfusion and DAT-SPECT in LBD [10, 15]. Nobili et al. previously evaluated the correlation between brain perfusion and DAT-SPECT in patients with PD and found that brain perfusion in the posterior cingulate, parahippocampal gyrus, and middle temporal cortex (uncorrected \( p < 0.001, k > 100 \) voxels). Regression lines at notable regions are shown. CPR, caudate-to-putamen ratio; SPECT, single-photon emission computed tomography.

**Fig. 4** Correlations between brain perfusion SPECT and the CPR index. The CPR index correlated with brain hypoperfusion in the right temporoparietal cortex (FEW corrected \( p < 0.05 \)), right precuneus (uncorrected \( p < 0.001, k > 100 \) voxels), and bilateral temporal cortex (uncorrected \( p < 0.001, k > 100 \) voxels). Regression lines at notable regions are shown. CPR, caudate-to-putamen ratio; SPECT, single-photon emission computed tomography.
gyrus correlated with uptake in the caudate, whereas that in the posterior cingulate, parietal precuneus, and occipital cuneus correlated with uptake in the putamen [50]. However, their study enrolled only patients with PD, and they used the SBR of the caudate/putamen regions, not the PCR or CPR, as quantitative indices. The PCR/CPR

| Area                  | Cluster size | Coordinates          | Z-score | p values (uncorrected, k > 100) |
|-----------------------|--------------|----------------------|---------|---------------------------------|
| PCR                   |              |                      |         |                                 |
| Medulla oblongata     | 165          | 8 - 30 - 52          | 3.88    | <0.001                          |
| Mid Bbrain            | 168          | 8 - 24 - 18          | 3.41    | <0.001                          |
| CPR                   |              |                      |         |                                 |
| R temporoparietal lobe| 1295         | 54 - 54 - 4          | 4.26    | <0.05 (FWE corrected)           |
| R precuneus           | 427          | 8 - 66 50            | 3.52    | <0.001                          |
| L temporal lobe       | 137          | - 42 - 16 - 32       | 3.41    | <0.001                          |
| R temporal lobe       | 106          | 48 - 10 - 30         | 3.29    | <0.001                          |

PCR, caudate-to-putamen ratio; FWE, family-wise error; L, left; MMSE, mini-mental state examination; PCR, putamen-to-caudate ratio; R, right
indices have been suggested to be particularly valuable as they are background-, age-, and camera-independent [6]. These factors may explain the difference between our findings and theirs.

This study has some limitations. First, the number of patients analysed was relatively small. Additional studies with larger numbers of participants are needed to confirm our observations. Second, the diagnoses of PD, PDD, and DLB were clinical diagnoses and not pathologically confirmed. Finally, this was a single-centre study, and institution-specific factors might limit the generalizability of our results.

**Conclusion**

This study found that changes in striatal tracer accumulation on DAT-SPECT correlated with brain hypoperfusion in several specific regions (brainstem, temporoparietal cortex, or precuneus) in patients with LBD.

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**Author Contribution** YI, TS, and MJ were responsible for the design of the study; YI and RM collected the SPECT data; YI performed the statistical analysis; MS, DI, HU, and HT supported the selection of clinical data; and YI, TS, KM, MS, DI, HU, and HT drafted the manuscript. All authors read and critiqued the manuscript and approved the final version of the manuscript.

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**Data Availability** All data generated or analysed during this study are included in this published article.

**Declarations**

**Ethics Approval** This study was approved by the Ethics Committee of Keio University School of Medicine (registration number: 20211068). This article does not contain any data from experiments with animals performed by any of the authors. All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Consent to Participate** The institutional review board of the hospital granted permission for this retrospective review of imaging and clinical data and waived the requirement for obtaining informed consent from the patients.

**Competing Interests** MJ received research grants from Nihon Medi-Physics Co., Ltd. and GE Healthcare Corp. MK received a research grant from Nihon Medi-Physics Co., Ltd. Other authors declare no conflict of interest.

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**References**

1. Emre M, Aarsland D, Brown R et al (2007) Clinical diagnostic criteria for dementia associated with Parkinson’s disease. Mov Disord 22:1689–1707
2. Braak H, Del Tredici K, Rüb U et al (2003) Staging of brain pathology related to sporadic Parkinson’s disease. Neuropathol Aging Brain 24:197–211
3. Mito Y, Yoshida K, Yabe I et al (2004) Brain 3D-SSP SPECT analysis in dementia with Lewy bodies, Parkinson’s disease with and without dementia, and Alzheimer’s disease. Clin Neurol Neurosurg 107:396–403
4. Jokinen P, Scheinin N, Aalto S et al (2010) [(11)C]PIB- [(18) F]FDG-PET and MRI imaging in patients with Parkinson’s disease with and without dementia. Parkinsonism Relat Disord 16:666–670
5. Roberts G, Kane JPM, Lloyd JJ et al (2019) A comparison of visual and semiquantitative analysis methods for planar cardiac 123I-MIBG scintigraphy in dementia with Lewy bodies. Nucl Med Commun 40:734–743
6. Söderlund TA, Dickson JC, Prvulovich E et al (2013) Value of semiquantitative analysis for clinical reporting of 123I-2-[12]-carbomethoxy-3-[4-iodophenyl]-N-(3-fluoropropyl)nortropane SPECT studies. J Nucl Med 54:714–722
7. Mito Y, Yabe I, Yaguchi H et al (2020) Relations of clinical symptoms with dopamine transporter imaging in drug-naïve Parkinson’s disease. Clin Neurol Neurosurg 196:105960
8. Ravina B, Marek K, Eberly S et al (2012) Dopamine transporter imaging is associated with long-term outcomes in Parkinson’s disease. Mov Disord 27:1392–1397
9. Kuribara T, Enatsu R, Kitagawa M et al (2020) Neuroimaging and neurophysiological evaluation of severity of Parkinson’s disease. J Clin Neurosci 74:135–140
10. Iwabuchi Y, Kameyama M, Matussaka Y et al (2021) A diagnostic strategy for Parkinsonian syndromes using quantitative indices of DAT SPECT and MIBG scintigraphy: an investigation using the classification and regression tree analysis. Eur J Nucl Med Mol Imaging 48:1833–1841
11. Jolting M, Vriend C, van der Zande JJ et al (2018) Lower (123) I-FP-CIT binding to the striatal dopamine transporter, but not to the extrastriatal serotonin transporter, in Parkinson’s disease compared with dementia with Lewy bodies. Neuroimage Clin 19:130–136
12. Walker Z, Costa DC, Walker RW et al (2004) Striatal dopamine transporter in dementia with Lewy bodies and Parkinson disease: a comparison. Neurology 62:1568–1572
13. Gibb WR, Lees AJ (1988) The relevance of the Lewy body to the pathogenesis of idiopathic Parkinson’s disease. J Neurol Neurosurg Psych 51:745–752
