Presynaptic striatal dopaminergic function in atypical parkinsonisms: A meta-analysis of imaging studies

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ABSTRACT

Background. Multiple system atrophy (MSA), progressive supranuclear palsy (PSP) and corticobasal syndrome (CBS) have overlapping signs and symptoms with Parkinson's disease (PD), and these similarities complicate their clinical diagnostics. Although presynaptic dopaminergic brain imaging with PET and SPECT is clinically widely used for patients with suspected PD, the benefit of functional imaging in atypical parkinsonism syndromes remains unclear. We compared striatal presynaptic dopaminergic function in MSA parkinsonism variant (MSA-P), MSA cerebellar variant (MSA-C), PSP, CBS and PD using combined quantitative data from all published studies.

Methods. PubMed database was searched from inception to August 2018 for terms "dopamine" OR "dopaminergic" AND "PET" OR "SPECT" OR "SPET" and keywords related to PD, MSA, PSP and CBS. A total of 1711 publications were identified. PET or SPECT studies comparing patients with atypical parkinsonism to another diagnostic group (PD, MSA, PSP or CBS) were included. Tracers for dopamine transporter (DAT), aromatic amino acid decarboxylase (AADC) or vesicular monoamine type 2 (VMAT2) were investigated. Tracer binding data were extracted from the original articles. Heterogeneity of the data were examined using I^2 statistics and a random effect model was used to summarize data. Hedges *g* was used as an estimator of effect size in group comparisons. Results are reported according to PRISMA guidelines.

Results. Thirty-five studies (29 DAT, 6 AADC, no VMAT2 studies) with 356 MSA-P patients, 204 PSP patients, 79 CBS patients and 62 MSA-C patients were included in the meta-analysis. Caudate nucleus and putamen DAT functions were clearly lower in PSP as compared to PD (caudate: 34.1% difference, *g*=-1.08, 95%CI= -1.52 to -0.64; putamen: 18.2% , *g*=-0.86, 95%CI=-1.50 to -0.21) and MSA-P (striatum: 31.4%, *g*=-0.70, 95%CI=-1.21 to -0.19), and in MSA-P as compared to MSA-C (striatum: 46.0%, *g*=1.46,

95%CI=0.23 to 2.68). Although not significant due to limited data, aromatic L-amino acid decarboxylase (AADC) results paralleled the DAT findings.

Conclusions. Striatal presynaptic DAT function is clearly lower in PSP patients as compared to PD and MSA-P patients, and in MSA-P patients as compared to MSA-C patients.

Key words: PET, SPECT, dopamine, parkinsonism, multiple system atrophy, progressive supranuclear palsy, Parkinson's disease, human

INTRODUCTION

Multiple system atrophy (MSA), progressive supranuclear palsy (PSP) and corticobasal syndrome (CBS) have been termed as atypical parkinsonian disorders and they are characterized by a more rapid progression and poorer prognosis than the typical parkinsonian disorder - Parkinson's disease (PD). Clinicopathological studies have pointed out that the diagnostic accuracy of atypical parkinsonisms is not optimal; these disorders are underdiagnosed, and many patients that carry a diagnosis of PD in fact have MSA, PSP or CBS (*1*). The sensitivities of the MSA and PSP diagnoses are low at 53% and 64%, respectively, when diagnosed by general neurologists, and at 88% and 84%, when diagnosed by movement disorders specialists (*2,3*). Given that there are distinct proteinopathic disease mechanisms in different atypical parkinsonian syndromes, and that there are active attempts to develop protein-specific therapies, biomarkers that could be used to improve diagnostic accuracy would be valuable.

Functional brain imaging with positron emission tomography (PET) or single photon emission computed tomography (SPECT) enables the investigation of central neurotransmitter function at the system level *in vivo*. When PD patients are compared to healthy individuals via striatal dopaminergic PET/SPECT, the PD patients show a wide-spread presynaptic defect with practically no overlap with healthy controls (*4*). However, it remains unclear whether presynaptic dopamine imaging can be used in the differential diagnosis of atypical parkinsonisms. Protein-specific tracers for tau and alpha-synuclein hold promise as possible future diagnostic tools (*5*), but in the current clinical imaging of movement disorders, presynaptic dopaminergic imaging dominates the field. A major limitation in individual dopaminergic neuroimaging studies of atypical parkinsonisms has

been the small sample sizes, which has led to insufficient statistical power to make reliable clinical inferences.

A quantitative meta-analysis offers an opportunity to investigate a large number of small studies with improved power to detect differences. A previous meta-analysis using diagnostic odds ratios has suggested that presynaptic dopaminergic tracers cannot distinguish between PD and atypical parkinsonisms (*6*). To investigate the role of presynaptic dopaminergic PET and SPECT in the diagnosis of atypical parkinsonisms in more detail, we carried out a meta-analysis of all available imaging data using regional binding values in each study.

MATERIALS AND METHODS

Aims of Meta-Analysis

The primary aim of the meta-analysis was to investigate differences in striatal dopamine signaling as measured by PET/SPECT among atypical parkinsonism disorders as compared to PD. Ethics Committee approval was waived because this study did not involve any human participants or animals.

Study Collection and Screening

The preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement was followed (*7*). Studies for initial screening were identified through PubMed for initial screening using a search query of keywords related to parkinsonism disorders (Fig. 1). The final database search was conducted on the 8th of August, 2018. The initial screening and assessment for eligibility were performed by two investigators (V.K. and T.K.). Criteria for screening and data extraction are presented in supplemental methods.

Statistical Analysis

The synthesis of study results and group comparisons were conducted using Meta-Essentials (Version 1.1, Erasmus Research Institute of Management, Rotterdam, The Netherlands) (*10*). Statistical significance was set at two-tailed P-value of <0.05. Hedges' *g* was used as an estimator of effect size in group comparisons using random effects model. Heterogeneity of the data was examined using I^2 statistics. If substantial heterogeneity (I^2 > 50%) was detected, meta-regression analyses of the moderators age, disease duration, and disease severity as indicated by the motor UPDRS and Hoehn and Yahr scale scores were also performed.

RESULTS

Study Characteristics

Twenty-nine DAT studies (Supplemental Table 1) and 6 AADC studies (Supplemental Table 2) were included in the meta-analysis. There were no suitable VMAT2 studies. Four studies (*11-14*) that had combined MSA-P patients with MSA-C patients were excluded from the MSA-analysis (Supplemental Table 3). Only one study reported binding values also in PSP parkinsonism variant (PSP-P) patients (*15*), which were not included to the analysis. The final sample thus included 35 studies that described DAT or AADC binding in 958 PD, 356 MSA-P, 204 PSP, 79 CBS and 62 MSA-C patients. The demographic and clinical characteristics of the patients are presented in Table 1. The quality evaluation of the included studies is presented in Supplemental Table 4. Twenty-five studies received 5-6 stars and 10 studies received 3-4 stars (out of 6 stars) in the Newcastle-Ottawa scale. The overall quality of the studies was therefore sufficient but the PET/SPECT imaging methodology and resolution were suboptimal in studies that had been published in the 1990s. There was some variation in diagnostic criteria as well (Supplemental Table 5) although many studies used published and commonly used criteria for PD (*16*), PSP (*17*) and MSA (*18,19*).

The DAT-studies were published between 1998 and 2018. The tracers used were ^{123}I-β-CIT, ^{123}I-FP-CIT, ^{99m}Tc-TRODAT, ^{18}F-FP-CIT and ^{123}I-IPT. The majority of the included studies had calculated striatal specific binding ratios using the occipital cortex as the reference region, and the values were expressed as (region-of-interest – occipital cortex)/occipital cortex (Supplemental Table 1). The AADC-studies were published between 1990 and 1997 and used 6-^{18}F-fluoro-L-dopa as the tracer.

Atypical Parkinsonisms vs PD

The PSP patients had lower DAT binding than did the PD patients in the mean caudate (weighted relative difference=34.1%, Table 2), mean putamen (18.2%, Table 2), mean striatum, contralateral caudate, ipsilateral caudate and anterior putamen (Fig. 2, Table 2, Supplemental Table 7). The MSA-P patients had lower DAT binding than did the PD patients in the mean caudate (Fig. 2, Table 2, Supplemental Table 7). There were no differences between the PD patients and patients with MSA-C or CBS but the total numbers of patients and studies were low (Table 2). There were no differences in AADC activity between the PD and PSP or MSA-P patients although directions of differences were similar to the DAT analysis (Supplemental Table 5). There were insufficient data for other AADC comparisons.

Differences Between Atypical Parkinsonisms

The PSP patients had 31.4% lower mean striatal DAT binding (weighted relative difference) than did the MSA-P patients (Table 2, Supplemental Table 7). The MSA-P patients had 46.0% lower DAT binding than did the MSA-C patients in the striatum (Table 2, Supplemental Table 7). No other significant differences were observed. The primary results with DAT imaging remained the same when only studies that had used similar diagnostic criteria (Supplemental Table 5) were included in the analysis. There were no suitable studies that had compared PSP to MSA-C patients, or CBS patients to those with other atypical parkinsonisms. There were no differences in AADC activity between PSP and MSA-P patients, and there were insufficient data for other comparisons (Supplemental Table 6).

Meta-Regression Analyses and Publication Bias

There were no significant associations in meta-regression analyses using disease duration or the mean motor UPDRS values as moderators. The only significant relationship observed was between the H&Y stage and the effect size for caudate DAT binding in the PD vs MSA-P comparison (Supplemental Table 8), indicating that a higher difference in the H&Y stage scores between the PD and MSA-P groups was associated with a greater difference in caudate nucleus DAT binding between these groups. Funnel plots of the comparisons that had sufficient numbers of studies, did not suggest missing studies that would have suggested publication bias (Egger regressions, $p>0.05$).

DISCUSSION

The results of this meta-analysis indicate that the striatal DAT binding is lower in PSP patients than in both MSA-P and PD. Another important finding was that the caudate DAT binding is lower in MSA-P than in PD patients without significant differences in the putamen. The third major finding was that the striatal DAT binding is clearly lower in MSA-P than in MSA-C patients. Although not significant due to limited data, AADC results paralleled the findings with DAT. The data concerning VMAT2 and CBS are currently insufficient.

Dopaminergic Function in PSP is Lower than in both MSA-P and PD

Our results show that presynaptic dopaminergic function, as measured by DAT binding, is up to 34% lower in PSP than in MSA-P and PD. It has been demonstrated that there is a profound loss of nigral dopaminergic neurons in PSP (*20*) and on the basis of the present results, this loss may exceed that seen in other degenerative parkinsonisms, at least when patients are examined by means of functional brain imaging 3-5 years after symptom onset. Comparative neuropathological data are needed to investigate whether the greater loss of presynaptic dopamine function in PSP is present at all disease stages and whether this loss of dopamine function is based on greater neuronal loss or a functional difference in the nigrostriatal tract. There are data suggesting that PD and PSP patients may have similar losses of A9 dopamine neurons in the substantia nigra (*21*), whereas the number of A10 neurons is clearly lower in PSP than in PD (*22*). From a clinical perspective, it is important to note that the markedly lower DAT binding in the PSP patients compared to the PD or MSA-P patients does not seem to be directly related to clinical differences in motor symptom severity. For example, although the motor symptoms of the PSP patients were less advanced compared to those of the MSA-P patients (motor

UPDRS score 33 vs 37, respectively), the striatal dopaminergic degeneration was clearly more progressed (31.4% lower in the PSP patients than in the MSA-P patients).

Relative differences in the striatal DAT binding between PSP and MSA-P/PD were large, at 18-34% (Hedges' $g > 0.70$). The magnitudes are possibly diagnostically significant. Currently, many semi-automatic analysis systems used clinically for DAT SPECT have taken advantage of published cohorts of healthy subjects (e.g. Varrone et al.(*23*)) and clinical diagnostics is aided by the automatic flagging of abnormal striatal values as compared to the reference values. In the future, automated analysis could possibly be extended to atypical parkinsonisms by including reference values for PD, PSP, MSA-P and MSA-C. However, this would not be an easy task, as the level of pathology is not constant across the disease course, and the system would need to contain information about not only the age and sex of the patients, but also the motor symptom severity and disease duration. This may not be possible in the immediate future, but an endeavor for this purpose could possibly be carried out via the international collection of large numbers of scans of patients with atypical parkinsonisms (*24*).

Caudate Dopaminergic Loss Differentiates MSA-P from PD

The results also showed that while there does not seem to be a difference in putaminal dopaminergic function between MSA-P and PD, there is a difference in the caudate nucleus. Indeed, one previously suggested possibility for improving the dopaminergic diagnostic accuracy of atypical parkinsonisms is the utilization of caudate-putamen or putamen-caudate ratios, as it has been suspected that the rostro-caudal gradient of the dopaminergic deficit is lost in atypical parkinsonisms (e.g. (*25,26*)). We were unable to perform meta-analytical calculations of these ratios because the

measurements were variably reported. Nevertheless, the results indirectly support the notion that the caudate-putamen ratio may be affected in MSA. This is another issue that merits the further large multisite collection of clinical scans for comparison. An automated comparison of the caudate-putamen ratio to those from a large pool of clinically well-characterized patients with PD and atypical parkinsonisms could prove valuable. These data would optimally be based on measurements from PET scans due to the superior spatial resolution which allows clearer separation of striatal subregions in PET as compared to SPECT (*25*). In the included studies, the binding values for the hemispheres contra- and ipsilateral to the predominant motor symptoms were also only sporadically reported. The lack of reported subregional and hemispheric values conveys a message to the neuroimaging community. To successfully perform similar meta-analyses in the future, more precise reporting of regional binding values (each contra- and ipsilateral region for each group together with SDs) or open data sharing is needed.

MSA-P and MSA-C Differ in Striatal Dopamine Function

There was a strikingly large 46.0% difference in striatal DAT binding between the MSA-P and MSA-C patients (Hedges' g = 1.46, four studies with 133 patients). DAT imaging therefore appears useful in the differentiation of MSA subtypes. However, rather than being dichotomically different pathological entities, MSA-P and MSA-C are likely to represent a neuropathological continuum with mixed neuropathology (*27*). It is possible that MSA-P and MSA-C patients included in neuroimaging trials are particularly well characterized and represent extreme ends of the continuum. Therefore, the large difference in striatal DAT binding between the MSA-P and MSA-C patients possibly does not fully represent clinical reality, where patients with mixed phenotypes are more frequent. Nevertheless, the magnitude of the difference is noteworthy, and we argue that

striatal DAT imaging could be one of the auxiliary diagnostic tools for patients with mild parkinsonism, dysautonomic features and variable levels of cerebellar findings. The second consensus diagnostic criteria of MSA suggested that in the absence of parkinsonian features in a patient with cerebellar ataxia, imaging evidence of a nigrostriatal presynaptic deficit points to the diagnosis of MSA-C (*19*). The present results do not directly contradict this interpretation, but the results demonstrate that it is not the MSA-C subtype but rather the MSA-P phenotype that shows the robust loss of dopamine function. Further studies comparing MSA-C to other degenerative parkinsonisms will be of importance.

Limitations

The results presented herein were derived almost solely from DAT imaging using various tracers. We did not identify suitable VMAT2 studies, and also the number of AADC studies was low (six studies published in the 1990s). Therefore, we do not currently know if the diagnostic value of DAT imaging in atypical parkinsonisms is superior to or worse than other presynaptic imaging targets. Although AADC function may be somewhat upregulated in PD and the DAT is possibly downregulated (*28*), we do not consider it likely that the differences reported herein would be markedly different if VMAT2 or AADC was the target. Another limitation is that the level of the present evidence precludes definitive conclusions about the dopaminergic function in CBS because the numbers of studies and patients were low. It is also debatable whether it is useful to classify PSP and CBS as different disorders (*29,30*). It should also be noted that the results of the present meta-analysis do not necessarily represent well the clinical diagnostic reality as many of the included studies were performed with patients that had already been clinically diagnosed

at the time of imaging. Finally, medications were variably reported and it was therefore impossible to perform subanalyses between treatment groups.

CONCLUSION

The results of this meta-analysis demonstrate that PSP is associated with the greatest presynaptic dopaminergic loss compared to other degenerative parkinsonian syndromes. The observed large difference between MSA-P and MSA-C may also be clinically useful in patients with dysautonomia. Given the magnitude of the differences between the diagnostic groups, an effort could be initiated for the collection and analysis of clinical scans that could be used to create reference and of cut-off values for research and clinical work.

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Statement of Disclosure

No potential conflicts of interest relevant to this article exist.

Table 1. Summary of demographic and clinical details of the samples in the included studies. N or weighted* mean values and weighted standard deviations are presented.

Target	Variable	PD	MSA-P	PSP	CBS	MSA-C
DAT	Samples (n)	26	18	16	5	5
	Patients (n)	877	285	181	77	62
	Age (yrs)	64(9)	63(9)	67(7)	68(8)	62(8)
	Sex (m/f ratio)	1.5	1.0	1.3	0.7	1.1
	Disease duration (yrs)	4.6(3.6)	3.2(1.9)	3.2(1.9)	3.0(1.3)	3.2(1.9)
	H&Y score	2.1(0.7)	3.4(0.8)	3.2(0.9)	3.0(0.8)	3.5(1.1)
	Motor UPDRS score	23(11)	37(13)	33(11)	35(13)	30(11)
AADC	Samples (n)	6	5	3	1	0
	Patients (n)	81	71	23	2	0
	Age (yrs)	58(6)	57(7)	66(5)	65(5)	-
	Sex (m/f ratio)	2.1	1.6	3.3	1.0	-
	Disease duration (yrs)	8.3(6.3)	4.7(3.3)	3.3(1.8)	4.0(0)	-
	H&Y score	2.7(0.8)	3.3(0.8)	3.3(-)	-	-
	Motor UPDRS score	-	-	-	-	-

*Weighted for number of subjects for each study

Table 2. Summary of DAT results. *g* = Hedges' *g*, CI = 95% confidence interval for *g,* n = number of studies/number of patients, I^2= heterogeneity index. There were no available studies that have compared MSA-C patients to PSP or CBS patients. There were also insufficient data for an MSA-P vs. CBS comparison. Statistically significant comparisons are highlighted with bold text. Hemispheric values and ratios are presented in Supplemental Table 6.

	PD vs MSA-P	**PD vs PSP**	**PD vs MSA-C**	**PD vs CBS**	**MSA-P vs PSP**	**MSA-P vs MSA-C**	**PSP vs CBS**
Caudate	***g*=-0.39 CI=-0.77 to -0.01 n=10/609, I^2=63.2%**	***g*=-1.08 CI=-1.52 to -0.64 n=11/356, I^2=56.6%**	*g*=0.73 CI=-1.18 to 2.63 n=2/92, I^2=0.0%	*g*=-0.33 CI=-1.08 to 0.43 n=3/122, I^2=0.0%	*g*=-0.37 CI=-1.13 to 0.39 n=5/114, I^2=47.7%	*g*=1.20 CI=-0.20 to 2.59 n=3/99, I^2=45.6%	Insufficient data n=1/17
Putamen	*g*=-0.27 CI=-0.58 to 0.04 n=9/451, I^2=29.5%	***g*=-0.86 CI=-1.50 to -0.21 n=8/291, I^2=73.3%**	*g*=1.51 CI=-0.57 to 3.59 n=2/92, I^2=0.0%	*g*=0.55 CI=-0.42 to 1.53 n=3/122, I^2=26.8%	*g*=-0.47 CI=-1.22 to 0.28 n=4/101, I^2=27.5%	***g*=1.87 CI=0.46 to 3.29 n=3/99, I^2=34.1%**	Insufficient data n=1/17
Striatum	*g*=-0.34 CI=-1.01 to 0.33 n=4/255, I^2=46.6%	***g*=-1.05 CI=-1.68 to -0.43 n=9/390, I^2=73.3%**	Insufficient data n=1/55	*g*=0.98 CI=-0.65 to 2.62 n=4/142, I^2=81.3%	***g*=-0.70 CI=-1.21 to -0.19 n=3/83, I^2=0.0%**	***g*=1.46 CI=0.23 to 2.68 n=4/133, I^2=63.5%**	*g*=1.30 CI=-5.49 to 8.09 n=2/29, I^2=40.1%

Key points

Question: It is unclear whether presynaptic dopamine imaging with PET or SPECT can be used in the differential diagnosis of atypical parkinsonisms.

Pertinent findings: Striatal dopamine transporter (DAT) function was clearly lower in progressive supranuclear palsy (PSP) as compared to Parkinson's disease and parkinsonism variant of multiple system atrophy (MSA-P), and in MSA-P as compared to the cerebellar variant (MSA-C).

Implications for patient care: The results demonstrate group-level differences in presynaptic dopamine function between atypical parkinsonism syndromes.

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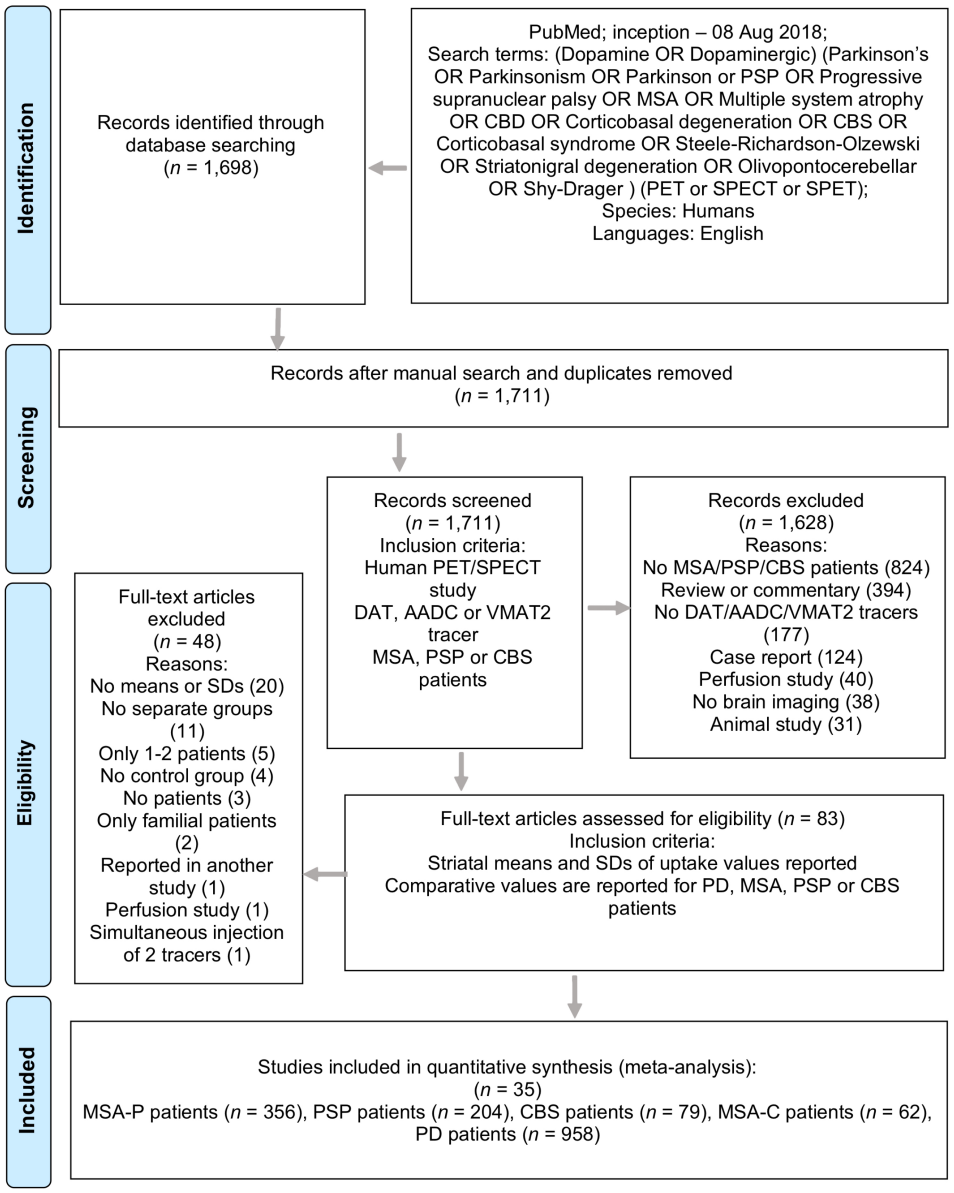
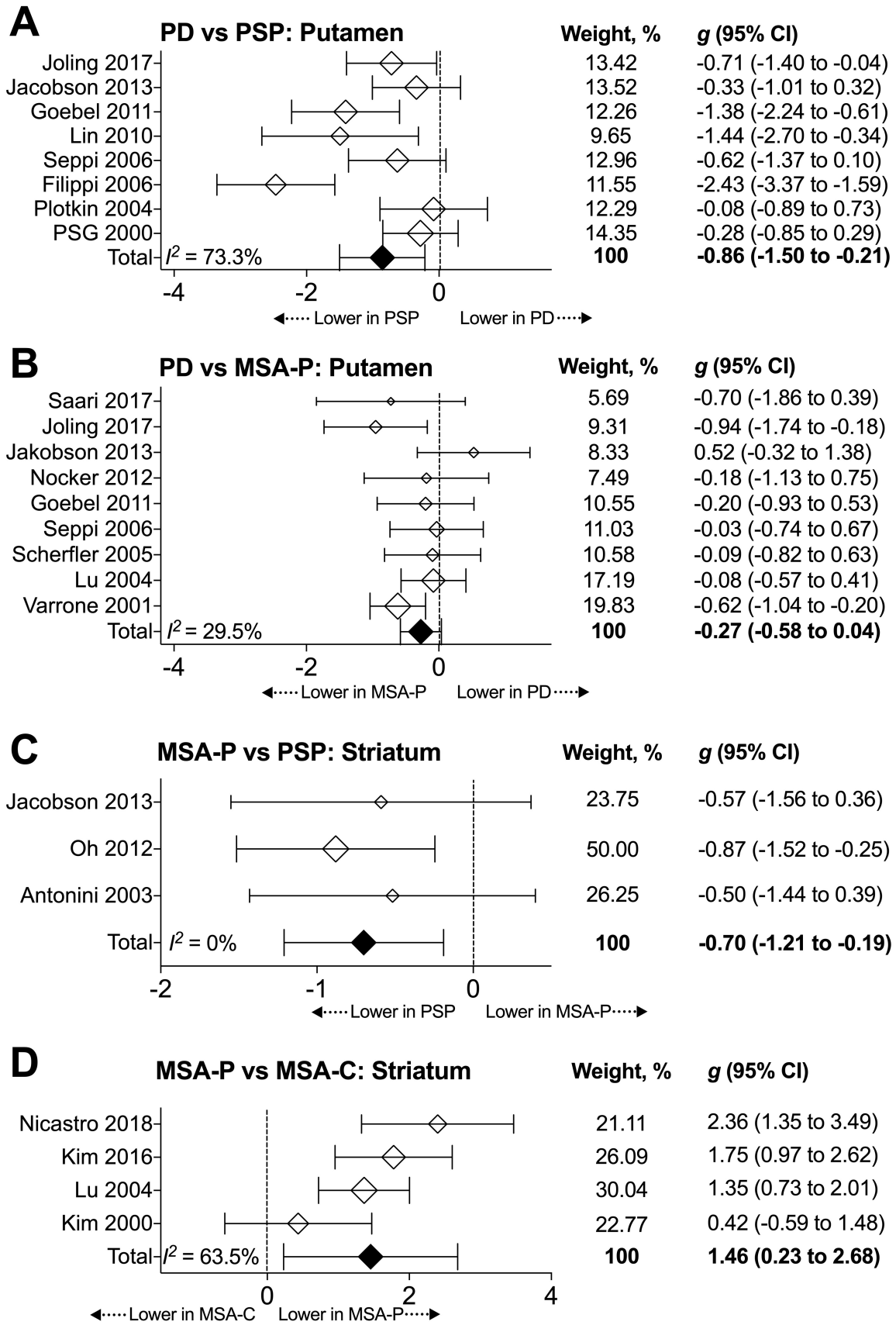
Figure 1. Flow chart of study inclusion and exclusion. PSP=progressive supranuclear palsy, MSA=multiple system atrophy, CBD=corticobasal degeneration, CBS=corticobasal syndrome, PET=positron emission tomography, SPECT=single photon emission computed tomography, DAT=dopamine transporter, AADC=aromatic amino acid decarboxylase, VMAT2=vesicular monoamine transporter type 2, SD=standard deviation, MSA-P=multiple system atrophy parkinsonism variant, MSA-C=multiple system atrophy cerebellar variant.

Figure 2. Forest plots of key comparisons in DAT studies. A. Significant putaminal difference between PD and PSP. B. Non-significant putaminal difference between PD and MSA-P. C. Significant striatal difference between MSA-P and PSP. D. Significant striatal difference between MSA-P and MSA-C.


Identification
Records identified through database searching (n = 1,698)
PubMed; inception – 08 Aug 2018;
Search terms: (Dopamine OR Dopaminergic) (Parkinson's OR Parkinsonism OR Parkinson or PSP OR Progressive supranuclear palsy OR MSA OR Multiple system atrophy OR CBD OR Corticobasal degeneration OR CBS OR Corticobasal syndrome OR Steele-Richardson-Olzewski OR Striatonigral degeneration OR Olivopontocerebellar OR Shy-Drager) (PET or SPECT or SPET);
Species: Humans
Languages: English
Screening
Records after manual search and duplicates removed (n = 1,711)
Records screened (n = 1,711)
Inclusion criteria:
Human PET/SPECT study
DAT, AADC or VMAT2 tracer
MSA, PSP or CBS patients
Records excluded (n = 1,628)
Reasons:
No MSA/PSP/CBS patients (824)
Review or commentary (394)
No DAT/AADC/VMAT2 tracers (177)
Case report (124)
Perfusion study (40)
No brain imaging (38)
Animal study (31)
Eligibility
Full-text articles excluded (n = 48)
Reasons:
No means or SDs (20)
No separate groups (11)
Only 1-2 patients (5)
No control group (4)
No patients (3)
Only familial patients (2)
Reported in another study (1)
Perfusion study (1)
Simultaneous injection of 2 tracers (1)
Full-text articles assessed for eligibility (n = 83)
Inclusion criteria:
Striatal means and SDs of uptake values reported
Comparative values are reported for PD, MSA, PSP or CBS patients
Included
Studies included in quantitative synthesis (meta-analysis):
(n = 35)
MSA-P patients (n = 356), PSP patients (n = 204), CBS patients (n = 79), MSA-C patients (n = 62), PD patients (n = 958)


A
PD vs PSP: Putamen
Weight, %
g (95% CI)
Joling 2017
13.42
-0.71 (-1.40 to -0.04)
Jacobson 2013
13.52
-0.33 (-1.01 to 0.32)
Goebel 2011
12.26
-1.38 (-2.24 to -0.61)
Lin 2010
9.65
-1.44 (-2.70 to -0.34)
Seppi 2006
12.96
-0.62 (-1.37 to 0.10)
Filippi 2006
11.55
-2.43 (-3.37 to -1.59)
Plotkin 2004
12.29
-0.08 (-0.89 to 0.73)
PSG 2000
14.35
-0.28 (-0.85 to 0.29)
Total
I2 = 73.3%
100
-0.86 (-1.50 to -0.21)
-4
-2
0
Lower in PSP
Lower in PD
B
PD vs MSA-P: Putamen
Weight, %
g (95% CI)
Saari 2017
5.69
-0.70 (-1.86 to 0.39)
Joling 2017
9.31
-0.94 (-1.74 to -0.18)
Jakobson 2013
8.33
0.52 (-0.32 to 1.38)
Nocker 2012
7.49
-0.18 (-1.13 to 0.75)
Goebel 2011
10.55
-0.20 (-0.93 to 0.53)
Seppi 2006
11.03
-0.03 (-0.74 to 0.67)
Scherfler 2005
10.58
-0.09 (-0.82 to 0.63)
Lu 2004
17.19
-0.08 (-0.57 to 0.41)
Varrone 2001
19.83
-0.62 (-1.04 to -0.20)
Total
I2 = 29.5%
100
-0.27 (-0.58 to 0.04)
-4
-2
0
Lower in MSA-P
Lower in PD
C
MSA-P vs PSP: Striatum
Weight, %
g (95% CI)
Jacobson 2013
23.75
-0.57 (-1.56 to 0.36)
Oh 2012
50.00
-0.87 (-1.52 to -0.25)
Antonini 2003
26.25
-0.50 (-1.44 to 0.39)
Total
I2 = 0%
100
-0.70 (-1.21 to -0.19)
-2
-1
0
Lower in PSP
Lower in MSA-P
D
MSA-P vs MSA-C: Striatum
Weight, %
g (95% CI)
Nicastro 2018
21.11
2.36 (1.35 to 3.49)
Kim 2016
26.09
1.75 (0.97 to 2.62)
Lu 2004
30.04
1.35 (0.73 to 2.01)
Kim 2000
22.77
0.42 (-0.59 to 1.48)
Total
I2 = 63.5%
100
1.46 (0.23 to 2.68)
0
2
4
Lower in MSA-C
Lower in MSA-P