

SUPPORTING INFORMATION

Asymmetric dopamine transporter loss affects cognitive and motor progression in Parkinson's disease

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SUPPORTING METHODS

DAT-SPECT – additional methodological details

The reconstructed data was transferred to the PMOD (PMOD Technologies, Zurich, Switzerland) for processing purposes. Site-specific attenuation correction was applied to the reconstructed data by means of an automated ellipse drawing method and Chang's zero attenuation correction using an attenuation coefficient, μ , which was empirically derived from the phantom data acquired during the technical site visit. Hermes (Hermes Medical Solutions, Stockholm, Sweden) and PMOD (PMOD Technologies, Zurich, Switzerland) were used as brain software for quantification. After the attenuation correction step, a standard Gaussian 3D 6.0 mm filter was applied, and spatial normalization was performed in PMOD software, normalizing these files to the standard Montreal Neurologic Institute space to enable the same anatomical alignment for all scans.

Then, the transaxial slice with the highest striatal uptake was identified, and the eight hottest striatal slices around it were averaged to generate a single slice image. Count densities were extracted and used to calculate striatal specific binding ratios (SBRs) for each of the four striatal regions, based on this formula: $SBR = (\text{striatal region})/(\text{occipital})-1$. Images were checked for registration accuracy.

SUPPORTING TABLES

Table e-1 Age-normative data (mean and SD) based on the healthy control sample of PPMI dataset: at baseline, 2- and 4-year follow-up

Age ranges (years)	Baseline				Follow-up							
	30-45	46-60	61-75	76-90	2-year				4-year			
					30-45	46-60	61-75	76-90	30-45	46-60	61-75	76-90
<i>n</i>	23	66	85	11	15	55	81	15	10	41	81	22
MoCA#	28.44 (1.26)	28.07 (1.11)	28.00 (1.10)	27.83 (1.27)	28.4 (1.64)	27.73 (2.20)	26.48 (2.43)	27.00 (2.14)	28.40 (1.51)	27.98 (1.77)	27.32 (2.48)	26.64 (2.72)
Benton JLO	26.70 (3.44)	26.88 (3.37)	25.60 (4.50)	25.27 (4.59)	23.87 (7.76)	26.98 (3.17)	25.41 (5.45)	25.2 (4.65)	26.60 (3.53)	26.15 (5.61)	25.58 (4.95)	24.00 (6.76)
HVLT-R Immediate Recall	26.57 (4.69)	27.15 (4.33)	25.34 (4.58)	24.36 (4.65)	29.00 (4.41)	27.49 (4.51)	25.05 (5.09)	23.33 (4.85)	30.60 (4.01)	27.37 (5.13)	26.11 (4.38)	22.91 (5.71)
HVLT-R Delayed Recall	10.04 (2.03)	9.47 (2.38)	8.95 (2.38)	9.00 (2.53)	11.20 (0.86)	9.67 (2.37)	8.96 (2.45)	7.87 (2.88)	11.00 (1.70)	9.80 (2.04)	8.99 (2.49)	7.64 (2.38)
HVLT-R Recognition	11.7 (0.56)	11.55 (0.79)	11.39 (0.86)	11.36 (1.21)	11.87 (0.35)	11.64 (0.8)	11.38 (1.47)	10.73 (2.82)	11.60 (0.70)	11.61 (0.83)	11.47 (1.48)	10.73 (1.64)
LNS	12.26 (2.14)	11.02 (2.49)	10.45 (2.79)	10.09 (2.3)	13.80 (3.17)	11.55 (2.16)	10.20 (2.27)	10.20 (2.24)	13.00 (3.33)	11.85 (2.84)	10.43 (2.54)	10.05 (2.48)
SDMT	56.26 (10.54)	50.45 (9.69)	43.06 (8.81)	37.18 (7.78)	61.60 (11.96)	50.44 (8.73)	43.44 (8.09)	35.93 (7.40)	67.70 (11.97)	51.05 (9.53)	44.48 (7.98)	36.55 (7.53)
Semantic fluency	52.65 (10.93)	54.89 (10.48)	50.52 (11.84)	46.27 (9.48)	55.80 (10.83)	55.31 (11.31)	51.93 (11.22)	47.47 (13.83)	61.00 (12.53)	56.76 (11.33)	49.91 (10.22)	46.09 (12.35)

Note: Values are mean and SD. # Sample 30-45 (n = 25), 46-60 (n = 70), 61-75 (n = 89), 76-90 (n = 12). MoCA, Montreal Cognitive Assessment; JLO, Judgment of Line Orientation; HVLT-R, The Hopkins Verbal Learning Test-Revised, LNS, Letter Number Sequencing; SDMT, Symbol Digit Modalities Test.

Table e-2 Neuropsychological features of PD patients

	PD-right	PD-left	F	P value
MoCA, corrected score#	27.06 (2.48)	27.29 (2.25)	0.251	0.617
Z scores§				
Benton JLO	-0.19 (1.02)	-0.16 (1.06)	0.001	0.969
HVLТ-R Immediate Recall	-0.44 (0.96)	-0.27 (1.09)	0.727	0.395
HVLТ-R Delayed Recall	-0.45 (0.96)	-0.28 (1.02)	1.197	0.275
HVLТ-R Discrimination Recognition	-0.37 (1.34)	-0.26 (1.55)	<0.001	0.986
LNS	0.01 (0.90)	-0.12 (1.02)	1.345	0.247
SDMT	-0.36 (1.10)	-0.62 (0.90)	6.628	0.011
Semantic fluency	-0.35 (1.00)	-0.33 (1.05)	0.002	0.963

Note. # PD-right n=106 and PD-left n=143. § PD-right n=102 and PD-left n=136. PD-right, PD right putaminal asymmetry; PD-left, PD with left putaminal asymmetry; MoCA, Montreal Cognitive Assessment; JLO, Judgment of Line Orientation; HVLТ-R, The Hopkins Verbal Learning Test-Revised, LNS, Letter Number Sequencing; SDMT, Symbol Digit Modalities test. MDS-UPDRS-III was used as covariate, if pertinent.

Table e-3 Mixed model analysis results for clinical, neuropsychological and imaging measures

	<i>F</i>	Num df	Den df	<i>p</i>
<u><i>Clinical measures</i></u>				
MDS-UPDRS (<i>motor score</i>)				
Time	13.45	2	398.02	< .001
Asymmetry	5.31	1	239.5	0.022
Asymmetry × Time	0.43	2	398.02	0.654
Conditional R² = .52				
LEDD				
Time	314.54	2	441.97	< .001
Asymmetry	2.04	1	247.08	0.154
Asymmetry × Time	1.9	2	441.97	0.151
Conditional R² = .57				
CSF - Aβ₄₂				
Time	5.26	2	286.35	0.006
Asymmetry	4.46	1	233.24	0.036
Asymmetry × Time	0.08	2	286.35	0.41
Conditional R² = .83				
<u><i>Neuropsychological measures</i></u>				
SDMT (<i>z-scores</i>)				
Time	4.84	2	396.91	0.046
Asymmetry	2.93	1	245.55	0.032
Asymmetry × Time	0.08	2	375.62	0.825
Conditional R² = .64				
<u><i>DAT imaging</i></u>				
DAT-SPECT (<i>mean putamen</i>)				
Time	226.85	2	359.154	< .001
Asymmetry	1.753	1	241.545	0.187
Asymmetry × Time	5.087	2	359.154	0.007
Conditional R² = .80				
DAT-SPECT (<i>mean caudate</i>)				
Time	249.51	2	358.44	< .001
Asymmetry	0.79	1	244.87	0.374
Asymmetry × Time	3.16	2	358.44	0.044
Conditional R² = .86				

Table e-4 Mixed model analysis results for hemispheric striatal DAT-SPECT measures

	<i>F</i>	Num df	Den df	<i>p</i>
Putamen - left				
Time	174.76	2	361.37	<.001
Asymmetry	50.37	1	240.53	<.001
Asymmetry × Time	63.57	2	361.37	<.001
Conditional R² = .80				
Putamen - right				
Time	166.12	2	361.43	<.001
Asymmetry	80.36	1	242.22	<.001
Asymmetry × Time	21.82	2	361.43	<.001
Conditional R² = .82				
Caudate - left				
Time	216.73	2	360.02	<.001
Asymmetry	20.09	1	245.01	<.001
Asymmetry × Time	7.04	2	360.02	.001
Conditional R² = .84				
Caudate - right				
Time	206.63	2	358.75	<.001
Asymmetry	36.11	1	244.52	<.001
Asymmetry × Time	1.02	2	358.75	.360
Conditional R² = .86				