The Electronic Supplementary Material file includes Abbreviations, eight Tables, and three Figures.

Title: Deficits in task-set maintenance and execution networks in Parkinson's disease

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Abbreviations:

BA: Brodmann area
BC: Betweenness centrality
B/l: Bilateral
CC: Clustering coefficient
dAI: Dorsal anterior insula
FG: Frontal gyrus
HV: Healthy volunteer
H & Y: Hoehn and Yahr
IFG: Inferior frontal gyrus
ITG: Inferior temporal gyrus
L: Left
LE: Local efficiency
MFG: Middle frontal gyrus
MidCG: Mid cingulate gyrus
MNI: Montreal Neurological Institute
MTG: Middle temporal gyrus
NS: Node strength
OFI: Orbitofrontal insula
op: Operculum
Op: Opercularis
Orb: Orbicularis
PD: Parkinson's disease patients
PFC: Prefrontal cortex
postCG: Postcentral gyrus
preCG: Precentral gyrus
R: Right
SFG: Superior frontal gyrus
SMA: Supplementary motor area
SMG: Supramarginal gyrus
STG: Superior temporal gyrus
TPJ: Temporoparietal junction
Tri: Triangularis
sup med: Superior medial
UPDRS total: Unified Parkinson's disease rating scale total score
UPDRS III: UPDRS motor examination score

Table 1 Anatomical labels and MNI coordinates of nodes[1]

	x	y	z
Cingulo-opercular Network			
R anterior PFC	27	49	26
R ventral PFC	34	32	7
L anterior cingulate cortex	-2	30	27
R ventral frontal cortex	51	23	8
R anterior insula	38	21	-1
R dorsal anterior cingulate cortex	9	20	34
L anterior insula	-36	18	2
L dorsal cingulate cortex	-6	17	34
Medial frontal cortex	0	15	45
L basal ganglia	-20	6	7
R basal ganglia	14	6	7
L ventral frontal cortex	-48	6	1
R mid insula	37	-2	-3
L thalamus	-12	-3	13
L thalamus	-12	-12	6
R thalamus	11	-12	6
R mid insula	32	-12	2
L mid insula	-30	-14	1
R basal ganglia	11	-24	2
L posterior insula	-30	-28	9
R temporal	51	-30	5
L posterior cingulate	-4	-31	-4
R fusiform	54	-31	-18
R precuneus	8	-40	50
R parietal	58	-41	20
R temporal	43	-43	8
L parietal	-55	-44	30
R superior temporal	42	-46	21
L angular gyrus	-41	-47	29
L temporal	-59	-47	11
L temporoparietal junction	-52	-63	15
Frontoparietal Network			
R anterior PFC	29	57	18
L anterior PFC	-29	57	10
R ventral anterior PFC	42	48	-3
L ventral anterior PFC	-43	47	2
R ventrolateral PFC	39	42	16
R dorsolateral PFC	40	36	29
L anterior cingulate cortex	-1	28	40
R dorsolateral PFC	46	28	31
L ventral PFC	-52	28	17

L dorsolateral PFC	-44	27	33
R dorsal frontal cortex	40	17	40
R dorsal frontal cortex	44	8	34
L dorsal frontal cortex	-42	7	36
L inferior parietal lobule	-41	-40	42
R inferior parietal lobule	54	-44	43
L posterior parietal	-35	-46	48
L inferior parietal lobule	-48	-47	49
L inferior parietal lobule	-53	-50	39
R inferior parietal lobule	44	-52	47
L intraparietal sulcus	-32	-58	46
R intraparietal sulcus	32	-59	41
Sensorimotor Network			
R frontal	58	11	14
R dorsal frontal cortex	60	8	34
L ventral frontal cortex	-55	7	23
R pre-SMA	10	5	51
R ventral frontal cortex	43	1	12
SMA	0	-1	52
R frontal	53	-3	32
R precentral gyrus	58	-3	17
L mid insula	-42	-3	17
L precentral gyrus	-44	-6	49
L parietal	-26	-8	54
R precentral gyrus	48	-8	24
L precentral gyrus	-54	-9	23
R precentral gyrus	44	-11	38
L parietal	-47	-12	36
R mid insula	33	-12	16
L mid insula	-36	-12	15
R temporal	59	-13	8
L parietal	-38	-15	59
L parietal	-47	-18	50
R parietal	46	-20	45
L parietal	-55	-22	38
L precentral gyrus	-54	-22	22
L temporal	-54	-22	9
R parietal	41	-23	55
R posterior insula	42	-24	17
R parietal	18	-27	62
L parietal	-38	-27	60
L parietal	-24	-30	64
L posterior parietal	-41	-31	48
L temporal	-41	-37	16
L temporal	-53	-37	13

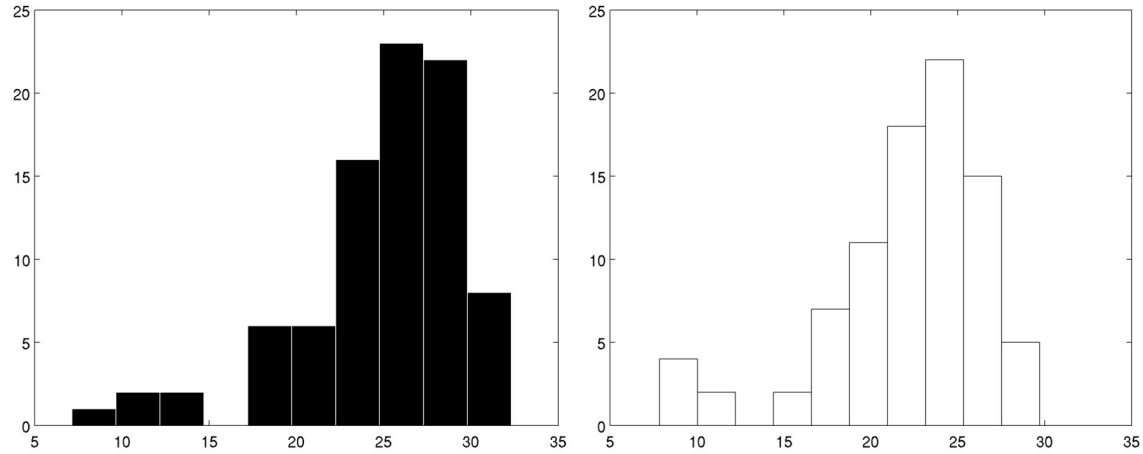
R superior parietal	34	-39	65

[1]: Dosenbach et al., 2010

Skewness Calculations of the Unthresholded Node Strength Distributions

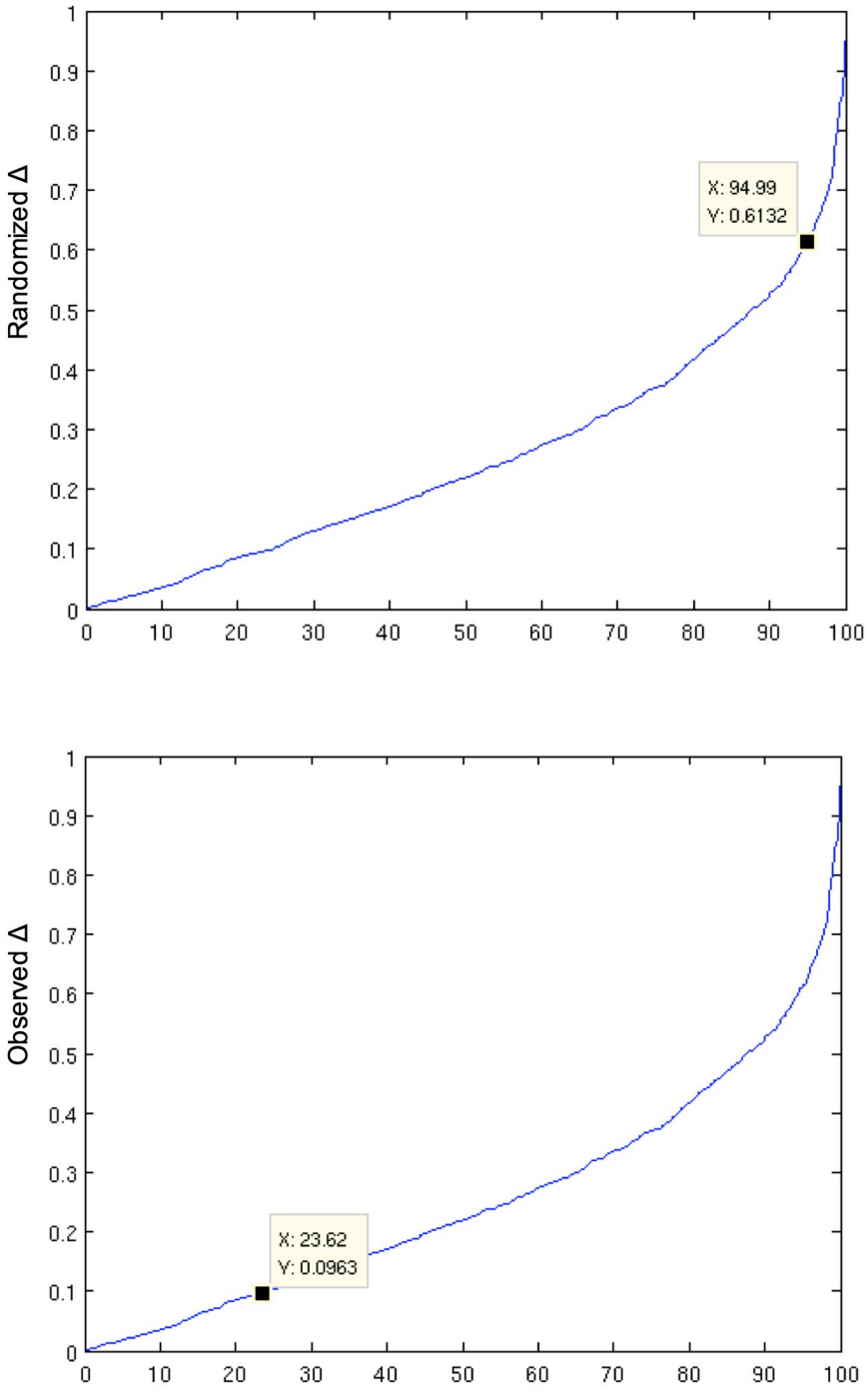
The histograms of the unthresholded node strength values for both groups are shown in Fig. 1 (black bars: HV, white bars: PD). The distributions were skewed for both groups.

Fig. 1 Histograms



Using the skewness function in Matlab 2013a, we also established quantitatively using a bootstrapping method that the skewness was not significantly different between the groups. To do so, the average unthresholded node strength values of 86 nodes were calculated for each group yielding a an 86 x 1 vector per group. Then, the skewness of each group vector was calculated and the absolute difference between the skewness values (observed difference) was computed. Subsequently, the data were randomly sorted into two group vectors (1000 permutations) and the absolute difference between the skewness values was calculated for each permutation (randomized difference). Whenever the randomized difference was greater than the observed, this was counted as a "hit." In the end, a p value was determined as a hits/permutations ratio. All of the randomized differences were sorted along an x-axis, and the value corresponding to the 95% confidence interval threshold was identified. The observed skewness difference (0.096) was much smaller than the value corresponding to the 95% threshold (0.6); therefore, it was insignificant (Fig. 2).

Fig. 2 Plots



The top plot shows the randomized differences sorted along the x-axis by size after bootstrapping. The 95% threshold corresponds to a difference of 0.6. The bottom plot demonstrates the position of the actual observed difference on the curve, which corresponds to a threshold of 23%.

Table 2 Demographic and clinical data of patients in "OFF" state

ID	Age	H & Y	UPDRS total	UPDRS III
PD1	68.5	2.5	61	41
PD2	59.6	3	78	52
PD3	59	2.5	54	35
PD4	68.6	2.5	68	53
PD5	64.6	2	38	32
PD6	46.5	2	48	33
PD7	75.6	3	38	26
PD8	67.7	2	36	28
PD9	73.2	2.5	62	46
PD10	62	2.5	50	31
PD11	73	2.5	36	26
PD12	69	2.5	63	39
PD13	59	3	58	38
PD14	61	2.5	47	34
PD15	54.8	2.5	45	32
PD16	54	2	51	31
PD17	59.4	2.5	65	35
PD18	64	2	32	14
PD19	50.3	3	60	23
PD20	68	2	31	21
PD21	42	3	54	22

PD22	61	3	62	25
PD23	65.6	2	19	7
PD24	66.6	2.5	33	21
PD25	64.3	2	25	6
PD26	61.6	3	53	29
PD27	55.8	2.5	28	16
PD28	62.4	2	35	22
PD29	43	2	20	10
PD30	54.8	2	45	24

Table 3 Left dAI within-group functional connectivity

HV	BA	x	y	z	# of voxels
L OFI	47/12	-42	19	-4	706
R OFI	47/12	31	23	-7	563
L midCG	32	-4	9	42	509
R SMG	40	63	-37	35	71
R midCG/paracentral	31	7	-33	49	18
L midCG/precuneus	5	-11	-39	50	13
R STG/SMG	42/40	66	-30	21	12
L IFG (pars Tri)	45	-42	26	24	12
R MFG	9	38	44	28	12
R precuneus	7	21	-61	28	10
L putamen		-25	5	-7	7
L MFG	46	-42	40	31	7
R MFG	10	35	44	7	5
R calcarine	17	17	-68	10	4
R calcarine	17	21	-65	7	2
L calcarine	17	-14	-72	14	2
R Rolandic op	44	59	2	14	2
L cuneus/calcarine	17	-14	-68	21	2
R midCG	23	3	-23	31	2
L midCG	24	-7	-9	38	2
R precuneus	7	10	-68	52	2

PD	BA	x	y	z	# of voxels
R Rolandic op/IFG	44/45	56	12	0	763
L insula/IFG	47/13	-32	19	0	682
L SMA/midCG	6/32	3	9	49	410
L MFG	46	-42	40	21	75
R midCG	23	7	-23	28	15
R midCG/paracentral	31/6	10	-30	45	9
R precuneus	7	21	-68	42	4
R thalamus		17	-12	10	3
L SMG	40	-63	-26	42	2

Top 5% of correlations are shown. Cutoff for HV is Z = 6.27 and for patients Z = 6.12.

Table 4 Left TPJ within-group functional connectivity

HV	BA	x	y	z	# of voxels
L TPJ		-56	-68	10	626
R TPJ		52	-54	17	515
R precuneus	31	7	-61	21	272
R IFG (pars Orb)	47	42	30	-14	156
L IFG/Insula (pars Tri)	47/13	-42	26	7	138
L calcarine	18	-21	-61	10	70
L MTG	21	-53	-19	-4	43
R sup med FG	9	3	47	35	27
L sup med FG	9	-7	47	21	25
R MFG/preCG	6	45	-5	52	21
L ITG/fusiform	37	-46	-40	-25	18
R SFG	9	14	58	28	16
R insula	13	49	2	0	12
R Rolandic op/insula	13	45	-12	17	11
R lingual	17	17	-61	0	10
L preCG	6	-39	-2	45	10
R STG	22	63	-12	3	5
R MTG	21	52	-9	-18	4
R STG	22	56	5	-14	4
R paracentral	4	3	-40	70	4
L hippocampus		-21	-30	-4	3
R temporal pole	38	63	12	0	3
L IFG	45	-49	26	17	3
R IFG (pars Tri)	45	38	16	28	3

R postCG	2	59	-16	35	3
R fusiform	37	42	-44	-21	2
R IFG (pars Orb)	47	24	23	-18	2
R lingual		10	-51	-4	2
R insula	13	35	-16	7	2
R insula	13	38	-12	7	2
R midCG	24	7	-2	45	2
R SMA	6	10	-5	52	2

PD	**BA**	**x**	**y**	**z**	**# of voxels**
B/l calcarine	18	14	-61	17	464
B/l sup med FG	8	-7	33	52	453
L TPJ		-53	-68	10	452
R TPJ		49	-65	17	298
L midCG/precuneus	5	-7	-40	49	157
L SFG	10	-18	61	28	34
R IFG (pars Tri)	45	56	30	17	29
L MTG	21	-60	-12	-11	12
R MTG	21	70	-33	-4	11
R ITG/MTG	21	52	2	-35	10
L sup med FG	10	-0	65	17	10
L MTG	21	-70	-44	3	9
L preCG	6	-39	-2	52	9
L IFG (pars Op)	44	-53	16	35	7
L paracentral	4	-7	-40	77	7
R IFG (pars Orb)	47	45	30	-14	6
R hippocampus		21	-33	-4	6
R IFG (pars Op)	44	45	16	35	6
L parahippocampus	36	-28	-26	-18	5
L parahippocampus	36	-28	-33	-11	5
L IFG (pars Orb)	47	-56	26	-7	5
L olfactory		-0	16	-11	4
L postCG	3	-39	-16	38	4
R preCG	6	49	5	42	4
L medial temporal pole	38	-49	19	-28	3
R MTG	21	56	-5	-18	3
L fusiform	37	-32	-40	-14	3
R MTG	21	56	-19	-7	3
R SFG	10	31	58	14	3
L medial temporal pole	38	49	9	-28	2
R SFG	10	17	58	24	2
R postCG	3	52	-16	52	2
R precuneus	7	3	-51	63	2

Top 5% of correlations are shown. Cutoff for HV is Z = 5.69 and for patients, Z = 5.58.

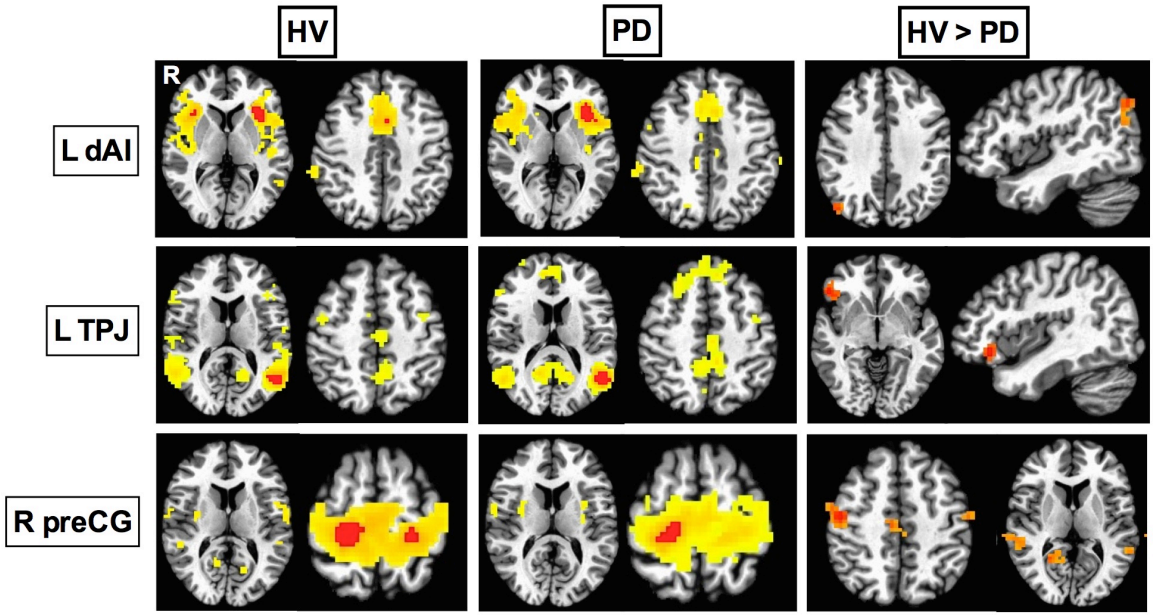
Table 5 Right preCG1 functional connectivity

HV	BA	x	y	z	# of voxels
B/l preCG and SMA	4/6	-28	-30	59	1913
R calcarine gyrus	18	17	-61	17	40
L lingual	18	-11	-65	-4	11
R putamen/insula		31	-5	14	11
L calcarine / cuneus	18	-0	-75	17	11
L STG	41	-53	-37	14	9
R fusiform	37	28	-58	-11	8
L calcarine	17	-14	-68	10	5
R STG	41	52	-37	10	4
L insula/putamen	13	-35	-5	3	3
R cuneus	18	17	-75	31	3
L MTG	21	-46	-30	3	2
L cuneus	17	-14	-86	17	2

PD	BA	x	y	z	# of voxels
B/l preCG and SMA	4/6	28	-33	59	1870
R putamen		31	2	7	49
R MFG	8	31	26	42	12
L putamen/insula		-32	-12	7	9
L insula	13	-32	2	10	9
R temporal pole (STG)	22	59	5	0	6
R STG	22	56	-12	0	4
R STG	41	56	-23	3	4
R STG	22	59	-26	3	3
R STG	42	63	-33	14	3
L Rolandic op	6	-53	2	14	3
L mid occipital		-42	-72	17	2
L MFG	9	-32	33	38	2

Top 5% of correlations are shown. Cutoff for HV is Z = 6.44 and for patients Z = 5.79.

Fig. 3



Axial and sagittal sections of within- and between-group seed-based whole-brain functional connectivity maps are shown. See corresponding tables for coordinates.

Table 6. Correlations between the UPDRS total scores and average graph metrics across the whole network in the PD group

	Degree		NS		CC		BC		LE	
threshold	**r**	**p**	**r**	**p**	**r**	**p**	**r**	**p**	**r**	**p**
0.1	0.42	0.021	0.37	0.040	0.37	0.040	- 0.46	0.010	-	-
0.15	0.4	0.028	0.36	0.050	0.38	0.038	- 0.46	0.010	0.36	0.050
0.2	0.39	0.035	-	-	0.39	0.035	- 0.45	0.013	0.37	0.040
0.25	0.38	0.038	-	-	0.37	0.040	- 0.44	0.016	-	-
0.3	0.36	0.050	- -	- -	0.36	0.050	- 0.41	0.024	0.38	0.038
0.35	-	-	- -	- -	0.36	0.050	- 0.39	0.035	0.41	0.024
0.4	-	-	-	-	-	-	- 0.39	0.035	0.4	0.028

Correlations between the UPDRS total scores and seed-based functional connectivity maps

We used the significance threshold: voxel p value= 0.001, cluster size = 25 voxels, and kept the cluster size constant.

We found that the functional connectivity between the right preCG1 and left inferior frontal gyrus (x = -49, y = 47, z = 3) showed a strong trend for positive correlation with the UPDRS total scores (voxel p value = 0.0012, cluster size = 25 voxels, Z = 4.28).

As an exploratory analysis, we also correlated the UPDRS III motor exam scores with the seed-based functional connectivity maps using the same significance threshold: voxel p value= 0.001, cluster size = 25 voxels, and kept the cluster size constant. We observed the following results:

- There was a significant positive correlation between the UPDRS III scores and between the right preCG1 - right posterior insula (x = 42, y = -23, z = 3) functional connectivity (Z = 4.64).

The other two seeds demonstrated trends:
- The functional connectivity between the left dAI and left inferior temporal gyrus (x = -60, y = -58, z = -11) showed positive correlation with the UPDRS III scores (voxel p value = 0.0035, cluster size = 25 voxels, Z = 4.16).
- The functional connectivity between the left TPJ and left superior medial gyrus (x = -7, y = 33, z = 35) showed positive correlation with the UPDRS III scores (voxel p value = 0.01, cluster size = 25 voxels, Z = 3.51).

Whole-brain functional connectivity of the striatal-thalamic nodes

There are two striatal and three thalamic nodes included in our composite network all of which belong to the CON. One may argue that the striatal-thalamic nodes were underrepresented in the network and therefore, did not yield between-group differences. As we pointed out in the Discussion, “More recent seed-based resting-state fMRI studies also showed abnormal striatal functional connectivity and striatal-cortical remapping in PD (Helmich et al. 2010; Wu et al. 2011b; Hacker et al. 2012; Luo et al. 2014).” In these studies (except for Wu et al., 2011), striatal connectivity was considered in a seed-based whole brain functional connectivity framework, i.e., outside the confines of a network topology. To examine this issue further, we performed an additional exploratory whole brain functional connectivity analysis using the striatal-thalamic nodes of the composite network as seeds. We used the significance threshold: voxel p value= 0.001, cluster size = 25 voxels, and kept the cluster size constant.
We found between-group differences. The striatal nodes showed stronger functional connectivity with the contralateral striatum in the HV > PD comparison. The reverse contrast did not reveal any differences. The functional connectivity of the thalamic nodes was not significantly different between the groups either.

Table 7. Left striatum functional connectivity (coordinates: x = -20, y = 6, z = 7), cluster size always 25 voxels

HV > PD	BA	x	y	z	Z	Voxel p value
R putamen		21	9	3	4.08	0.001
Lower thresholds						
L putamen		-21	9	10	4.48	0.002
R supramarginal gyrus	40	49	-40	42	3.20	0.008
R supplementary motor area	6	14	19	45	3.30	0.01

Table 8. Right striatum functional connectivity (coordinates: x = 14, y = 6, z = 7), cluster size always 25 voxels

HV > PD	BA	x	y	z	Z	Voxel p value
L caudate		-18	12	14	4.86	0.001
Lower thresholds						
R caudate		17	9	17	3.65	0.003
R superior frontal gyrus	8	21	16	42	3.03	0.01