SUPPLEMENTARY MATERIAL

Structural brain signature of cognitive decline in Parkinson's disease: DTI-based evidence from the LANDSCAPE study

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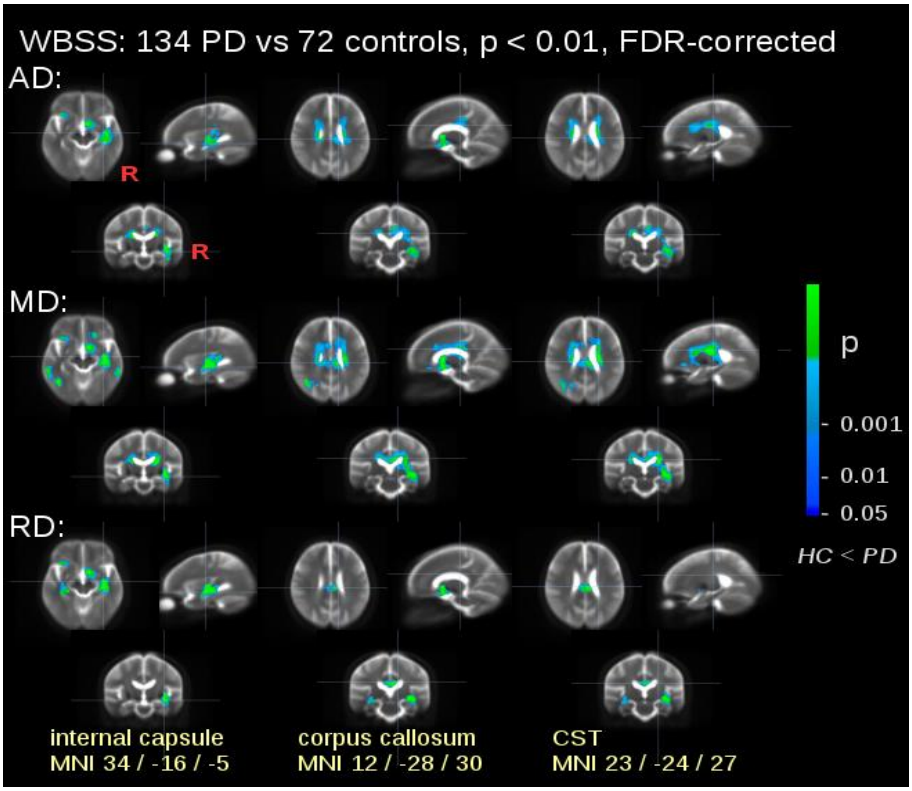
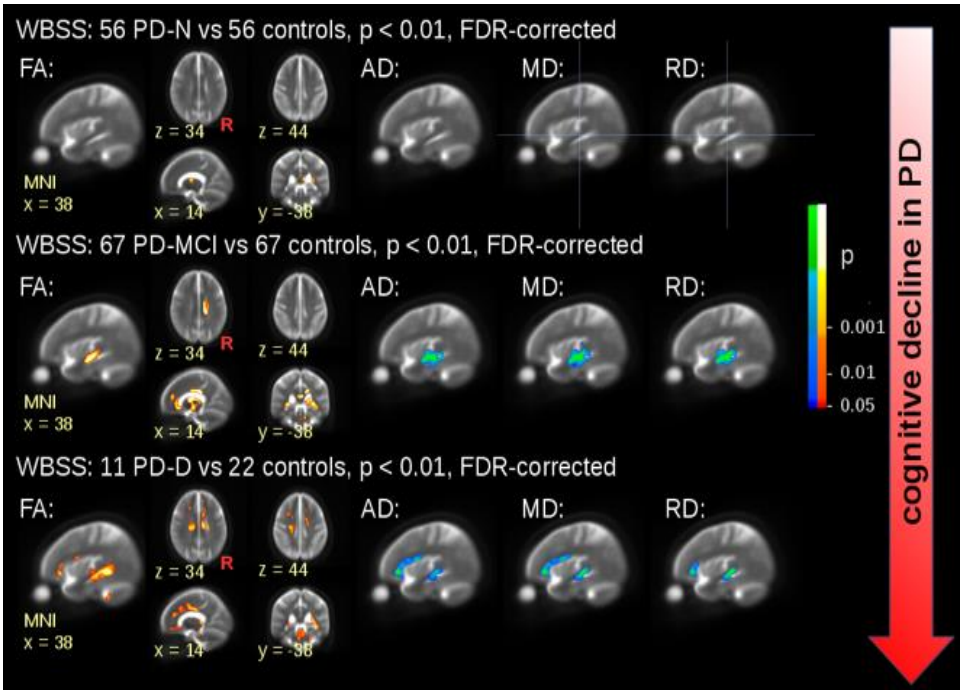
	PD-N *n*=56 (42%)	HC1 *n*=56 (78%)	*p*	PD-MCI *n*=67 (50%)	HC2 *n*=67 (93%)	*p*	PD-D *n*=11 (8%)	HC3 *n*=22 (15%)	*p*
Gender M/F	41/15	27/29	0.007	48/19	36/31	0.032	9/2	13/8	0.248
Age/y	66±8 (45-78)	65±7 (47-79)	0.616	68±8 (48-79)	67±6 (49-79)	0.225	71±4 (63-76)	72±5 (62-79)	0.898
Education/y	13±3 (8-19)	15±2 (10-18)	0.048	13±3 (7-20)	16±4 (10-30)	<0.001	13±4 (7-11)	15±3 (10-21)	0.097
MMSE	29±1 (26-30)	29±1 (26-30)	0.020	28±2 (22-30)	30±1 (26-30)	<0.001	24±2 (21-27)	29±1 (26-30)	<0.001

Supplementary Table 1: Demographic and neuropsychological characteristics. Demographic and neuropsychological characteristics of cognitively normal (PD-N), mildly cognitively impaired (PD-MCI), demented patients (PD-D), in comparison with age-matched healthy controls, i.e. HC1, HC2, and HC3, respectively, that were sampled from the overall control cohort (*n*=72). Data are given as mean±std (min-max) except for gender. The provided p-values refer to unpaired two-sample *t*-tests for unequal variances for continuous variables and χ^2-Test for categorical variables.



Supplementary Figure 1: **whole-brain-based spatial statistics (WBSS) of the DTI metrics maps showing results of group comparison for PD patients compared to healthy controls.** Cold colours indicate cluster of significant reduction of axial diffusivity (AD), mean diffusivity (MD), and radial diffusivity (RD) in PD patients after correction for confounding multicentric factors (p<0.01, false-discovery-rate (FDR) corrected with further cluster-wise correction to reduce false positive errors). Shown are triplets of most representative orthogonal slices displayed on a multicentre study specific averaged *b*0-template as background. MNI – Montreal Neurological Institute.



Supplementary Figure 2: Whole-brain-based spatial statistics (WBSS) of the fractional anisotropy (FA) maps showing results of different cognitive PD subtypes compared to healthy controls. Hot colours indicate clusters of significant decrease of FA in PD patients with normal cognition (PD-N, upper row), mild cognitively impaired PD patients (PD-MCI, centre row), and patients with PD-associated dementia (PD-D, lower row) after correction for confounding multicentric factors (p<0.01, false-discovery-rate (FDR) corrected with further cluster-wise correction). Shown are most representative orthogonal slices displayed on a multicentre study specific averaged *b*0-template as the background. Cold colours indicate clusters of significant increase of axial diffusivity (AD), mean diffusivity (MD), and radial diffusivity (RD) in PD-N patients, PD-MCI patients, and PD-D patients (right columns, MNI x=38). MNI – Montreal Neurological Institute.

	MNI (x y z)		size	p	anatomical localization	correlation (p)*						
						CERAD	BNT	CP	VF	WLD	WLL	WLR
FA												
	35 -16 -6	R	33028	< 0.00001	internal capsule, cingulate cortex, CST, CC, frontal lobe, pons, striatum	0.0002	0.06	0.005	0.01	0.62	0.06	0.06
	-7 -14 -4	L	7317	< 0.00001	internal capsule	0.045	0.08	0.052	0.16	0.83	0.98	0.59
	-28 -64 7	L	4360	< 0.00001	optic tract	0.006	0.27	0.001	0.19	0.40	0.03	0.07
	29 -65 21	R	2563	< 0.00001	optic tract	0.12	0.35	0.008	0.33	0.21	0.41	0.27
	7 -34 -22	R	2160	< 0.00001	midbrain	0.25	0.33	0.38	0.37	0.29	0.49	0.90
AD												
	37 -18 -2	R	25489	< 0.00001	internal capsule, CST, CC	< 0.00001	0.0048	0.0004	0.0003	0.12	0.0067	0.0047
	-21 -18 23	L	7059	< 0.00001	CST	0.0001	0.026	0.006	0.004	0.53	0.038	0.15
	-39 21 -2	L	1384	< 0.00001	frontal lobe	0.0008	0.015	0.037	0.21	0.34	0.014	0.010
MD												
	38 -18 -5	R	62753	< 0.00001	internal capsule, CST, CC	< 0.00001	0.010	0.0005	0.0008	0.27	0.006	0.007
	-44 -63 -3	L	10417	< 0.00001	optic tract	< 0.00001	0.039	0.0008	0.25	0.24	0.047	0.022
	-62 -43 -7	L	3303	< 0.00001	temporal lobe	0.0037	0.089	0.089	0.09	0.32	0.16	0.51
	62 -42 -9	R	2534	< 0.00001	temporal lobe	0.26	0.039	0.17	0.40	0.82	0.40	0.06
	19 25 -5	R	1360	< 0.00001	frontal lobe	0.022	0.14	0.03	0.046	0.33	0.96	0.96
RD												
	36 -14 -5	R	7531	< 0.00001	internal capsule	< 0.00001	0.003	0.0006	0.0062	0.12	0.018	0.005
	10 3 -4	R	3780	< 0.00001	cerebrum	0.0007	0.0005	0.025	0.069	0.15	0.017	0.46
	-3 18 14		3599	< 0.00001	cingulate cortex	0.016	0.32	0.053	0.19	0.39	0.17	0.023
	-27 -32 -7	L	2925	< 0.00001	internal capsule	< 0.00001	0.0032	0.0009	0.0027	0.33	0.024	0.028
	3 -26 26		2624	< 0.00001	CC	0.0001	0.012	0.011	0.0091	0.21	0.024	0.0022
	-40 20 -3	L	1845	< 0.00001	frontal lobe	0.018	0.028	0.052	0.34	0.61	0.34	0.025

Supplementary Table 2: Clusters of significant alterations of whole brain-based spatial statistics (WBSS) of PD patients vs controls for DTI metrics. Correlations of DTI-metrics within the alteration clusters and neuropsychological scores are provided as p-values (*correlation was positive for FA, and negative for AD, MD, RD, significant correlation ($p<0.01$, corrected) is marked in red). AD – axial diffusivity, MD – mean diffusivity, RD – radial diffusivity, CERAD – Consortium to Establish a Registry for Alzheimer's Disease, BNT – Boston naming test, CP – constructional praxis, VF – verbal fluency, WLD – word list discrimination, WLL – word list learning, WLR – word list recall.