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

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 χ²-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 $b0$-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 $b0$-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.
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.