Conclusions: Our findings reveal that fPDRP represents a replicable imaging marker across independent multicenter cohorts of IPD patients. These results provide further support for the stability of the fPDRP topography as well as the consistency of its relationship to motor symptoms across different patient populations.

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Diffusion tensor imaging changes in the corpus callosum and cognitive impairment in Parkinson's disease
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Objective: To evaluate diffusion characteristics of the corpus callosum in Parkinson's disease (PD) patients with varying degrees of cognitive impairment using Diffusion Tensor Imaging (DTI).
Background: The majority of PD patients eventually develop dementia (PDD), often preceded by a prodrome of mild cognitive impairment (PD-MCI). Prior studies have demonstrated volumetric and DTI changes in the corpus callosum in PD participants with cognitive impairment, but with limited information regarding the subregions of the callosum affected.
Methods: 75 PD and 24 healthy control (HC) participants received clinical and neuropsychological evaluation, MRI brain scans including DTI sequences with 26 non-collinear directions, and cognitive classification by Movement Disorder Society criteria (cognitively normal [PD-NC], n=23; PD-MCI, n=35; demented [PDD], n=17). Z-scores for cognitive domain performance (attention/working memory, executive function, memory, language, visuospatial function) were calculated. Diffusion weighted imaging volumes were pre-processed using FSL, including calculation of Fractional Anisotropy (FA), Mean Diffusivity (MD), Radial Diffusivity (RD), and Axial Diffusivity (AD) scalar values which were non-linearly registered to the IIT Brain Atlas mean-FA map (Varentsova, 2014). The callosum was divided into 5 parcellated segments (Hofer & Frahm, 2006). Scalar values of the 5 callosal segments were compared between PD and HC cohorts and among PD cognitive groups using MANCOVA models, covarying for age, sex, and PD duration. Regression analyses were performed on cognitive domain scores and callosal scalar values.
Results: PD participants showed increased AD values in the anterior 2/3rds of the corpus callosum compared to HCs. PDD participants had increased AD, MD, and RD values in the anterior 1/2 of the callosum compared to PD-NC and the anterior 1/6 of the callosum compared to PD-MCI participants. DTI scalar values and cognitive domain z-scores showed the strongest associations in the most anterior callosal region.
Conclusions: The corpus callosum appears to undergo white matter microstructural changes in PD. These changes may contribute to PD cognitive dysfunction due to altered information transfer among connected cortical areas.?

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A neuroimaging-based model for disease progression in Parkinson's disease
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Objective: We model the rate of disease progression over 4 years in subjects with Parkinson's disease based on neuroimaging features acquired at baseline.
Background: DaTSCAN is a radiotracer with high affinity for the presynaptic dopamine transporter (DAT) in the striatum. The putamen binding ratio (PBR) is the ratio of the tracer uptake between the putamen and the reference region (the occipital cortex). We use PBR data from 95 PD subjects from the PPMI database that have completed scans at baseline (year 0) and at years 1, 2 and 4. At baseline, PBR values were found to be significantly correlated with UPDRS motor score (Figure 1).
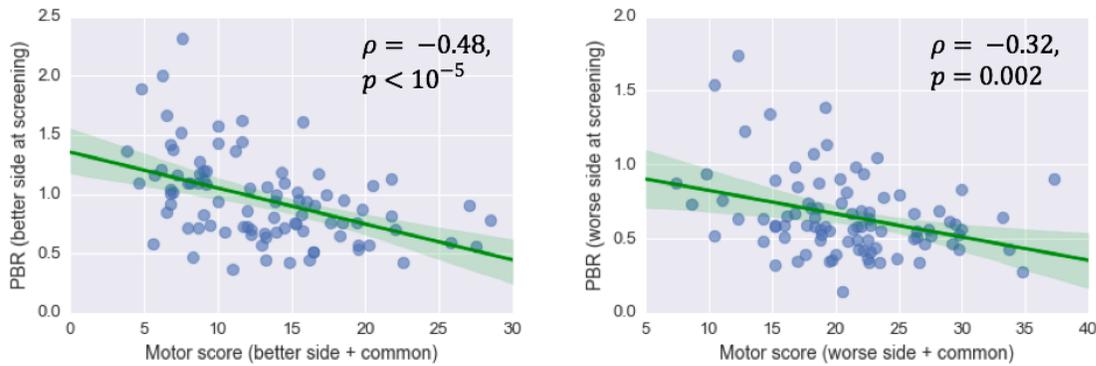
Figure 1. Cross-sectional correlation of the of the PBRs and the motor score (measured at baseline). The motor score is split into (better side + common) and (worse side + common) and correlated with the corresponding imaging side. The Spearman rho correlation was computed.

Methods: A hierarchical model is fitted to estimate the rate of progression as estimated by the change in PBR values. Our assumption is that the imaging data would contain relevant and objective information on disease progression as related to dopaminergic deficit. We identify the following image features, <u>all measured at baseline</u>: 1) PBR values for the more and less affected sides, 2) difference between the PBR values of the better and worse sides, and 3) difference between the putamen and caudate binding ratios (PBR – CBR). The model parameters were obtained in a training phase using a subset of the data. Next, the predicted yearly change of the PBR is estimated for each subject based on the baseline image features only and the estimated model parameters. This yearly change is used to predict the PBR at years 1, 2 and 4 (see Figure 2 for examples). The model is applied separately to the better and to the worse sides of the putamen. Cross-validation (5 folds) was used to estimate the error rate for year-4 PBR predictions.
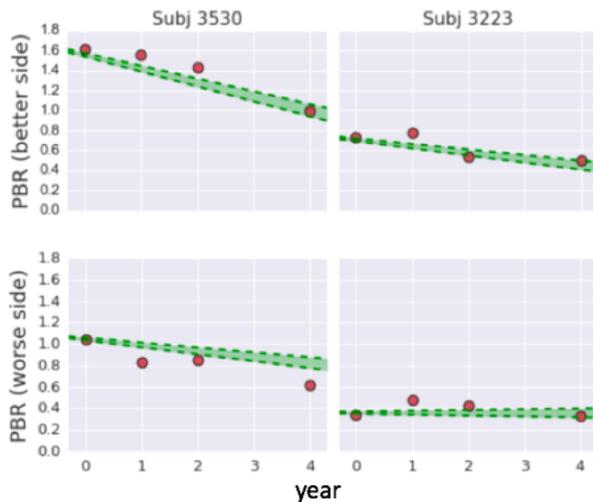
Figure 2. Examples of the measured PBR values (red points) and the predicted progression (green band) for two subjects in the study.

The model predicts the yearly change in PBR which is the slope of the green band in the figure. Only baseline imaging metrics are used to estimate the slope for the next 4 years.

Results: The median error for year-4 predictions is 18% for the better side and 24% for the worse side (Figure 3) and smaller errors were observed at years 1 and 2. The most important image feature for predicting the progression is the PBR value at baseline. The best predictor is obtained using the better side with the baseline PBR values ($p < 0.001$) and the PBR difference between the better and worse ($p < 0.01$). The (PBR – CBR) term is not significant.