Background: The Parkinson’s Progression marker initiative (PPMI; http://www.ppmi-info.org) is a multicenter longitudinal study that collects both MRI and 123-I Ioflupane SPECT. Several studies have shown diffusion tensor MRI (DTI) differences, specifically lower fractional anisotropy (FA), in cerebral or cerebellar white matter in PD patients in comparison to healthy controls (see Cruciger C and D’Esposito M, Neurology 2012; 80(1): 67-74 for a recent review). Whether these DTI differences are a consistent finding in large databases, and whether they reflect pathological changes related to PD, is not known. The 123-I Ioflupane SPECT striatal binding ratio (SBR) is an independent biomarker for the severity of striatal dopamine transporter depletion in Parkinson’s disease.

Objective: To compare FA, a DTI-based index of white matter microstructural integrity, to striatal binding ratio (SBR), a SPECT-based index of nigrostriatal projections, in Parkinson’s disease (PD) and control subjects.

Hypothesis: Lower SBR will be associated with lower FA in frontal and cerebellar white matter tracts.

METHODS: Data from 227 PPMI subjects (155 PD, 72 HC) with both SPECT (at screening) and DTI (at baseline) available as of March 2015 were analyzed. Preprocessed FA maps from the PPMI database, resampled to 1 mm T1 space, were first normalized in tract-based spatial statistics (Smith SM, Jenkinson M, Johansen-Berg H, et al. Neuroimage. 2006 Jul 15;32(3):1470-5); voxel-wise analyses were then conducted in SPM12 (http://www.fil.ion.ucl.ac.uk/spm).

• Initially, FA maps from the Parkinson’s and control groups (227 subjects) were compared in a regression model with covariates of group, age, and gender.

• To evaluate relationships between the striatal binding ratio (SBR) and FA in the Parkinson’s group (155 subjects), a regression model with the same covariates except group as well as a SPECT covariate (putamen SBR) was run. FA in several clusters (T = 4.2-4.3, n = 70-85; Figure 3A) in the left anterior thalamic radiation was related to higher Fa.

RESULTS: Age effect: Greater age was associated with diffusely lower FA throughout the central white matter (T = 4.10; Figure 1).

Group differences: Parkinson’s subjects had higher FA than control subjects in a cluster at the pons-midbrain junction (T = 4.43; MIN 10, -24, -23; Figure 2). There were no significant clusters in which the control group’s FA values exceeded those of Parkinson’s subjects.

Relationship between SBR and FA: Within the Parkinson’s group, lower minimum putamen SBR was related to higher FA in one cluster (T = 4.28, n = 77, MIN 29, -73, 14; Figure 3A) within the parieto-occipital white matter, and lower mean SBR was related to higher FA in several clusters (T = 4.2-4.3, n = 90.55; Figure 3B) in the left anterior thalamic radiation (cluster 1), superior (cluster 2), and genu/anterior body of corpus callosum (cluster 3).

CONCLUSIONS: Analysis of this multi-center data did not suggest that FA within major white matter tracts is lower in Parkinson’s patients; however, by restricting the analysis to regions of FA < 0.2, we excluded gray matter regions such as the substantia nigra. It is also possible that certain cognitive groups such as PD-dementia or PD-DLBD predict DTI differences in frontal white matter, but were not specifically evaluated for this abstract. Furthermore, the voxel-wise approach may lack sensitivity to differences in specific tracks, which can be better investigated in an a priori design.

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