Supplementary Files

Methodological details

In all subjects the following clinical features were recorded: presence of parkinsonism assessed by Hoehn and Yahr Staging and Unified Parkinson’s Disease Rating Scale Motor Section (UPDRS - part III; range 0-108) (1); functional ability at the time of investigation, assessed by the modified Rankin Scale (RS, range 0-6) (2); overall cognitive functioning, rated on Global Deterioration Scale (GDS; range 1-7) (3).

Brain MRI (1.5 T MRI system Symphony, Siemens) was performed in all subjects. Distribution of brain lesions was assessed by a semi-quantitative scale which assigns a score from 0 to 6 to each region (4). A total of 15 individual regions were scored separately, and the total score (range 0-90) was calculated as an index of overall severity of lesion load. MR images were also examined for abnormal signal intensities in the deep brain nuclei to calculate a basal ganglia score.

To investigate nigrostriatal function SPECT studies were performed 3 hours after IV injection of about 185 MBq of $^{[123]}$I-FP-CIT (DaTscan, GE Healthcare). The studies were processed using the Basal Ganglia Matching Tools ver. 2 software to obtain a semiquantitative striatal DAT uptake evaluation by measurement of (Caudate-Background)/Background and (Putamen-Background)/Background ratios, and left-to-right side uptake percent asymmetry $[100 \times (\text{Left-Right})/\frac{1}{2}(\text{Left+Right})]$. This method is operator-independent, based on 3D template of the striatum derived from Talairach and Tournoux’s anatomical atlas. The normal values (mean ± SD) obtained for caudate-to-background and putamen-to-background are: $4.21 \pm 0.67$ and $3.59 \pm 0.66$ (5). The software compared the proband patient vs. an Italian population of 96 normal subjects. Caudate and putamen background-normalized values for each patient were graphically plotted vs healthy subjects at two C.I. levels: 90% and 97%. Values below these levels were considered slightly or definitely abnormal (6). Finally, each study was scored according a visual scale (range: 0-3) specifically designed for vascular parkinsonism (7).
Myocardial $^{123}$I-meta-iodobenzylguanidine (MIBG) scintigraphy was performed in four patients with parkinsonism to investigate myocardial sympathetic denervation for differential diagnosis with idiopathic PD. $^{123}$I MIBG (AdreView, GE Healthcare, 185 MBq) was injected intravenously and two anterior planar studies of thorax were acquired after 10 minutes and after 4 hours. Regions of interest (ROI) were drawn over left heart ventricle (H) and mediastinum (M) and H/M ratios were calculated for early (H/M$_{10m}$) and late study (H/M$_{4h}$) (8). In our laboratory, we use a late ratio cut-off value <1.39 to suggest the diagnosis of a myocardial sympathetic impairment as found in idiopathic PD.

Analysis of MRI, $^{123}$I- FP-CIT SPECT, and $^{123}$I-MIBG scintigraphy was done by an investigator (AM for MRI, AB for molecular imaging studies) blinded to the patients’ clinical status in relation to parkinsonism.

All subjects gave their informed consent to participate in the present study according to the principles of the Declaration of Helsinki as revised in 2000. The study was approved by ethics committee.

References


Legend to Supplementary Figure.

Upper row. Axial brain MRI showing: multiple lacunae of the basal ganglia, more evident on the right pallidus and left caudate head on T2-weighted images in Case 1 (a); small basal ganglia lacunae and ischemic lesions of the left ventral thalamus and right globus pallidus on T2-weighted spin echo image in Case 2 (b); cortical infarct in the left temporo-occipital region and lacunae in the left pallidus and right thalamus on T2-weighted images in Case 3 (c); ischemic infarction of the right lentiform nucleus on T2-weighted spin echo images in Case 5 (d).

Lower row. [\(^{123}\)I]-FP-CIT showing: slight reduction of left putamen uptake in Case 1 (e); bilateral low putaminal uptake in Case 2 (f); bilaterally reduced uptake in the caudate and putamen in Case 3 (g); moderate low uptake at the right caudate and bilaterally reduced putaminal uptake in Case 5 (h).