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Diffusion tensor imaging differentiates vascular parkinsonism from parkinsonian syndromes of degenerative origin in elderly subjects

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ABSTRACT

Background and Purpose: The etiologic diagnosis of parkinsonian syndromes is of particular importance when considering syndromes of vascular or degenerative origin. The purpose of this study is to find differences in the white-matter architecture between those two groups in elderly patients.
Materials and Methods: Thirty-five patients were prospectively included (multiple-system atrophy, $n=5$; Parkinson's disease, $n=15$; progressive supranuclear palsy, $n=9$; vascular parkinsonism, $n=6$), with a mean age of 76 years. Patients with multiple-system atrophy, progressive supranuclear palsy and Parkinson's disease were grouped as having parkinsonian syndromes of degenerative origin. Brain MRIs included diffusion tensor imaging. Fractional anisotropy and mean-diffusivity maps were spatially normalized, and group analyses between parkinsonian syndromes of degenerative origin and vascular parkinsonism were performed using a voxel-based approach.
Results: Statistical parametric-mapping analysis of diffusion tensor imaging data showed decreased fractional anisotropy value in internal capsules bilaterally in patients with vascular parkinsonism compared to parkinsonian syndromes of degenerative origin ($p=0.001$) and showed a lower mean diffusivity in the white matter of the left superior parietal lobule ($p=0.01$).

Fractional anisotropy values were found decreased in the middle cerebellar peduncles in multiple-system atrophy compared to Parkinson's disease and progressive supranuclear palsy. The mean diffusivity was increased in those regions for these subgroups.
Conclusion: Clinically defined vascular parkinsonism was associated with decreased fractional anisotropy in the deep white matter (internal capsules) compared to parkinsonian syndromes of degenerative origin. These findings are consistent with previously published neuropathological data.

Abbreviations: DeP, Parkinsonian syndromes of degenerative origin; DTI, diffusion tensor imaging; FA, fractional anisotropy; FLAIR, fluid-attenuated inversion recovery; MD, mean diffusivity; MSA, multiple-system atrophy; PD, Parkinson's disease; PSP, progressive supranuclear palsy; VP, vascular parkinsonism; WM, white matter.

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1. Introduction

Parkinson's disease (PD) is the most common, but not the only, cause of parkinsonian syndromes. This diagnosis is specially challenging in elderly subjects due to the frequency in this population of other causes of parkinsonian syndromes [1], comorbidities and the heterogeneity of clinical expression and evolution. Other parkinsonian syndromes could be separated into degenerative, toxic or vascular syndromes and include progressive supranuclear palsy (PSP), parkinsonian multiple-system atrophy (MSA), corticobasal degeneration syndrome, dementia with Lewy's bodies, and secondary causes (i.e., toxic origins). Parkinsonian syndromes of degenerative origin (DeP) comprise PD, PSP and MSA. The differentiation of PD from other parkinsonian syndromes is of particular importance because their progression, prognosis and treatment might be very different. In elderly subjects, vascular parkinsonism (VP) may be diagnosed based on Zijlman's criteria. VP accounts for 4.4% to 12% of all cases of parkinsonism [2].

VP is typically associated with macroscopic infarcts in the basal ganglia or microscopic small-vessel disease, leading to changes in deep white matter (WM) [3].

Computerized tomography and MRI support the concept of VP [4], and neuroimaging changes appear to be correlated with changes seen on post-mortem examination [5].

There are no clear biomarkers for differential diagnosis between VP and DeP, and SPECT imaging [6] and conventional MRI are often insufficient, although MRI morphometric and volumetric studies of the brain seem promising [7]. Diffusion-weighted imaging and especially diffusion tensor imaging (DTI) permit the quantification of brain-water movements and allow a specific and indirect examination of structural changes in the WM. Diffusion tensor imaging is differently restricted in various tissues; in WM, for example, the directions of diffusion are more limited. Anisotropy represents the limited directionality of diffusion and is higher in WM than in the less organized gray matter. This difference allows the calculation of FA and MD values for the entire cerebral parenchyma and the generation of parametric maps. Fractional anisotropy (FA) ranges from 0 to 1, where 0 is isotropic diffusion (no directional organization) and 1 is anisotropic diffusion (well-organized tissues like WM). Mean diffusivity (MD) is a measure of the average molecular motion, independent of tissue directionality. It is modified by cellular size and integrity [8]. Applications of DTI have been increasing in recent years because it may help qualify and quantify structural changes in cerebral WM with greater sensitivity than the usual visual evaluation of WM hyperintensities used with conventional MRI data [9]. DTI parameters are altered in PD [10], and DTI may distinguish DePs [11,12]. Recent works also show that VP is associated with architectural abnormalities in WM that are visible via DTI [13].

To the best of our knowledge, DTI parameters have not been compared between VP and other DePs. The main goal of this study is to compare DTI-derived indices between elderly subjects with DeP and VP. In parallel, we will also investigate the use of DTI to distinguish between the different subgroups of DeP, comparing our findings to the published literature.

2. Materials and methods

2.1. Population

Forty-two patients with late-onset parkinsonian syndromes without dementia were prospectively recruited for this study, and each individual gave informed consent. Three patients were excluded because of an uncertain diagnosis. Thirty-nine patients (23 males/16 females; mean age 76 years, range 56–90 years) were included, but 3 could not continue with the MRI and the MRI data were not usable for one subject. We thus have a total of 35 subjects in the MRI study. Fig. 1 summarizes the study participation.

2.2. Clinical evaluation

Diagnoses were verified by a neurologist experienced with parkinsonian syndromes (C.G.) according to established guidelines: the UK Parkinson's Disease Society Brain Bank criteria for idiopathic PD, the National Institute of Neurological Disorders and Stroke (NINDS) and the Society for Progressive Supranuclear Palsy (SPSP) criteria for PSP, Gilman's criteria for MSA, and Zijlmans's criteria for VP.

All patients were examined within 2 months before the MRI exam. Clinical data included age, disease duration, and age at onset. Neurological impairment was assessed using the Hoehn and Yahr scale and MDS-UPDRS. No patient had a history of head injury, stroke, intra-cerebral bleeding, exposure to neuroleptic drugs before onset of symptoms, or psychiatric comorbidity.

According to the previously listed criteria, patients were classified in 4 subgroups: sixteen patients met the criteria for idiopathic PD (10 males/6 females; mean age 74.3 ± 7.8 y-o); 5 patients met the criteria for MSA (5 males; mean age 73 ± 7.6 y-o); 11 patients met the criteria for PSP (6 males/5 females; mean age 75.3 ± 4.2 y-o); and 7 patients met the criteria for VP (2 males/5 females; mean age 82.6 ± 5 years).

Because PD, MSA and PSP are of neurodegenerative etiology, i.e., are characterized by neuronal loss and brain atrophy, we grouped them as parkinsonian syndromes of degenerative origin to clearly differentiate them from parkinsonian syndromes of vascular origin.

2.3. Neuropsychological evaluation

Neuropsychological evaluation was performed to rule out dementia with Lewy bodies within 2 months before the MRI exam. The evaluation was composed of the Mattis Dementia-Rating Scale, the Grober and Buschke verbal-learning test, the Span Task, the Stroop Word-Color Test, the Trail-Making Test, the Rey-Osterrieth Complex-Figure Test and a semantic-processing task (LEXIS test). It also included the Frontal Assessment Battery, which estimates frontal subcortical-dysfunction syndrome, the Isaac test for verbal fluency and the clock-drawing test to assess visuospatial activities. Finally, educational attainment (EA) was recorded. Global cognitive evaluation was assessed using the Mini Mental-Status Examination.

2.4. MRI acquisitions

Brain MRIs were performed on a 1.5T magnet (Siemens Avanto, Erlangen, Germany). The acquisition protocol contained an anatomic 3D T1 weighted sequence, a fluid-attenuated inversion recovery (FLAIR) acquisition, susceptibility-weighted imaging (repetition time = 62 ms, echo time = 12.26 ms and 52.65 ms, flip angle = 15°, slice thickness = 2 mm) and a DTI acquisition (64 directions, 55 slices, thickness = 2.5 mm, repetition time = 6700 ms, echo time = 82 ms, number of excitations = 1, voxel: $2.5 \times 2.5 \times 2.5$ mm, b = 1000 s/mm^2).

2.5. Data analysis

2.5.1. Morphologic analysis

2.5.1.1. Susceptibility-weighted imaging analysis. One board-certified neuroradiologist (S.M.C.) independently counted the number of cerebral microbleeds on susceptibility-weighted imaging and was blinded to individual diagnoses. The total number of cerebral microbleeds was compared between groups (DeP and VP) and subgroups (PSP, MSA, DP and VP).