Brain Atrophy and White Matter Hyperintensities in Early Incident Parkinson Disease. A Large Case-Control Study.

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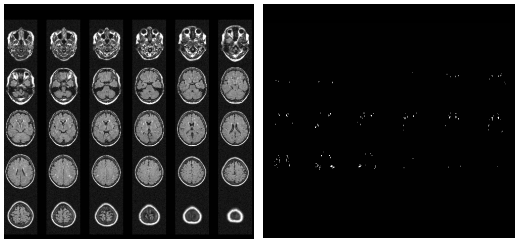
Overview. We wanted to examine the extent of whole brain, gray and white matter atrophy in a sample of early clinical Parkinson Disease (PD) patients compared to age-matched normal controls (NC). A secondary aim was to investigate the total volume of white matter hyperintensities (WMH) between groups and to further explore the relationship between cognition and WMH in PD.

Background. Previous magnetic resonance imaging (MRI) studies on PD have found gray matter atrophy in patients with advanced disease and linked this to cognitive dysfunction(1). The relationship between brain WMH and cognition is not yet clear(2). Therefore, we conducted the first study on atrophy and WMH in early incident PD and examined its impact on cognition.

Methods. The normalized brain and lateral ventricle volumes were calculated at baseline on 156 PD patients (age 65.8±9.2 years, disease duration 26.9±20.0 months) and 102 NC (age 65.6±9.4 years) on 3D-T1-WI using SIENAX software(3). The patients and NC were included in a multicenter (4 sites) prospective longitudinal study. For a well matched subgroup of 37 PD and 37 NC at one site, we also performed gray (neocortical and deep) and white matter segmentation analysis. WMH volume was calculated on axial fluid-attenuated inversion recovery (FLAIR) scans using a semi-automated method (Java Image software) on 156 PD and 99 NC. Correlation analysis and linear regression analysis were conducted to investigate the impact of different MRI variables on cognition as measured by the Mini Mental State Examination (MMSE).

Results. The analysis did not reveal significant differences between PD and NC controls in any MRI variables. A novel finding was the significant correlation between total WMH and the MMSE score found in PD (ρ=-.308 , $p< 0.0001$) but not in NC (ρ=-.035, p=0.658). The relationship in PD patients remained significant when partial correlation analysis, controlled for age, sex, cerebrovascular risk, depression, education and center (r= -.186, p=.023) was applied. Multiple linear regression, with the MMSE score as a dependent variable covariated for age, education, total WMH, depression score, presence of one or more cerebrovascular risk factors and center, retained WMH as a significant predictor, $p <0.0001$ and ß= -.272. This model predicted about 32% of the variance in the MMSE score.

Conclusions. We found no significant whole brain, gray or white matter atrophy in our cohort of recently diagnosed PD compared to age-matched NC. Our finding that WMH may predict the MMSE score in PD contributes to the ongoing discussion on possible causes of the cognitive impairment found in PD(4). Further studies on regional distribution of WMH in PD versus NC are needed in order to explore this further.



Axial FLAIR MRI, (left) shows white matter hyperintensities in PD female patient, 56 years of age and with 24 months of disease duration.
Lesion masks contoured with Java Image software are shown on the right. This patient had a total lesion load of 12,669 m3.

References:
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