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The biology of cognitive decline and reduced survival in Parkinson disease

Prognostic factors in a population-based cohort

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Akademisk avhandling

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Title
The biology of cognitive decline and reduced survival in Parkinson disease. Prognostic factors in a population-based cohort.

Abstract
Parkinson disease (PD) is a progressive neurodegenerative disease that affects about 1% of the population over 60 years. The cardinal symptoms are motor disabilities but cognitive decline is also common. About 50% of all persons with PD develop dementia within 10 years after disease onset. Dementia in PD account for high social costs and has large, negative effects on quality of life.
Aims. The aim of the study was to investigate clinical, neurobiological and genetic factors of importance for progression and for the prognosis in PD and parkinsonism. First, we aimed to describe mortality and risk factors for death, including possible associations with cognitive dysfunction, in patients with idiopathic parkinsonism. Second, we aimed to study if biomarkers in the cerebrospinal fluid (CSF) are useful for the diagnosis of different forms of idiopathic parkinsonism and prediction of cognitive decline in PD.
Methods. A population-based cohort consisting of patients with new-onset, idiopathic parkinsonism was studied prospectively. After screening in a catchment area of ~142 000 inhabitants in Sweden, 182 patients with parkinsonism were included. The patients were investigated comprehensively, including neuropsychological testing, multimodal neuroimaging and genetic and biosample analyses. During follow up, 143 patients were diagnosed with PD, 13 with multiple system atrophy (MSA), and 18 with progressive supranuclear palsy (PSP). A total of 109 patients died.
Results. Patients with MSA and PSP had the shortest life expectancy. PD patients who presented with normal cognitive function had a largely normal life expectancy. In contrast, the mortality was increased in PD patients with cognitive impairment, freezing of gait, hyposmia, and mildly elevated leukocytes in the CSF. Also of importance for the prognosis, patients with PD with an early CSF pattern of high Neurofilament light protein, low β-amyloid, and high heart fatty acid binding protein had an 11.8 times increased risk of developing PD dementia (95% CI 3.3-42.1, $p < 0.001$), compared with PD patients with a more ”normal” CSF pattern. Variation in genes associated with dopamine function was also associated with some effects on cognitive functions in PD.
Conclusions. PD subtypes, for instance the subtype characterized by cognitive decline, have distinguishing clinical, neurochemical and neurobiological traits, which are of importance for the prognosis and the survival. An early CSF analysis is useful for predicting cognitive decline. The finding of a low-grade immune reaction in the CSF of patients with PD may have clinical implications. In clinical practice, CSF biomarkers could be useful for improving diagnosis and prognostication.
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Keywords
Parkinson disease, multiple system atrophy, progressive supranuclear palsy, natural history, cognitive impairment, dementia, predictors of mortality, cerebrospinal fluid biomarkers, prospective, population-based.

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