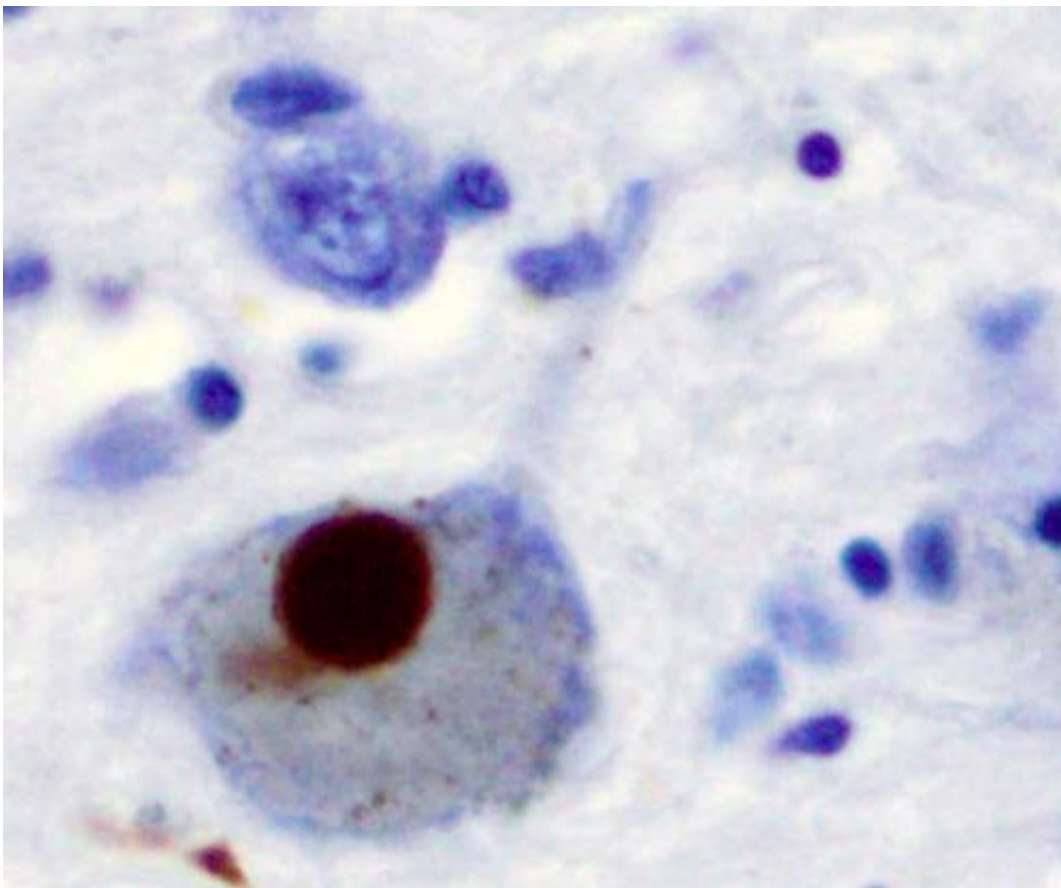


# Researchers identify biomarker for early cognitive decline in Parkinson's disease patients

February 17 2016

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Immunohistochemistry for alpha-synuclein showing positive staining (brown) of an intraneuronal Lewy-body in the Substantia nigra in Parkinson's disease. Credit: Wikipedia

Many patients with Parkinson's Disease (PD) develop mild cognitive impairment (MCI) or dementia. Identifying biomarkers for cognitive impairment could be instrumental in facilitating both early diagnosis of MCI and developing new cognitive-enhancing treatments. New research published in the *Journal of Parkinson's Disease* indicates that lower concentrations of  $\alpha$ -synuclein in cerebrospinal fluid (CSF) is associated with reduced performance on several cognitive tests.

"This is the largest study exploring the association between CSF biomarkers and cognition in PD, and one of few to explore if  $\alpha$ -synuclein is associated with [cognitive impairment](#)," explained lead investigator Ragnhild E. Skogseth, MD, of Haraldsplass Deaconess Hospital and the Department of Clinical Medicine, University of Bergen (Norway).

CSF markers beta-amyloid42 (abeta42), total tau protein (t-tau), phosphorylated tau protein (p-tau), and  $\alpha$ -synuclein reflect pathophysiological changes relevant to cognition in PD. If changes in these biomarkers can predict [cognitive decline](#), patients could be informed to seek possible treatments.

Part of the Parkinson's Progression Markers Initiative (PPMI), an international project focusing on development of biomarkers of progression in PD, this study was comprised of 414 patients with untreated PD without dementia and 196 health control (HC) subjects from 24 clinical sites worldwide. The patients were evaluated for multiple cognitive skills, including visuospatial functions, verbal memory, executive function, and attention. Patients were defined as having MCI (PD-MCI) if they showed impairment on two or more tests, while patients not fulfilling criteria for MCI were classified as having normal cognition (PD-NC). The Unified Parkinson's Disease Rating Score (UPDRS) was used to evaluate the progression of the disease in the PD patients.

The investigation determined that lower  $\alpha$ -synuclein was associated with reduced performance in cognition testing in the whole PD-group.

Abeta42 was significantly decreased in PD with [mild cognitive impairment](#) compared with controls, while values in PD without MCI were identical to the HC group controls.

After analyzing demographics and the results of CSF analysis, there were no significant differences in gender, age, or education between PD and HC patients. Among the PD patients, 140 PD-MCI subjects were significantly older, had less formal education, and had higher UPDRS scores than the 274 PD-NC subjects.

"The association between reduced CSF  $\alpha$ -synuclein concentrations and cognition suggests that  $\alpha$ -synuclein pathology contributes to early cognitive impairment in PD, in particular to executive-attentional dysfunction. Longitudinal analyses are needed to determine if this and other CSF biomarkers in early Parkinson's disease are associated with the risk of future cognitive decline and dementia," noted Dr. Skogseth.

"This is a very important study that not only gives insight into the mechanisms that might underlie cognitive decline in Parkinson's disease, but it might also represent the first steps in the development of a much needed biomarker that can predict which [patients](#) will develop dementia," commented Patrik Brundin, MD, PhD, Editor-in-Chief of the *Journal of Parkinson's Disease* and Director of the Center for Neurodegenerative Science at Van Andel Research Institute in Grand Rapids, MI.

**More information:** Ragnhild E. Skogseth et al. Associations between Cerebrospinal Fluid Biomarkers and Cognition in Early Untreated Parkinson's Disease, *Journal of Parkinson's Disease* (2015). [DOI: 10.3233/JPD-150682](#)

Provided by IOS Press

Citation: Researchers identify biomarker for early cognitive decline in Parkinson's disease patients (2016, February 17) retrieved 3 May 2024 from <https://medicalxpress.com/news/2016-02-biomarker-early-cognitive-decline-parkinson.html>

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