Blood proteins may help to track the pathological progression of Lewy body disease

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Early detection of Alzheimer's disease-related changes in Parkinson's disease and dementia with Lewy bodies could be made possible by monitoring the amyloid-β (Aβ) and phosphorylated tau (p-tau) proteins. Researchers at Nagoya University in Japan have also discovered that the blood levels of neurofilament light chain (NfL) protein are elevated at an early stage of Parkinson's disease (PD) and dementia with Lewy bodies (DLB). This discovery may provide a method to identify potential patients and to make early interventions. The findings were published in npj Parkinson's Disease.

The two forms of Lewy body disease are PD and DLB. Recent discoveries indicate that patients with these diseases share characteristics with Alzheimer's disease, including the presence of Aβ and p-tau proteins in the brain.

Recently, researchers have directed their attention toward the early stage of these diseases, called the prodromal stage. During the prodromal stage, abnormal protein buildup begins, leading to the eventual development of the disease about 10–20 years after the onset of motor and cognitive symptoms.

A research group led by Professor Masahisa Katsuno and Dr. Keita Hiraga from Nagoya University Graduate School of Medicine measured plasma biomarkers for Alzheimer's disease (Aβ and p-tau) and
neurodegeneration (NfL) in patients with PD and DLB, as well as high-risk individuals in the prodromal stage. The study was a collaboration with the National Center for Geriatrics and Gerontology and National Institutes for Quantum Science and Technology.

Changes in the expression of proteins Aβ and p-tau were observed in patients with PD dementia (PDD) and DLB, but not in those in the prodromal stage. On the other hand, both individuals in the prodromal stage and those suffering from the diseases exhibited elevated levels of NfL.

"These findings suggest that the proteins associated with comorbid Alzheimer's disease pathology in PDD and DLB are not present in the prodromal phase, but instead develop after the onset of the disease," Hiraga said. "On the other hand, neuronal damage caused by α-synuclein-induced neurodegeneration leads to the release of NfL in PD and DLB. Therefore, the elevation of NfL in high-risk individuals, despite the absence of increased Alzheimer's disease-related biomarkers, suggests that NfL may be used to detect α-synuclein-induced neurodegeneration, a key marker of disease, in the prodromal phase."

"In PD and DLB patients, Aβ and p-tau are not present in the prodromal stage before onset but rather appear after the disease has manifested," Katsuno added. "This chronological pattern is quite different from Alzheimer's disease, in which Aβ and p-tau start to deposit a few decades before the onset of dementia."

The team's findings indicate that anti-Aβ antibody treatments for early-stage Alzheimer's disease could be effective in treating Lewy body diseases.

"Our findings suggest that Aβ accumulation in PD and DLB may occur after disease onset," Hiraga said. "Recently, lecanemab, an anti-Aβ
antibody drug, was approved for early-stage Alzheimer's disease. This drug could also be effective against Alzheimer's pathology in PD and DLB.

**More information:** Plasma biomarkers of neurodegeneration in patients and high risk subjects with Lewy body disease, *npj Parkinson's Disease* (2024). DOI: [10.1038/s41531-024-00745-8](https://doi.org/10.1038/s41531-024-00745-8)

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