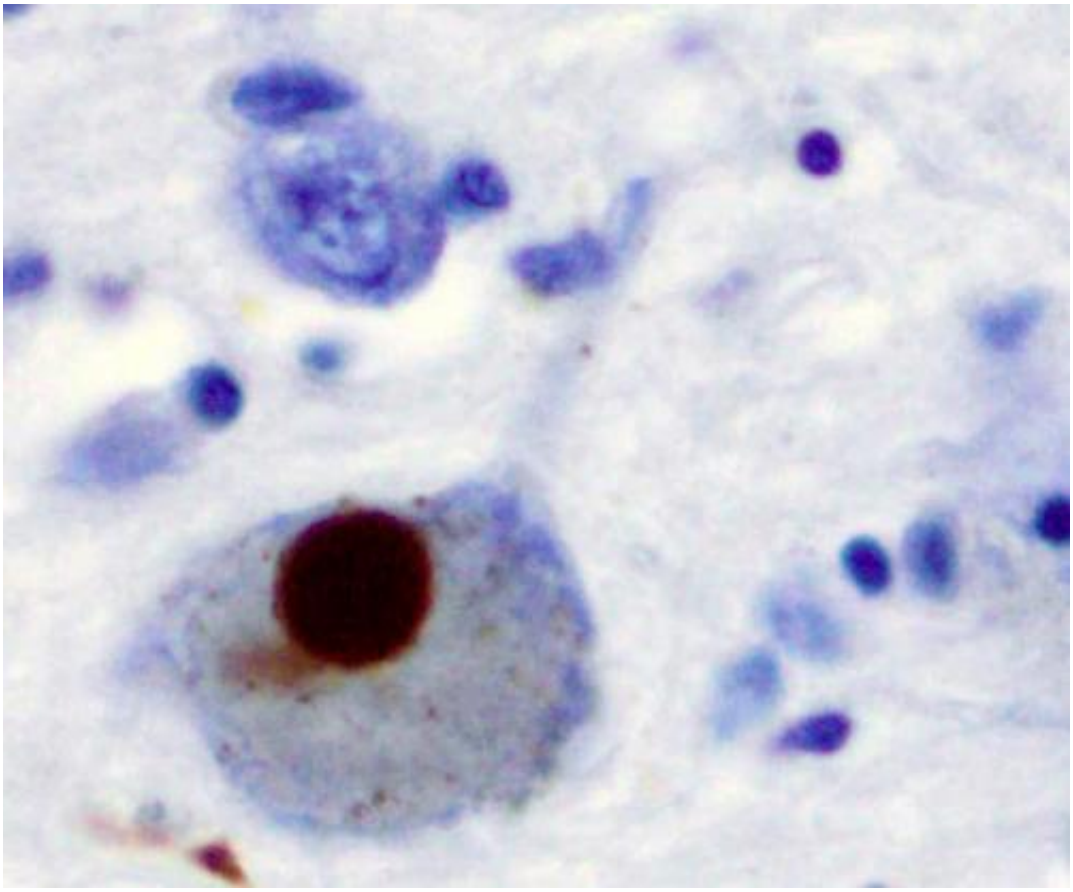
Experts propose revising the criteria for diagnosis of Parkinson's disease

February 5 2019



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

In the past 25 years it has become clear that some symptoms of

Parkinson's disease (PD) occur decades before the development of motor symptoms and clinical diagnosis, and that monitoring these emerging symptoms may provide important insights into the origin and development of the disease. Understanding this "prodromal" phase, along with the development of new treatments, may enable earlier treatment to prevent the disease from developing, according to experts writing in a supplement to the *Journal of Parkinson's Disease*.

PD is a slowly progressive disorder that affects movement, muscle control, and balance. "Brilliant work of many in different scientific fields has paved the way for the concept of prodromal PD; that is, a phase of years to decades in which non-motor and subtle motor symptoms may indicate spreading PD pathology, but do not meet the threshold for diagnosis according to the classic motor-based clinical criteria," explained authors Daniela Berg, MD, of the Department of Neurology, Christian-Albrechts-University of Kiel, Kiel, Germany, and Ronald B. Postuma, MD, MSc, of the Department of Neurology, Montreal General Hospital, Montreal, Canada.

The authors define the main anchors of the concept of the prodromal phase as:

- The broadly accepted fact that the neurodegenerative process in PD spreads slowly, possibly starting in the gut or olfactory system and finally encompassing much of the nervous system
- Increasing knowledge of risk factors and clinical symptoms that precede the typical motor manifestations by years to decades and can be correlated to imaging and histopathological findings
- Longitudinal studies that observed conversion to PD in groups of patients with different combinations of risk and prodromal markers

The authors and colleagues have constructed a mathematical model that

makes it possible to calculate an individual's personal risk of being in the prodromal phase of PD. As they point out, there are several limitations to this model, such as the time taken to conversion to PD, age and sex factors, and subtypes with undetectable prodromal stages. "The prodromal PD criteria are meant to be research criteria and constitute a first step in what should be a continually-updated process," noted the authors.

Biomarkers and wearable technology such as mobile phones are expected to play a role in greater accuracy of diagnosis in the prodromal phase. The goal of biomarker research, as well as quantitative motor assessment, is to use new data arising from objective measurements to enable earlier detection of the neurodegenerative process and possibly motor symptoms. It would also facilitate the development of neuroprotective trials in early stages.

Key questions that the authors hope to see resolved are: When is the starting point of PD? What will define the disease; will it still be motor symptoms (possibly typical subtle ones), or will it be biomarker evidence of nigrostriatal system neurodegeneration without motor symptoms? Will it be a certain combination of non-motor signs? Or will it be based upon non-clinical biomarkers, similar to changes in Alzheimer's disease?

By 2040, the authors hope that prodromal criteria will be incorporated into active neuroprotective treatment programs, allowing a program of population-based screening followed by early treatment and ultimately the prevention of clinical PD from ever becoming manifest.

"Our review highlights the importance of making an earlier diagnosis of neurodegenerative diseases, and in particular PD, for now primarily to understand the disease better," said Dr. Berg and Dr. Postuma. "However, in the future, once we have preventive therapy, it will become critical to find patients in the earliest stages of disease, so that we can

prevent the disease from developing and affecting quality of life."

"Today we somewhat artificially define the transition for the Parkinson prodrome into overt PD by the emergence of motor symptoms," commented Patrik Brundin, MD, Ph.D., Van Andel Research Institute, Grand Rapids, MI, USA, and J. William Langston, MD, Stanford Udall Center, Department of Pathology, Stanford University, Palo Alto, CA, USA, Editors-in-Chief of the *Journal of Parkinson's Disease*. "By 2040, these definitions will likely be revised, and we will understand the whole continuum of the disease process much better. This will open up therapies that are applied much earlier and hopefully can arrest the pathogenesis."

More information: Daniela Berg et al, From Prodromal to Overt Parkinson's Disease: Towards a New Definition in the Year 2040, *Journal of Parkinson's Disease* (2018). DOI: 10.3233/JPD-181457

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