# Parkinson's disease: early detection crucial, new therapy approaches on the horizon

*Detecting Parkinson's disease before non-reversible symptoms occur: New approaches to early detection are meant to ensure just that. They are based on detection of alpha-synuclein in the skin or intestines. New therapy approaches such as a potential "vaccination" could improve the prognosis of affected individuals in future. Prof Günther Deuschl, President of the European Academy of Neurology (EAN), summarized the latest findings in research on Parkinson's' disease.*

**Amsterdam, 24 June 2017** – New findings on the early detection and treatment of Parkinson's disease are being discussed at the 3rd Congress of the European Academy of Neurology (EAN) in Amsterdam. "We are getting closer to the big goal of being able to detect Parkinson's disease at a very early stage," said EAN President Prof Dr Günther Deuschl from University Hospital Schleswig-Holstein in Kiel. The diagnosis of Parkinson's disease is difficult particularly in the early phase of the disease (prodromal stage). Although complaints such as sleep disorders, loss of smell, bouts of depression or digestive disorders have been identified as possible early signs of Parkinson's disease, diagnosis today cannot be carried out with greater certainty until the typical movement disorders manifest themselves, such as tremors and slow, stiff movements. These symptoms are preceded by years of nerve cells dying off. About 80 per cent of the dopaminergic nerve endings and as many as 50 per cent of the nerve cells in the substantia nigra area of the brain are already destroyed by that stage. A therapy capable of stopping the disease from taking its course is no longer possible at that point in time. The pathological hallmark of Parkinson's disease is the deposit of pathologic alpha-synuclein in cells of the nervous system.

**Early detection with biopsies**

Different research groups have reported biopsies of the skin (Donadio *et al.*, 2016), submandibular glands (Adler *et al.*, 2016, Vilas *et al.*, 2016) and colon biopsies (Schneider *et al.*, 2016) showing such alpha synuclein at a very early stage of Parkinson's disease. A further major success in early detection was reported recently (Doppler *et al.*, 2017): Pathologic alpha synuclein was demonstrated in REM-sleep behavioural disorder, a condition which leads in about 85 per cent of the sufferers to Parkinson's disease with the aid of a skin test – and thus, this is many years before the onset of the typical movement disorders. The skin biopsy requires taking only a five millimetre large sample. Detection of pathological deposits of the protein alpha-synuclein in the fine nerve endings of the skin indicates the genesis of the disease.

It has long been known that a high percentage of people suffering from REM sleep behaviour disorders entailing aggressive dreams and violent movements while sleeping will contract Parkinson's within 15 to 20 years. The study has now been able to identify the biomarker alpha-synuclein in the skin of these patients at risk. Alpha-synuclein is also found in healthy individuals but is present in pathological clumped form in Parkinson's patients. That results in a malfunction of cell metabolism and ultimately in the degeneration of nerve cells. Prof

Deuschl: "The method has great potential for identifying patients for Parkinson's prevention studies and for winning them over to take part in clinical studies to test disease-modifying medications." In future, this diagnostic marker should be able to detect Parkinson's disease at an early stage also in individuals who do not have REM sleep behaviour disorders.

## Biomarkers detectable in intestines and salivary glands

However, this is not the only early detection method that is currently the subject of intensive research. Pathologic alpha-synuclein aggregations also form in the enteric nervous system, which consists of the myenteric plexus between the muscle layers of the intestinal wall and the submucous plexus. The protein accumulations in this area cannot be viewed automatically as diagnosis criterion for Parkinson's disease, however, because they also occur in healthy individuals. Prof Deuschl: "But if aggregations exhibit certain patterns, we can distinguish Parkinson's patients from healthy individuals with a refined morphometric analysis. Nonetheless, further studies are needed to prove that Parkinson's can be diagnosed by means of gastrointestinal biopsies." A Spanish study was also able to prove that alpha-synuclein deposits are detectable by means of a needle biopsy also in the submandibular salivary glands in patients with REM sleep behaviour disorders and thus with early signs of Parkinson's.

## New therapies for mitigation of symptoms

New therapeutic approaches rely on treating the disease already in its early stages and stopping nerve cells in the brain from dying off. In recent years, experts have gained an ever better understanding of how Parkinson's originates and how it spreads. Prof Deuschl: "Today we know that nerve cells sick from Parkinson's disease can 'infect' other nerve cells in a manner similar to prion diseases. The disease gradually spreads in this way throughout the entire nervous system." New therapy approaches are being developed based on this finding. Studies pursue the goal developing a "vaccine" against Parkinson's disease and rely on two different strategies in these efforts: Either stimulate the immune system to generate antibodies against alpha-synuclein or administer synthetic antibodies.

Another new therapy approach relies on binding larger quantities of iron. That is because oxidative stress in the cells also contributes to the development of Parkinson's disease. This in turn is caused by excessive amounts of iron in certain regions of the brain, which accelerate the demise of the cells.

## New definition of diagnostic criteria

One important advance in the early detection of Parkinson's disease is the new definition of diagnostic criteria for the prodromal stage, during which the classic diagnosis based on motor symptoms is not yet possible. To this end, the Movement Disorder Society drew on clinical studies and statistical studies to create a criteria list that is meant to standardise the clinical research and to facilitate diagnosis in the very early stage (Berg *et al.*, 2015). Prof Deuschl: "The new system for assessing the risk of Parkinson's disease consists of the age of the patient, environmental triggers such as smoking or caffeine consumption, genetic factors, the results of biomarker tests or prodromal symptoms such as constipation and loss of smell. This system can be expanded at any time if new tests are added for early detection – such as skin biopsies for example."

Parkinson's disease is second only to Alzheimer's as the most frequent neurodegenerative disease of the central nervous system. Parkinson's affects about two per cent of the population over age 65 and is one of the most common neurodegenerative diseases

throughout Europe with 1.2 million people suffering from it. Estimates indicate that the number of cases might at least double by 2030 due to ever longer life expectancy figures.

**Sources:** *Adler CH, Dugger BN, Hentz JG, Hinni ML, Lott DG, Driver-Dunckley E, et al. Peripheral Synucleinopathy in Early Parkinson's Disease: Submandibular Gland Needle Biopsy Findings. Mov Disord. 2016 Feb;31(2):250-6.*

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