Smell tests, biomarkers and colon biopsies—new approaches to early identification of Parkinson's disease

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Early diagnosis and starting treatment as early as possible are decisive factors in achieving improved quality of life for Parkinson's sufferers. Experts are discussing a wide range of new insights into the early stages of the disease at the Congress of the European Academy of Neurology in Copenhagen.

"New, neuroprotective or disease-modifying therapies against Parkinson's could be far more effective if administered at an early stage of the disease. Fortunately, we are increasingly able to decipher the mechanisms by which the condition develops thanks to the latest findings and methods, which enables us to identify persons at risk of developing Parkinson's early on," commented Prof Günther Deuschl of the University Medical Center Schleswig-Holstein in Kiel, and President of the European Academy of Neurology (EAN), at the second EAN Congress in Copenhagen. New insights into the early stages of Parkinson's are among the main topics under discussion at this major medical event.

EAN President Günther Deuschl underlined the growing importance of early recognition, particularly in light of current demographic trends: "Parkinson's disease affects around 2 percent of over-65s and is one of the most common neurodegenerative conditions in Europe, with about 1.2 million cases across the continent. In view of increasing life expectancy, the number of sufferers is expected to double by 2030."

Parkinson's is also highly significant in terms of disability-adjusted life years (DALYs), a measure of the number of years of life lost to illness and premature death. "In the EU, some 640,000 healthy years of life are being lost to this disease. Today, Parkinson's is ranked fifth in the list of the most expensive neurological conditions facing Europe's health systems. That makes it all the more important to devise innovative approaches that prevent the progression of the disease as effectively as possible," Prof Deuschl explained.

Keeping an eye open for risk markers – from impaired sense of smell to muscle weakness

The pathology of Parkinson's disease begins long before clinical diagnosis. More and more studies have shown that many symptoms appear several years prior to the identifiable degeneration of nerve cells and the onset of typical motor impairment. These include hyposmia, constipation, dizziness and urinary dysfunction. A special type of sleep disorder, known as REM-sleep behaviour disorder, is another such symptom. In healthy individuals, motor functions are inhibited during this phase of sleep, but sufferers of this condition actually physically enact their dreams.

"A long line of studies being presented at the EAN Congress confirm the existence of risk markers that are not necessarily associated with Parkinson's disease at first glance, and as such are easily missed," said Prof Deuschl. One of these studies, an analysis of 40 Parkinson's patients compiled by French researchers, shows that the respiratory function of those with the disease is significantly weaker than that of healthy individuals. It appears that in the early stages of the disease, the function of the muscles involved in breathing is impaired.

An Italian study also presented at the EAN Congress looked at the

olfactory performance of Parkinson's patients at an early, undiagnosed stage of the disease, and compared this with the sense of smell of a control group consisting of healthy people of the same age. The control group's stronger sense of smell may be the result of a better cortical connection to the caudate nucleus, a part of the basal ganglia that is involved in controlling voluntary movements. Researchers from Russia, who studied 104 patients, illustrated the prevalence of olfactory dysfunction among Parkinson's sufferers. Eight out of ten participants in the study had hyposmia, while almost one in five were anosmic and only two subjects had no impairment.

Biomarkers and intestinal biopsies as tools for early recognition

Risk markers are only one of the areas where researchers have gained new insights. It appears that alpha-synuclein, a protein, plays a decisive part in the progression of the disease. "Alpha-synuclein agglutination in the brain is a significant factor. It seems that this pattern of damage is passed on from cell to cell – so future therapies should be aimed at stopping or at least delaying this chain reaction," Prof Deuschl pointed out. There is increasing evidence that pathological changes occur not only in the brain, but also in other nerve cells, for instance in the intestines, and that they possibly "migrate" from there to the brain. Typical protein damage has also been found in skin cells and the salivary glands. "These findings are opening the door to new approaches for the early recognition and treatment of Parkinson's disease. Detailed research is under way to establish whether a biopsy of the nerves in the intestines, salivary glands or skin permits a conclusive early diagnosis of the condition," said Prof Deuschl.

More reliable estimate of the probability of developing Parkinson's

The definition of criteria for diagnosing Parkinson's in the prodromal phase of the condition – in other words, a very early stage when conventional clinical diagnosis based on motor symptoms is not possible – is a major step forward in terms of early recognition of the disease. "The criteria were recently published by the Movement Disorder Society. They are designed to standardise clinical research and provide diagnostic support," Prof Deuschl explained. "There are still no reliable tests for early diagnosis of Parkinson's, so doctors have had to rely on experience alone. But now we have developed a completely novel neurological approach that links clinical examinations and statistical calculations of probability." The starting point is the likelihood that an individual will develop the condition, based on their age. As much diagnostic information as possible is then collected and evaluated using a likelihood ratio. The information can include environmental risks such as smoking or caffeine consumption, genetic factors, the results of biomarker tests and prodromal symptoms such as constipation or olfactory dysfunction. This means that risk factors can be considered as either positive or negative influences. "The risk assessment system can be extended as required when new tests to support early diagnosis are developed," according to Prof Deuschl.

More information: G. Baille et al: Ventilatory disturbance in early Parkinson's disease: a prospective study; EAN 2016 Abstract

S. Marino et al: Resting state functional connectivity in olfactory network in de novo Parkinson's disease; EAN 2016 Abstract

M. Titova et al: Objective olfactory testing and self-assessment of olfactory function in patients with Parkinson's disease

R.B. Postuma et al: The new definition and diagnostic criteria of Parkinson's disease, in *The Lancet* Volume 15, No. 6, p546-548, May 2016

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