

PD BEGINS IN THE PERIPHERAL NERVOUS SYSTEM: YES

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Parkinson's disease (PD) follows a rather uniform pattern of progression. There are roughly 10% of all patients in Europe suffering from a genetically defined PD while the others have a so-called idiopathic Parkinson syndrome. These patients present with preclinical signs such as hyposmia, which is present in about 80-90% , REM sleep behavior disorder, constipation and depression. If there are more than one of these preclinical signs present in a person his risk to develop PD increases steadily. Only after years with just a preclinical sign patients develop a typical Parkinson syndrome, i.e. a movement disorder consisting of bradykinesia, rigidity, tremor and postural instability.

There is good evidence that Lewy bodies with α -synuclein pathology are present in the enteric nervous system before they can be found in the basal ganglia. A possible hypothesis for these findings of Braak and others is that an exogenous toxin or virus may be inhaled and swallowed and then start to cause abnormal α -synuclein accumulation in the enteric nervous system of the stomach and gut. In line with these neuroanatomical findings is the work by Shannon and others who demonstrated that patients with PD present with Lewy bodies in the colon which was shown by colon biopsies. In addition, this group could gain colon biopsies who presented with PD and had colonoscopy years before they developed motor symptoms. In these biopsies again Lewy bodies with abnormal α -synuclein could be found. In addition, our group could demonstrate that the application of rotenone via a tubing system to the gut could create in mice Lewy bodies and typical PD pathology via the vagal nerve to the brain. In summary there is ample evidence from post-mortem studies, from animal models and from clinical observations that PD begins in the gut.