

## Research on Parkinson's Pre-Motor Symptoms

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The aim of my research is to identify environmental factors that contribute to neurodegenerative diseases and aging, and to understand the natural history of debilitating neurodegenerative diseases. The ultimate goal is disease prevention and healthy aging. In pursuit of these goals, I have chosen to focus on Parkinson's disease (PD) – the second most prevalent neurodegenerative condition after Alzheimer's. My research has contributed to the documentation of a wide range of environmental (e.g. smoking, caffeine intake, exercise, pesticides, certain medications) and genetic (e.g. ~30 loci from recent GWAS analyses) risk factors for PD. PD may take decades to develop and to date all efforts to cure PD have failed. It is already too late to intervene at the time of PD motor/clinical onset; therefore, it is of ultimate importance to investigate the origins of the disease and to understand its early etiological process. I therefore recently shifted my research focus to a group of non-specific symptoms that may precede PD motor onset by years. These "pre-motor" symptoms include hyposmia, depression/anxiety, rapid eye movement sleep behavior disorder, excessive daytime sleepiness, and constipation. Accumulating evidence from clinical, epidemiological, and experimental research suggests that these symptoms may occur in the prodromal stage of PD. The Braak hypothesis further provides pathological underpinnings that these symptoms may be related to Lewy pathology in the brain and even in the periphery before the involvement of substantia nigra pars compacta. Therefore, research on pre-motor symptoms of PD may offer an excellent opportunity to characterize high-risk populations for PD and to better understand the origin and etiology of the disease. More importantly, such research may lead to evaluation of novel etiological hypotheses such as the possibility that environmental toxicants or viruses may initiate PD pathogenesis in the gastrointestinal tract or olfactory bulb. In this presentation, I will discuss my ongoing and future research on PD pre-motor symptoms and discuss potential gains and obstacles of research on PD pre-motor symptoms.