

## Parkinson's - Just another Infectious Disease

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### Abstract

Anatomic staging of PD progression suggests that an unidentified neurotropic pathogen in the intestinal lumen triggers abnormal synuclein aggregation that, in turn, initiates a "prion-like" process in the enteric nervous system (ENS) eventually achieving access to the central nervous system (CNS) via the vagus nerve (cranial nerve X). This protein aggregation, manifest as Lewy bodies, targets and destroys dopamine producing cells resulting in both the classic motor and non-motor symptoms of PD; with the non-motor symptoms predating the motor symptoms by years, or even decades.

### Commentary

Neuroscientists are turning - or shall we say returning - to the intestinal tract to study Parkinson's disease (PD). James Parkinson, in 1817, posed the following:

"Although unable to trace the connection by which a disordered state of the stomach and bowels may induce a morbid action in a part of the medulla spinalis, little hesitation need be employed before we determine on the probability of such occurrence" [1].

Anatomic staging of PD progression suggests that an unidentified neurotropic pathogen in the intestinal lumen triggers abnormal synuclein aggregation that, in turn, initiates a "prion-like" process in the enteric nervous system (ENS) eventually achieving access to the central nervous system (CNS) via the vagus nerve (cranial nerve X) [2-7]. This protein aggregation, manifest as Lewy bodies, targets and destroys dopamine producing cells resulting in both the classic motor and non-motor symptoms of PD [7,8]; with the non-motor symptoms predating the motor symptoms by years, or even decades [9].

Genetic studies reveal an association between (PD), leprosy and Crohn's disease and since discovered, these findings have been considered "surprising". Autophagy and ubiquitin-proteasome systems are cellular systems that both fight intracellular pathogens (xenophagy) and maintain cellular protein quality control. PD is a common neurodegenerative disease that manifests clinically as a profound movement disorder. The recognized genetic defects of PD create disruption of cellular homeostasis that result in protein folding abnormalities of PD called Lewy bodies. Those same genetic defects are associated with susceptibility to intracellular pathogens, including mycobacteria. It is now understood that PD Lewy body pathology starts in the enteric nervous system and "spreads" to the brain in a retrograde fashion via the vagus nerve [10].

An accurate early diagnostic test for Parkinson's disease (PD) is a critical unmet need [11]. Analysis of the ENS by routine colonoscopy biopsies is evolving as a tool for pre-mortem neuropathological diagnosis of PD, and also provides insight into the progression of motor and non-motor symptoms [12].

It seems that in PD something is perturbing the microbiome of the gut [13]. I have suggested a triggering role for *Mycobacterium avium* ss. *paratuberculosis* (MAP) [10]. It could be MAP and/or a host of other infectious/noxious precipitants of the protein cascade that results in PD, but the gut is a reasonable place to start; because when it comes to PD: what happens in the vagus does not stay in the vagus.

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