

The etiology of pd is predominantly genetic? No

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While we know, that more and more gene defects are related to PD it is also generally accepted that most patients do not suffer from a monogenetic form. This may be different in countries such as Israel and Northern Africa where many patients with PD present with a LRRK2 point mutation. In addition, there are reports that genetic abnormalities in the glucocerebrosidase (*GBA*) gene are important and common risk factors for Parkinson's disease and related disorders. Hypotheses proposed to explain this association include a gain-of-function due to mutations in glucocerebrosidase that promotes α -synuclein aggregation; substrate accumulation due to enzymatic loss-of-function, which affects α -synuclein processing and clearance; and a bidirectional feedback loop. But even if this is true, it is obvious that the majority of patients do not present with such genetic abnormalities. We and others could demonstrate in animal models that the exposure to toxins such as rotenone induce PD pathology and phenomenology. The most often used PD model, the MPTP-model also uses a toxin to destroy dopaminergic cells and from environmental medicine we know that farmers in Iowa and California who use herbicides and pesticides and drink their own dwelled water have a considerably higher incidence of PD. Finally patients who were exposed to manganese and carbon monoxide also develop PD. Since the pathology, i.e. accumulation of abnormal alpha-synuclein starts in the olfactory bulb and the enteric nervous system in the gut, it is intriguing to speculate that some substances from the environment may cause the initiation of this alpha-synuclein pathology. If this is true, it has to be discussed why not everybody develops PD. For this it is important to consider that there seem to be genetic patterns, but not monogenetic abnormalities, that may make patients prone to develop PD when they are exposed to toxins or other substances from the environment. Taken together, there seems to be a link between genetic and environmental factors that may explain the so-called idiopathic Parkinson syndrome.