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Parkinson's Disease: Cause and Therapy

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Description

Parkinson's disease (PD) is a neurodegenerative disease marked by the presence of Lewy bodies in the midbrain and the loss of dopaminergic neuron function, especially in the substantia nigra. Patients with PD have tremor, rigidity, postural alterations, and a decrease in spontaneous movements; hence, it is classed as a movement disorder. Prior to the diagnosis of PD, comorbidities such as anxiety, sadness, exhaustion, and sleep difficulties are recognised. The most important risk factor for Parkinson's disease is age, but sex also plays a role, with men being disproportionately afflicted. A number of studies have found that both known and unknown environmental factors can increase the risk of Parkinson's disease. Pesticide exposure, well water consumption, and head injury, as well as premotor symptoms such as constipation and depression, have all been linked to an increased risk of Parkinson's disease, while other factors such as tobacco, coffee, and alcohol consumption have controversially shown possible protective associations with the disease. Idiopathic PD has a complicated aetiology, with polygenic inheritance, environmental exposures, and gene–environment interactions all playing a role. Despite the fact that monogenic, inherited forms of PD are uncommon, accounting for just about 5% to 10% of all cases, 20% of individuals with PD have at least one affected first- or second-degree relative. More than 20 years after the discovery of a-synuclein gene mutations and multiplications as a cause of PD, extensive study and the identification of several genes connected to PD pathogenesis have followed [1,2].

Development of pd

The loss of dopaminergic neurons in the substantia nigra and basal ganglia causes Parkinson's disease. Tremor, postural instability, muscle rigidity, and slowness of movement are the four major symptoms. Subtypes of Parkinson's disease are not well defined, however they are classified according to their severity levels. The degrees of PD progression are described as mild PD, moderate PD, and advanced PD. Mutations in the LRRK2 (leucine-rich repeat kinase 2), PARK7 (Parkinsonism Associated Deglycase), PRKN (Parkin RBR E3 Ubiquitin Protein Ligase), PINK1 (PTENinduced putative kinase 1), or SNCA (alpha-synuclein) genes have been linked to an increased risk of Parkinson's disease. GBA (glucocerebrosidase) and UCHL1 (Ubiquitin C-Terminal Hydrolase L1) are thought to affect the likelihood of PD progression in some families.

Targeting a-Synuclein as a therapeutic

The presence of aggregated a-synuclein in specific brain regions is a characteristic of Parkinson's disease, suggesting that this protein plays a key role in the sporadic disease. Asynuclein is involved in the control of neurotransmitter release from presynaptic terminals in neurons. Familial PD is caused by mutations and multiplications in the SNCA gene. Aggregation and Lewy body disease originate from the production of synuclein oligomers and fibrils that are not efficiently removed by lysosomal or ubiquitin proteasome mechanisms. Before going into detail about the various techniques, it is important to note that medicines aimed at inhibiting a-synuclein aggregation and spread have significant hurdles. To begin with, there is no naturally occurring animal model of a-synucleinopathy in humans. As a result, preclinical testing of a-synuclein-targeting medicines is limited to animals that are at best comparable to human conditions [3,4]. A second key issue is that there is currently no defined way for assessing target engagement in the brain for a-synuclein-targeting treatments. It's unclear whether species of a-synuclein aggregates is pathogenic and causes dementia, therefore it's unclear whether lowering the development of oligomers or fibrils, or even reducing the availability of monomeric building blocks of the aggregates, is adequate. Third, imaging the severity of a-synuclein pathology in patient brains is currently impossible, and there is currently no biofluid-based biomarker that can assess the level of a-synuclein pathology in patient brains.

Reducing a-Synuclein Production: Several methods for reducing a-synuclein expression in the substantia nigra employing viral vector-mediated generation of short interfering RNA against a-synuclein have been effectively evaluated in animal models. In mouse investigations, antisense oligonucleotides that increase Ribonuclease H-mediated degradation of asynuclein messenger RNA were found to safely lower levels of a-synuclein message and protein while also protecting nigral dopaminergic neurons [4].

Aggregation inhibitors: Intrabodies are minute pieces of antibodies that can penetrate cells and range in size from 140 to 250 amino acids. They can be made to bind monomeric a-synuclein and prevent it from oligomerizing. In mice with viral vector-mediated asynuclein overexpression, intrabodies have been found to diminish a-synuclein aggregation and nigral neurodegeneration.

Autophagy enhancers: The activity of the mammalian target of rapamycin, which inhibits autophagy when activated by phosphorylation, is a critical predictor of autophagic pathway activity. In model systems, inhibitors of the mammalian target of rapamycin, such as rapamycin, have been demonstrated to improve autophagy and reduce a-synuclein disease.

Targeting the GBA pathway as a therapeutic approach

Glucosylceramide is converted to ceramide and glucose by GBA, a lysosomal hydrolase. Gaucher disease is caused by a lack of GBA, which leads to the buildup of undegraded substrates. Heterozygous GBA mutations increase the likelihood of developing PD and other synucleinopathies, whereas homozygous or compound heterozygous GBA mutations cause Gaucher disease. GBA mutations are the most common genetic risk factor for Parkinson's disease that has been identified to far, with 7 percent to 10% of PD patients possessing one of the approximately 300 GBA mutations. The primary obstacle to GBA-related therapies is a lack of knowledge about the precise processes through which GBA mutations enhance the risk of synucleinopathies and speed disease progression. A picture is starting to emerge, which is significant [4,5].

Increasing the activity of glucocerebrosidase (GCase): GBA-mediated loss of function generates an aberrant glycosphingolipid environment, which leads to cellular protein mishandling (proteinopathy) and neuronal dysfunction, according to the current leading hypothesis. GBA augmentation with adeno-associated virus 1 restored cognitive impairments in a mouse type of Gaucher-related synucleinopathy and lowered a-synuclein in an A53T-SNCA animal model, according to preclinical investigations. Clinical translation of the therapeutic benefit would necessitate a significant increase in GCase activity in the CNS. Prior to the development of GBA gene therapy for GBA-related PD, more research into the best serotype, delivery route, and brain distribution to crucial brain regions is needed.

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Conflict of Interest

The authors reported no potential conflict of interest.

References

1. Bhat, Shreya, U. Rajendra Acharya, Yuki Hagiwara and Nahid Dadmehr, et al. "Parkinson's disease: Cause factors, measurable indicators, and early diagnosis." *Com Bio Med* 102 (2018): 234-241.
2. Baiano, Chiara, Paolo Barone, Luigi Trojano and Gabriella Santangelo. "Prevalence and clinical aspects of mild cognitive impairment in Parkinson's disease: A meta-analysis." *Mov Disorder* 35 (2020): 45-54.
3. Gelders, Géraldine, Veerle Baekelandt, and Anke Van Der Perren. "Linking neuroinflammation and neurodegeneration in Parkinson's disease." *J Immunol Res* 20 (2018).
4. Zahoor, Insha, Amrina Shafi and Ehtishamul Haq. "Pharmacological treatment of Parkinson's disease." Exon Publications (2018): 129-144.
5. Monzio Compagnoni, Giacomo, Alessio Di Fonzo, Stefania Corti and Giacomo P. Comi, et al. "The role of mitochondria in neurodegenerative diseases: The lesson from Alzheimer's disease and Parkinson's disease." *Mol Neurobiol* 7 (2020): 2959-2980.

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