Original Article

Advancement of biomolecular engineering in Parkinson disease

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Abstract

Parkinson's Condition (PD) is the second most common degenerative neurological disease, affecting 10 million people globally. Nigrostriatal degeneration is linked to decreased motor and non-motor functioning in this chronic illness. Resting tremor, stiffness, akinesia (or bradykinesia), and postural instability are the four cardinal symptoms of Parkinson's disease. Because the symptoms of Parkinson's disease are similar to those of other age-related disorders like SWEDD (scans without evidence of dopaminergic deficit), essential tremors, and Parkinson's disease, early diagnosis is difficult. A synucleinopathy is Parkinson's disease (PD) with Lewy Bodies (DLB).

Although both genetic and environmental variables are assumed to play a role in Parkinson's disease (PD), there was no direct evidence to support either as a causal component until recently. Six distinct genes have been discovered as producing familial PD in the last eight years. They back up the idea that similar pathogenetic pathways exist across the spectrum of Parkinson's disease etiologies. Mutations in α-synuclein, parkin, UCHL1, DJ1, PINK1, and LRRK2 cause.

Parkinson's disease, which is inherited in a Mendelian form. Overexpression of α- synuclein and parkin causes mitochondrial issues, but DJ1 and PINK1 are mitochondrial proteins. These same proteins regulate proteasomal function and play a role in the oxidative stress response.

Doped carbon nanotubes, especially phosphorus-doped carbon nanotubes, can efficiently prevent the formation of α- synuclein amyloid, suggesting that they could be utilized to treat Parkinson's disease. More in vitro and clinical research is, however, necessary. As previously stated, αsynuclein could be a therapeutic target for Parkinson's disease and other synucleinopathies. The most promising option would be small chemicals that may modify the structure of protofibrillar forms of α-synuclein and render them nonpathogenic. Given the pathogenic consequences of αsynuclein's feed-forward amplification loops, a range of therapeutic options will almost certainly be required.

Keywords: Parkinson diseases, α- synuclein.

INTRODUCTION

According to Politis (2014), Parkinson's Disease (PD) is the second most common progressive neurodegenerative condition, affecting 10 million individuals globally. Nigrostriatal degeneration is linked to impaired motor and non-motor functioning in this chronic disease (1) (2). Tremor at rest, Rigidity, Akinesia (or bradykinesia), and Postural instability are the four cardinal signs of Parkinson's disease (3). It's difficult to diagnose Parkinson's disease early on because either patients don't have these key symptoms or the symptoms are similar to those of other age-related disorders like SWEDD (scans without evidence of dopaminergic deficit) (4) (5) , essential tremors, and Parkinson's disease.

Synucleinopathies, such as Parkinson's disease (PD) with Lewy Bodies (DLB), are caused by human-synuclein, which is the causal protein in various neurodegenerative illnesses (5). αSynuclein is a naturally unfolded protein with unclear function that is abundant in central nervous system neurons. The fact that synuclein is the predominant fibrillar protein component of Lewy Bodies (LBs) in both sporadic and familial PD strongly supports its causal role in PD development. It is also reinforced by the fact that three separate α-synuclein missense mutations (A30P, A53T, and E46K), as well as the duplication and triplication of its locus, induce autosomal-dominant PD

ETIOLOGY

Although both hereditary and environmental variables are assumed to have a role in the aetiology of Parkinson's disease (PD), there has been no direct evidence to support either as a causal factor until recently. Six distinct genes have been discovered as producing familial PD in the last eight years. They back up the idea that common pathogenetic processes exist across the etiologic spectrum of Parkinson's disease. Specifically, mutations in -synuclein, parkin, UCHL1, DJ1, PINK1, and LRRK2 cause Parkinson's disease, which is inherited in a Mendelian fashion. Overexpression of -synuclein and parkin causes mitochondrial abnormalities, while DJ1 and PINK1 are mitochondrial proteins. These same proteins are implicated in the oxidative stress response and have an impact on proteasomal function. Environmental influences, on the other hand, have received little attention. Those toxins, however, are still present.(6)

PATHOPHYSIOLOGY

Parkinson's disease (PD) is a movement disorder caused by the loss of dopaminergic neurons in the substantia nigra. Although the cause of Parkinson's disease is unknown, recent discoveries of genes linked to rare monogenic forms of the disease, in combination with previous research and new experimental animal models, have provided important and novel insights into the molecular pathways involved in disease pathogenesis. Increasing evidence suggests that mitochondrial dysfunction, oxidative and nitrosative stress, the accumulation of aberrant or misfolded proteins, and ubiquitin- proteasome system dysfunction are the main molecular pathways or events underlying the pathogenesis of both sporadic and familial forms of PD.(7)

METHODOLOGY

This review paper was mostly based on the PubMed, Scopus, and Web of Science databases, which were utilised to search for publications addressing Parkinson disease, biomolecular engineering using regular keywords. The search yielded a number of documents, including editorials, review articles, free full texts, and abstracts. After a thorough review, pertinent articles and their references were used to perform a search for other publications.

The following criteria were used to choose these review articles: English language publication, articles published within the last ten years, human subjects and observational research, including review articles. The content of these books was prioritised over their location while selecting them. Articles, on the other hand, were exempted because they were written in a language other than English, had been published for more than ten years, were non-human studies, or were metaanalyses or case series.

Parkinson disease, α-synuclein, biomolecular engineering in Parkinson disease.

DISCUSSION

1. The accumulation of α-synuclein proteins in the brain, including amyloids and Lewy bodies, is one of the fundamental causes of Parkinson's disease. The goal of this research is to see if doped carbon nanotubes (CNTs) can prevent amyloid aggregation. Materials and procedures: The influence of CNTs doped with phosphorus, nitrogen, and bromine and nitrogen on the development of α-synuclein amyloid was simulated using molecular dynamics methods. The CNTs interacted strongly with α-synuclein, with the phosphorusdoped CNTs showing the most significant interactions. Conclusion: Doped- CNTs, particularly phosphorus- doped carbon nanotubes, can successfully suppress the development of α-synuclein amyloid, and hence could be considered as a potential Parkinson's disease treatment. However, additional in vitro and clinical research is required.(8-25)

2. α-Synuclein is a presynaptic neuronal protein that has been associated to Parkinson's disease both genetically and neuropathologically (PD). α- Synuclein may play a role in PD pathogenesis in a variety of ways, but it is widely assumed that its abnormal soluble oligomeric conformations, known as protofibrils, are the toxic species that disrupt cellular homeostasis and cause neuronal death by affecting intracellular targets such as synaptic function. Furthermore, secreted α-synuclein may have harmful consequences on nearby cells, such as seeding aggregation, perhaps contributing to disease development. Although it is unclear if α-synuclein is implicated in all cases of PD, addressing the protein's harmful effects when it is dysregulated could lead to novel therapeutic options not only for PD but also for other neurodegenerative diseases. As can be

seen from the foregoing, α-synuclein is a viable therapeutic target in PD and possibly other synucleinopathies. Small compounds with the capacity to change the structure of protofibrillar forms of α-synuclein and render them nonpathogenic would be the most promising option. The green tea derivative EGCG (9) or the natural substance scyllo inositol are two examples of such natural compounds(10).Given the feed- forward amplification loops involved in the pathogenic effects of α- synuclein, it's possible that numerous treatment approaches will be required (26-37).

CONCLUSION

Doped carbon nanotubes, particularly phosphorus-doped carbon nanotubes, can effectively restrict the development of α-synuclein amyloid, suggesting that they could be used as a Parkinson's disease treatment. However, more in vitro and clinical research is required. As seen above, αsynuclein is a possible therapeutic target for Parkinson's disease and possibly other synucleinopathies. Small compounds that could affect the structure of protofibrillar forms of αsynuclein and render them nonpathogenic would be the most promising alternative. Given the pathogenic implications of α-synuclein's feed-forward amplification loops, a variety of treatment approaches are likely to be necessary.

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