Approaches to multi-target treatment of Parkinson's and Alzheimer's disease

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ABSTRACT

Parkinson's Disease (PD), often known as Parkinson's disease, is a chronic degenerative condition of the central nervous system that primarily affects the motor system. Non-motor symptoms normally appear gradually, and as the disease progresses, they become more prevalent. Tremors, stiffness, slowness of movement, and trouble walking are the most noticeable early signs. Many patients with Parkinson's disease experience despair, anxiety, and apathy, which can lead to cognitive and behavioral issues. Parkinson's disease dementia grows prevalent as the condition progresses. Parkinson's patients may also experience issues with their sleep and sensory systems. The disease's motor symptoms are caused by the loss of ce--lls in the substantia nigra, a part of the midbrain, resulting in a dopamine shortage. Alzheimer's Disease (AD) is a neurological illness that often begins slowly and progresses over time. It is the root cause of 60–70% of dementia cases. The most frequent initial symptom is trouble recalling recent events. Language impairments, disorientation (including easily getting lost), mood changes, loss of motivation, self-neglect, and behavioral concerns can all occur as the condition progresses. As a person's health deteriorates, they frequently retreat from family and society. Body functions gradually deteriorate, eventually leading to death. Although the rate of progression varies, the average life expectancy after diagnosis is three to nine years.

Key Words: *Tremors; Stiffness.*

LETTER

Alzheimer's Disease (AD) and Parkinson's Disease (PD) are the most prevalent neurodegenerative illnesses and are incurable. C--urrent treatments for Alzheimer's and Parkinson's disease are primarily symptomatic, whereas a new effective pathogenesis-relevant medication that would stop the illness's progression and restore all lost capabilities is needed. The pathogeneses of Alzheimer's disease and Parkinson's disease are mostly connected with the buildup of neurotoxic protein aggregates in the brain, such as toxic forms of amyloid-beta (A), alpha-synuclein, and tau protein. As a result, boosting pathogenic protein removal has gained popularity. The FDA authorized Aducanumab in June 2021, based on a monoclonal antibody against amyloid. The introduction of this medicine into general clinical practice, on the other hand, causes some suspicion, owing to the uncertainty of the therapeutic impact or clinical benefit. There is also worry about directly targeting amyloid or alpha-synuclein because both are important in regular physiological function and so their content should not go below the crucial threshold. Failure of clinical trials of "A-oriented" medications may also be connected to their usage in the late stages of AD, although these treatments may be helpful when pathological aggregation of A occurs 10–20 years before the first indications of cognitive impairment in patients.

Furthermore, neurodegenerative disorders have a multifactorial aetiology and involve a variety of pathological processes, in addition to protein aggregate neurotoxicity, such as oxidative stress, neuro-inflammatory response, disturbed neurotrophic function and neurogenesis, synaptic and neurotransmission dysfunction, ion disbalance, and so on, which frequently interact and overlap. As a result, researchers create multifunctional medication combinations, Combination-Drugs-Multi-Targets, CDMT that have no negative side effects. A fresh trend seen as a potential technique for AD and PD therapy is multipurpose therapy directed targeting many major pathogenic hubs. Several research teams are now working on the CDMT approach. A recent Japanese study, for example, reported on the prevention of neurodegenerative dementia in mice using an intranasal rifampicin and resveratrol combo. A series of studies revealed that the antibiotic drug ceftriaxone, when used in a drug reprofiling strategy, has neuroprotective effects in both AD and PD models by suppressing glutamate-induced excitotoxicity, modulating the expression of genes related to A metabolism, enhancing neurogenesis, attenuating neuro-inflammatory response, and restoring neuronal density. Furthermore, combining ceftriaxone with erythropoietin allowed for a 20-fold reduction in ceftriaxone dose while maintaining efficacy in a Parkinson's disease animal. The goal of this article was to offer a current review of the multi- targeted th-

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-erapeutic strategy for AD and PD, as well as associated concerns. Several research groups presented fascinating points of view on this issue and shed light on critical contemporary facets of the situation. One of them masterfully presented the Topic's major issue by providing an accurate assessment of acylated ghrelin as a multi-targeted treatment for AD and PD. The review demonstrates the acylated version of the hormone ghrelin's broad neuroprotective characteristics and explores its potential to mitigate pathologic alterations in AD and PD, as well as the risks of long-term therapy with the medicine. We have published a paper in which we address the numerous neuroprotective benefits of the antibiotic ceftriaxone against AD-like pathology, with a particular emphasis on pathways associated to A load and neuro-inflammatory response. evaluated the detrimental function of inflammation in ageing, insulin resistance in the brain, and their interactions in ageing and neurodegeneration

The article summarizes current knowledge on immunosenescence, inflamm-aging, and metainflammation, as well as potential mechanisms of calorie restriction as a multi-purpose approach that may effectively break the vicious cycle of metainflammation, improve insulin resistance, and delay the onset of neurodegeneration. The majority of Parkinson's disease research has been on processes and targets in the central nervous system. In clinical practice, neuromodulation methods such as Deep Brain Stimulation (DBS) are used to treat drug-resistant Parkinson's disease symptoms.

They have presented a technique of bilateral Globus Pallidus Interna (GPi) combined with Subthalamic Nucleus (STN) variable frequency DBS implantation in a case report. The treatment of dystonia disorders with multi-electrode and multi-target stimulation is investigated in the instance of a young-onset Parkinson's disease patient with refractory dyskinesia.