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Investigating The Function of Micrornas in Parkinson's Disease-Related Neuroinflammation and Oxidative Stress: Mechanisms and Therapeutic Consequences

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Abstract

The progressive loss of dopaminergic neurons in the substantia nigra is the hallmark of Parkinson's disease (PD), a neurodegenerative condition that impairs motor and cognitive function. Recent studies demonstrate the crucial role that neuroinflammation plays in aggravating neuronal degeneration in Parkinson's disease (PD), which is mediated by activated microglia and astrocytes. Although microglia and astrocytes play a crucial role in preserving the homeostasis of the central nervous system (CNS), their activation in response to pathogenic stimuli, such as oxidative stress and alpha-synuclein aggregation, results in a complicated interaction between neuroprotective and neurotoxic effects. To lessen damage, activated glial cells first remove debris and produce anti-inflammatory cytokines. On the other hand, persistent activation leads to the generation of pro-inflammatory cytokines, chemokines, and reactive oxygen species (ROS), all of which exacerbate mitochondrial dysfunction, oxidative stress, and neuronal death. Moreover, glial scarring brought on by astrocytic activation may hinder the processes involved in neural healing. Therapeutic strategies that target glial activation pathways seek to improve neuroprotective properties and control inflammatory responses, providing potential means of slowing the progression of Parkinson's disease and improving patient outcomes. Subsequent investigations ought to concentrate on clarifying the specific processes of glial-mediated neurodegeneration and utilizing these discoveries to develop efficacious treatment approaches for Parkinson's disease control..

Keywords: Parkinson's disease, neuroinflammation, microglia, astrocytes, neuronal survival, oxidative stress, neurodegeneration, inflammatory cytokines, glial activation, therapeutic strategies.

1. INTRODUCTION

Parkinson's disease (PD) is a neurological condition that worsens with time and is characterized by the passing of dopaminergic neurons in the substantia nigra. This loss of neurons causes engine symptoms such as quake, bradykinesia, stiffness, and postural instability. Besides, notwithstanding these engine symptoms, non-engine symptoms such as mental hindrance, temperament problems, and autonomic dysfunction are also widespread and make a significant commitment to the general weight of the illness.

1.1.Role Of Neuroinflammation And Oxidative Stress In PD

Both neuroinflammation and oxidative stress are significant pathogenic processes that have been connected to the course of (PD). Neuroinflammation is a condition that occurs when the safe response is persistently enacted inside the focal nervous system (CNS). Microglia, which are the safe cells that are resident in the mind, are the essential cells engaged with this process. The overactivation of microglia in (PD) results in the release of favorable to fiery cytokines and chemokines, the two of which add to the destruction of neurons.

When contrasted with oxidative stress, which is characterized as an unevenness between the age of reactive oxygen species (ROS) and the cancer prevention agent defenses of the cell, oxidative stress is portrayed by the presence of a lopsidedness. oxidative stress might be caused by mitochondrial breakdown, damaged protein corruption pathways, and the collection of misfolded proteins such alpha-synuclein in dopaminergic neurons. These factors can all add to the advancement of oxidative stress. Specifically, dopaminergic neurons are susceptible to oxidative injury because of the great metabolic prerequisite they have and the relatively unfortunate cancer prevention agent limit they possess.

Parkinson's disease (PD) is characterized by the progressive debasement of dopaminergic neurons in the substantia nigra, which leads to a cascade of engine and non-engine symptoms. This degeneration contributes to the progression of the illness. Neuroinflammatory processes and oxidative stress are two significant pathogenic processes that have been connected to the course of (PD). The neurodegenerative pathology that is seen in Parkinson's disease is a result of several processes, which are closely connected.

❖ **Neuroinflammation in Parkinson's Disease**

The prolonged activation of the immune response inside the central nervous system (CNS) is responsible for the condition known as neuroinflammation. Microglia, which are immune cells that are located in the brain, are the primary participants in this process. When it comes to Parkinson's disease (PD), neuroinflammation is an essential characteristic that plays a big part in the course of the illness.

❖ **Oxidative Stress in Parkinson's Disease**

The expression "oxidative stress" refers to a situation in which there is an unevenness between the making of reactive oxygen species (ROS) and the cell reinforcement defenses of the cell. Oxidative stress is a significant part that contributes to neuronal loss and dysfunction in (PD).

Oxidative stress is a significant contributor to the pathogenesis of Parkinson's disease, and it does so via a number of important routes, including lipid peroxidation, protein oxidation, and DNA damage. The development of therapeutic techniques that target oxidative stress that seek to relieve neuronal damage and perhaps halt the course of illness requires an understanding of these pathways, which is vital for the development of such therapies. Through the mitigation of oxidative stress-induced damage to cellular components, researchers seek to provide new options for the successful treatment and management of Parkinson's disease.

2. LITERATURE REVIEW

Vallée, A., et.al.,(2020). In the substantia nigra pars compacta, Parkinson's disease (PD) is perhaps of the most unmistakable neurodegenerative disease. It is described by a slow degeneration of neurons that are composed of dopamine. The causes of Parkinson's disease are yet mystery. The most significant risk factor for Parkinson's disease is aging. The process of maturing may cause sub-atomic pathways that oversee cell homeostatic functions to become dysregulated. Parkinson's disease cells are the locations of various metabolic abnormalities, including neuroinflammation and oxidative stress at the same time. The circadian rhythms are the main impetus for metabolic structures. Physiological rhythms are mind boggling systems that are in constant correspondence with their surroundings and control various different physiological processes. Late research has shown that abnormalities in circadian rhythms are associated with Parkinson's disease (PD) and the metabolic dysregulations that are associated with it. The essential emphasis of this survey is on the powerful job that circadian rhythms play in Parkinson's disease, as well as their effect on neuroinflammation and oxidative stress conditions.

S. Saha, B. Buttari, E. Profumo, P. Tucci, and L. Saso (2022) are the authors of the study.Neuroinflammation is a significant calculate Alzheimer's disease (Promotion) and Parkinson's disease (PD), which are the two most normal degenerative diseases that lead to dementia. These neurological illnesses are distinguished by the collection of proteins that have been misfolded, including amyloid-ß (Aß), tau protein, and α-synuclein. These proteins add to the discontinuity of mitochondria, oxidative stress, and neuroinflammation. Misfolded proteins enact microglia, which thusly increases neuroinflammation and the release of supportive of fiery cytokines, which thusly accelerates synaptic debasement and the passing of neurons. As of not long ago, each and every one of the suggested medications has been based on the suppression of protein total, and every one of them have been unsuccessful in clinical trials. It is consequently that the numerous treatment choices for dementia keep on being a troublesome issue. As a result, examining several approaches to remedial treatment is

gainful. In this respect, there is a developing group of proof demonstrating that the transcription factor NF-E2 p45-related factor 2 (Nrf2) plays a basic job in the redox homeostasis and calming actions that are associated with neurodegenerative illnesses. Various interesting findings have been made in regards to the Nrf2 signaling pathway. These findings incorporate the overexpression of cell reinforcement genes, the suppression of microglia-interceded aggravation, and the improvement of mitochondrial capability in neurodegenerative illnesses.

Yang, L., et.al., (2020). The engine system is mostly impacted by Parkinson's disease (PD), which is the second most common age-related neurodegenerative state of the central nervous system. PD is portrayed by a general decrease in engine capability. Then again, the pathogenic processes are not yet completely understood. In Parkinson's disease (PD), the transaction among genes and the climate causes selective passing of dopaminergic neurons. The neuroinflammatory reactions that are engaged with the etiology of Parkinson's disease are supported by an increasing assemblage of research. This article provides a basic analysis of late research on the provocative response that occurs all through the degenerative phase of Parkinson's disease (PD). It is possible that neurodegenerative illnesses may be dealt with using the processes and tactics that incorporate the adjustment of physiological responses to aggravation.

Zhang, H., et.al., (2022). Alzheimer's disease is the most pervasive neurodegenerative illness, while Parkinson's disease is the second most regular neurodegenerative disease. Both of these diseases put a consistently increasing weight on society. Numerous investigations have uncovered the possibility that oxidative stress might have a significant impact in Parkinson's disease via different mechanisms that are associated with the breakdown or demise of neurons. Furthermore, it has been shown that this neurodegenerative illness is associated with various different subtypes of non-coding RNAs. The connection between oxidative stress and administrative non-coding RNAs in Parkinson's disease, then again, has not yet been completely understood. Inside the scope of this paper, we direct an exhaustive survey and give a diagram of the capability that administrative non-coding RNAs play related to oxidative stress in Parkinson's disease. The manner by which they associate with each other is also summarized. The purpose of this article is to give readers a somewhat fresh perspective on the pathophysiology of Parkinson's disease, which will ideally help to the improvement of pre-clinical diagnosis and treatment.

3. REGULATION OF INFLAMMATORY CYTOKINE EXPRESSION BY MICRORNAS

The ability of microRNAs (miRNAs) to regulate the synthesis and activity of cytokines involved in inflammatory responses inside the brain, especially in the context of Parkinson's disease (PD), is known as "regulation of inflammatory cytokine expression by microRNAs." Here's how this procedure is explained:

1. Targeting mRNA Degradation and Translation: Small RNA molecules known as microRNAs mainly attach to particular sequences on target messenger RNA (mRNA) molecules in order to carry out their intended function. There are two primary ways in which a miRNA can prevent the synthesis of proteins once it attaches to its target mRNA:

- **mRNA degradation:** By causing the mRNA to degrade, the miRNA can stop the mRNA from being translated into a useful protein.
- **Translation inhibition:** Without causing it to deteriorate, miRNA can prevent mRNA from being translated into protein.

Regulation of Cytokine mRNA Stability: MicroRNAs have the ability to target and regulate the stability of mRNA transcripts encoding different cytokines in the context of neuroinflammation in Parkinson's disease. In reaction to inflammation or cellular stress, immune cells and glial cells (including microglia and astrocytes) generate signaling chemicals known as cytokines. Dysregulated neuroinflammatory responses in Parkinson's

disease (PD) result in elevated cytokine production, which exacerbates neuronal damage and advances the disease.

Examples of MicroRNA Regulation: Certain microRNAs have been linked to Parkinson's disease (PD) by regulating neuroinflammatory pathways, including miR-7, miR-155, and miR-34b/c. Tumor necrosis factor alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1 beta (IL-1β) are a few examples of pro-inflammatory cytokines that these miRNAs can target. MiRNAs can lower the stability or translation efficiency of these cytokines by binding to their mRNA and therefore lowering their levels in the brain.

4. IMPACT OF MICROGLIAL AND ASTROCYTIC ACTIVATION ON NEURONAL SURVIVAL

One important component of neuroinflammation and neurodegenerative illnesses such as Parkinson's disease (PD) is the effect of astrocytic and microglial activation on neuronal survival. This is an explanation of the idea:

1. Microglial and Astrocytic Activation: In the central nervous system (CNS), glial cells such as microglia and astrocytes are crucial for preserving brain homeostasis and reacting to trauma or illness. These glial cells get activated in neuroinflammatory disorders like Parkinson's disease (PD) in response to many stimuli, such as misfolded protein aggregation (alpha-synuclein aggregates in PD), oxidative stress, and pro-inflammatory cytokines.

Roles of Microglia

- **Immune Response:**The major immune cells of the central nervous system (CNS), activated microglia, release pro-inflammatory cytokines (such as TNF-α and IL-1β), chemokines, and reactive oxygen species (ROS) in response to damage or infection.
- **Phagocytosis:**Through a process known as phagocytosis, microglia absorb and digest cellular waste, including damaged neurons and protein clumps.
- **Neurotoxicity:**Activated microglia can emit neurotoxic chemicals when they are dysregulated, which damages neighboring neurons and exacerbates neurodegeneration.

Roles of Astrocytes:

- **Neuroprotection:**By preserving the blood-brain barrier, supplying nutrients and metabolic support to neurons, and controlling neurotransmitter levels, astrocytes promote the health of neurons.
- **Inflammatory Response:**When a CNS injury or disease occurs, astrocytes, like microglia, can become reactive and release inflammatory mediators.
- **Scar Formation:**In chronic neurodegenerative disorders, astrocytes contribute to the creation of glial scars, which can separate areas of injury but may also impede neuronal repair and regeneration.

Impact on Neuronal Survival:

- **Supportive Roles:** Under normal conditions, activated microglia and astrocytes can exert neuroprotective effects by clearing cellular debris and promoting tissue repair.
- **Dysregulation in Neurodegeneration:**Chronic activation of astrocytes and microglia in neurodegenerative illnesses such as Parkinson's disease (PD) can result in oxidative stress and persistent inflammation, both of which are harmful to neurons. The release of reactive oxygen species (ROS) and pro-inflammatory cytokines by activated glial cells can cause direct neuronal apoptosis, or cell death, or damage neuronal connection and function.
- **Modulation of Disease Progression:**In order to reduce neuroinflammation and enhance neuronal survival in Parkinson's disease (PD), therapeutic approaches that modify microglial and astrocytic activation have been investigated. This involves encouraging anti-inflammatory and neuroprotective reactions or focusing on particular signaling pathways linked to glial activation.

5. CONCLUSION

Progressive dopaminergic neuronal degeneration is a hallmark of Parkinson's disease (PD), which is made worse by neuroinflammatory processes triggered by activated microglia and astrocytes. These glial cells, which are critical for preserving CNS homeostasis, get activated in response to pathogenic triggers such oxidative stress and alpha-synuclein aggregation. Chronic activation results in a neurotoxic state marked by the release of pro-inflammatory cytokines and reactive oxygen species (ROS), despite initially serving a neuroprotective effect through debris clearing and anti-inflammatory signaling. Through the induction of oxidative stress, mitochondrial malfunction, and apoptotic pathways, these variables lead to the damage and death of neurons. Furthermore, glial scarring brought on by astrocytic activation may impede neural healing. Therapeutic approaches that target glial activation seek to improve neuroprotective properties and regulate inflammatory responses; these approaches may be able to delay the progression of Parkinson's disease and improve patient outcomes. It is imperative that future studies concentrate on comprehending the dynamic roles of astrocytes and microglia and create targeted therapeutics in order to further Parkinson's disease treatment techniques.

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