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Letter to the Editor

PARKINSON'S IMMUNITY AND INFLAMMATION: NEW ASPECTS

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INTRODUCTION

Parkinson disease (PD) is a multisystem disorder which affects dopaminergic neurotransmission that is characterized by movement disorder with motor impairment, tremors, stiffness of the neck, trunk, and limbs, bradykinesia, postural instability, depression, anxiety, apathy, and soft voice. In PD, which typically develops around the age of 60 with an incidence of approximately 1.5% (1), there is neuroinflammation and a malfunction of the immune system that can lead to gastrointestinal dysfunction and sleep alterations (2,3). Individuals with PD present with a neurodegenerative syndrome involving both thalamocortical and non-motor motor circuits.

DISCUSSION

PD is one of the most frequent neurodegenerative diseases (4) and presents a degeneration of neurons in the substantia nigra causing motor dysfunction (5). The disease presents neuronal loss with the presence of proteins such as Lewy bodies (absent in mouse), but this mechanism still needs to be elucidated. The cause of these phenomena has often been attributed to oxidative stress, cytotoxicity, mitochondrial dysfunction, apoptosis, and low-grade inflammation (6-9). Inflammation is due to microglial activation, astrogliosis, and lymphocyte infiltration, contributing to neurodegeneration. Neurodegeneration could stimulate inflammatory proteins, causing brain dysfunction (10). Laboratory blood tests show that some cytokines such as IL-2, tumor necrosis factor (TNF), and IL-6 (11), as well as the chemokine RANTES (12), are increased in the serum of patients with PD. These highly inflammatory immune molecules could contribute to neurodegeneration. Autoantibodies against dopaminergic neurons may also be responsible or participate in this inflammatory process. Activated CD4+ and CD45RO+ T lymphocytes are involved in this immunopathological reaction, while naive CD45RA+ non-activated T lymphocytes are decreased. CD25 Treg lymphocytes are also increased in PD patients, demonstrating an immune reaction of the organism against the pathological phenomena. However, these results are still unclear and need to be confirmed.

The brain is an organ that has its own immune system in which cytokines can mediate both physiological and pathological phenomena. Pro-inflammatory cytokines such as IL-1, TNF, and IL-6, which can be generated by microglia and are important inflammatory markers, are also found in the cerebrospinal fluid of these patients (13). Microglia, which

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are sentinels of the central nervous system (CNS), exert a protective effect on the brain by maintaining homeostasis. These blood monocyte-like cells generate neurotrophic factors such as nerve growth factor (NGF) and fibroblast growth factor (FGF) (14). The activation of microglia by external insults leads to the production of pro-inflammatory cytokines, an effect that has also been confirmed in rodents (15). Inflammatory cytokines play a key role in the pathogenesis of neurodegenerative diseases (16,17). The cerebrospinal fluid of PD patients shows high levels of cytokines IL-1, IL-6, TNF, TGF-β1, VEGF, and the inflammatory chemokines MCP-1 and MIP-1α, highlighting that this disease also has inflammatory origins and that these cytokines/chemokines could be used as a target of this neurodegenerative pathology (18,11) (Table I).

Table I. *Some factors that mediate neuroinflammation.*

• Tumor necrosis factor (TNF)	• Interferon γ
• CD68, CD23	• β2-microglobulin
• Interleukin-1 (IL-1)	• Epidermal growth factor,
• Cyclooxygenase	• Transforming growth factors α and β
• Inducible nitric oxide synthase	• Interleukin-2 (IL-2)

CONCLUSIONS

PD can be relieved by treating the affected patient with the dopamine precursor levodopa or with dopaminergic inhibitors (19). Therapeutic treatment with levodopa proves to be effective in the long term with neurological improvement and quality of life. Patients with PD can also be treated with the surgical technique of brain stimulation which consists of a pulse generator that sends electrical stimuli to the brain.

However, studies underway in our laboratory as well as others aim to clarify the etiological and pathogenetic mechanisms, and the specific action of cytokines in PD, allowing for better therapeutic treatment for this neurodegenerative disease which ranks, by incidence, in second place in the world after Alzheimer's among brain disorders.

Conflict of interest

The author declares that they have no conflict of interest.

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