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NEUROBIOLOGICAL DETERMINANTS OF COGNITIVE DECLINE AND DEMENTIA IN PARKINSON'S DISEASE: THE ROLE OF NEUROINFLAMMATION AND STRUCTURAL CHANGES

Eldor Isroilovich Abduqodirov, Sharaf Khamrakulovich Babakulov, Sitora Oybekovna Inoyatova, Muxabbat Umarovna Karimova, Muxabbat Abdusattarovna Maxamadxodjayeva, Asliddin Baxriddinovich Kalanov
Tashkent State Medical University, Tashkent, Uzbekistan.

ABSTRACT

This comprehensive literature review examines the specific features of cognitive impairment and dementia in Parkinson's disease (PD), emphasizing their clinical, neurological, and neurobiological underpinnings. The study highlights the critical importance of early detection of mild cognitive impairment (MCI) and discusses contemporary diagnostic and therapeutic approaches. The review is based on an extensive analysis of publications from international scientific databases, reflecting the current state of research on the role of neuroinflammation and brain structural alterations in the progression of PD-related cognitive decline.

KEYWORDS

Parkinson's disease, cognitive impairment, dementia, mild cognitive impairment (MCI), α-synuclein, rivastigmine, neuropsychology, International Parkinson and Movement Disorder Society (IPMDS).

Аннотация

В настоящем литературном обзоре рассматриваются особенности когнитивных нарушений и деменции при болезни Паркинсона, их клинико-неврологические и нейробиологические аспекты. Подчёркивается важность раннего выявления лёгких когнитивных расстройств и обсуждаются современные подходы к диагностике и терапии. Обзор основан на публикациях в международных научных базах данных и отражает актуальное состояние проблемы.

Ключевые слова

болезнь Паркинсона, когнитивные нарушения, деменция, лёгкие когнитивные расстройства, α-синуклеин, ривастигмин, нейропсихология, IPMDS.

INTRODUCTION. Parkinson's disease (PD) is a progressive neurodegenerative disorder primarily characterized by the loss of dopaminergic neurons within the nigrostriatal system. Beyond the classical motor symptoms, PD is increasingly recognized for its significant impact on cognitive function, emotional stability, and the overall neuropsychological profile. Research indicates that the vast majority of PD patients will eventually develop varying degrees of cognitive impairment, dementia, and affective disorders [1].

Among the spectrum of non-motor symptoms, cognitive decline is considered one of the most debilitating challenges. Early longitudinal studies reported that approximately 30% of PD patients develop dementia, a clinical entity distinct from Alzheimer's disease (AD). While initial theories suggested that PD-related cognitive deficits were restricted to executive dysfunction and attentional deficits, contemporary data confirm a more global involvement, including

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impairments in memory, visuospatial functions, and language, even in the early stages of the disease [2].

EPIDEMIOLOGY AND PROGNOSIS. Long-term prospective data suggest a cumulative prevalence of dementia approaching 80% in patients with PD [3]. Approximately 25% of non-demented PD patients exhibit Mild Cognitive Impairment (PD-MCI) [4], which serves as a critical clinical predictor for rapid conversion to Parkinson's Disease Dementia (PDD) across both early [5] and advanced stages [6]. Furthermore, the presence of MCI at the onset of PD is associated with an increased mortality risk [7]. Recent findings indicate that 10–20% of newly diagnosed PD patients already fulfill the criteria for cognitive impairment [8]. Cognitive changes may even manifest in the prodromal phase [10], particularly among individuals with hyposmia, dopamine transporter (DAT) deficiency [13], or REM Sleep Behavior Disorder (RBD), the latter of which carries a profound risk for conversion to Dementia with Lewy Bodies (DLB) [15].

PATHOGENESIS AND NEUROBIOLOGY. The neurobiological substrate of cognitive decline in PD is multifactorial. The primary mechanism involves the widespread cortical deposition of fibrillar α-synuclein (Lewy bodies) [19]. However, at least one-third of PDD patients also exhibit co-pathologies typical of Alzheimer's disease, specifically β-amyloid plaques and, to a lesser extent, tau-pathology [20]. The synergy between α-synuclein and AD-type pathologies is considered one of the most robust predictors of dementia [8]. Furthermore, cerebrospinal fluid (CSF) biomarkers, such as reduced levels of β-amyloid 1-42, are closely linked to the progression of PDD [22].

OBJECTIVE. The objective of this review is to synthesize contemporary scientific evidence regarding the pathogenesis, clinical manifestations, and diagnostic frameworks of cognitive impairment and dementia in Parkinson's disease, with a specific focus on differential diagnosis, prognostic markers, and multi-modal therapeutic strategies.

MATERIALS AND METHODS. This review is based on a comprehensive analysis of peer-reviewed literature indexed in international databases, including PubMed, Scopus, Web of Science, and Google Scholar. The selection criteria focused on original research, systematic reviews, meta-analyses, and clinical guidelines published primarily within the last two decades.

DIAGNOSTIC FRAMEWORKS AND TOOLS. The International Parkinson and Movement Disorder Society (IPMDS) has revolutionized the field by establishing standardized diagnostic criteria and algorithms for PDD [2, 3]. Subsequent task forces have refined the criteria for PD-MCI, recommending specific neuropsychological batteries for clinical use [5, 24]. Validated tools adapted for PD include:

- Parkinson Disease-Cognitive Rating Scale (PD-CRS) [25]
- Montreal Cognitive Assessment (MoCA) [23]
- Mattis Dementia Rating Scale-2 (DRS-2) [26]
- Scales for Outcomes in Parkinson's Disease-Cognition (SCOPA-COG) [10]

THERAPEUTIC INTERVENTIONS. Pharmacological management of PDD has largely adapted strategies from AD. Currently, the cholinesterase inhibitor Rivastigmine remains the only FDA-approved treatment for PDD, following large-scale randomized controlled trials (RCTs) [19]. While statistically significant, its clinical efficacy is often modest and limited by side effects such as nausea, tremor, and dizziness. Notably, anticholinergic medications used for

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motor symptoms have been shown to accelerate cognitive decline and should be used with extreme caution [16, 17]. Non-pharmacological approaches, including cognitive training [18] and structured physical exercise [19], have demonstrated short-term benefits in specific cognitive domains. Additionally, managing comorbidities such as orthostatic hypotension (OH), obstructive sleep apnea (OSA), and vascular risk factors is essential for stabilizing cognitive function [21, 23].

DISCUSSION. The management of PD must transition from a motor-centric model to a holistic, multidisciplinary approach. Cognitive impairment in PD is not a late-stage complication but a progressive process that can precede motor symptoms. The pathogenesis is a complex interplay of α-synucleinopathy, amyloid deposition, and neurotransmitter dysregulation (including cholinergic and serotonergic systems). Early identification of MCI via validated scales is paramount for prognostic stratification and early intervention.

CONCLUSION.

1. Cognitive impairment in PD is a frequent and disabling complication that necessitates early diagnosis and a multidisciplinary management strategy.
2. The identification of specific prognostic factors and biomarkers offers a window of opportunity for early therapeutic intervention to delay the onset of dementia.
3. Modern standardized scales and international criteria have significantly improved the diagnostic accuracy of PD-MCI and PDD.
4. An integrative approach, combining optimized pharmacological therapy with non-pharmacological interventions (physical and cognitive training), is essential for improving the functional outcomes and quality of life for patients with Parkinson’s disease.

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