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A REVIEW OF NON-MOTOR SYMPTOMS IN PARKINSON'S DISEASE AND THEIR INFLUENCE ON QUALITY OF LIFE



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ABSTRACT

Purpose: This literature-based review explores the multifaceted impact of Parkinson's disease (PD) on patients' quality of life, with particular emphasis on non-motor symptoms. Building upon the findings of Karlsen et al., the article integrates contemporary evidence to highlight the role of chronic pain, sleep disturbances, fatigue, depression, emotional dysfunction, and social isolation in shaping patient wellbeing.

Methods: The review centers on the prospective study conducted by Karlsen et al. (1993–1997), which used the Nottingham Health Profile (NHP) to assess health-related quality of life in 111 patients with PD. Supplementary sources from recent decades, were analysed to provide an updated perspective on non-motor symptom prevalence, clinical relevance, and management strategies. These sources include data on physical activity, emotional health, digital health tools, and interdisciplinary care models.

Results: Non-motor symptoms frequently have a more significant negative impact on daily functioning and subjective quality of life than motor symptoms. These include not only chronic pain and sleep disturbances but also persistent fatigue, mood disorders, social disengagement, and reduced physical activity. Despite their prevalence, non-motor symptoms remain underrecognized and undertreated in clinical practice.

Conclusions: A holistic, multidisciplinary approach is essential for improving quality of life in patients with PD. Effective management should combine pharmacological therapies with psychological support, physical rehabilitation, group-based interventions, and the use of wearable technologies. Future research

should prioritize the development of integrated care models, the use of disease-specific quality-of-life assessment tools, and targeted strategies for fatigue, depression, and endocrine comorbidities such as hypothyroidism.

Keywords: Parkinson's disease, quality of life, non-motor symptoms, NHP, fatigue, sleep, depression, pain, social isolation, digital health, review

INTRODUCTION

Parkinson's disease (PD) is a progressive neurodegenerative disorder that primarily affects older adults, with a prevalence of approximately 1% in individuals over the age of 60 and up to 4% in those over 80 years [1]. It is characterized by motor symptoms such as bradykinesia, resting tremor, muscle rigidity, and postural instability. These manifestations result from the degeneration of dopaminergic neurons in the substantia nigra and are often accompanied by dysfunction in other neurotransmitter systems, including noradrenaline and acetylcholine, contributing to autonomic disturbances and cognitive decline.

Although the etiology of idiopathic PD remains partially understood, recent research suggests a multifactorial basis involving genetic predispositions—such as mutations in the PARK1 (alpha-synuclein) and PARK2 (parkin) genes—and environmental factors [2]. PD's clinical presentation is not limited to motor impairments; instead, patients frequently experience a broad range of non-motor symptoms (NMS) that can significantly diminish health-related quality of life (HRQoL).

These non-motor symptoms include chronic pain, fatigue, sleep disturbances, depression, anxiety, cognitive dysfunction, and social withdrawal. Mounting evidence indicates that NMS often exert a greater negative impact on QoL than motor symptoms, yet they remain underrecognized in clinical practice. A key early study by Karlsen et al. used the Nottingham Health Profile (NHP) to assess HRQoL in a cohort of PD patients and highlighted the critical role of non-motor symptoms—especially depression, sleep problems, and fatigue—in limiting daily functioning and psychological well-being [3].

These symptoms often overlap, making proper identification and selection of appropriate therapy difficult. An additional difficulty is the relatively low awareness among clinicians regarding the potential occurrence of additional disorders, such as depression or cognitive deficits, which can significantly affect the course and treatment of Parkinson's disease. [4]

Since that study, numerous reviews and clinical guidelines have emphasized the need for a patientcentered, multidisciplinary approach to PD management that addresses both motor and non-motor domains. Newer assessment tools, such as the PDQ-39 and MDS-UPDRS, provide a more detailed picture of symptom burden. Additionally, the incorporation of digital health technologies and community-based interventions is expanding the possibilities for personalized care.

This literature review revisits and contextualizes the findings of Karlsen et al. in light of contemporary evidence. It explores how non-motor symptoms shape the lived experience of PD and evaluates emerging strategies for their assessment and management, including pharmacological, behavioral, rehabilitative, and technological interventions.

METHODOLOGY

This paper is a narrative literature review aimed at analyzing the impact of Parkinson's disease on patients' quality of life, with a particular focus on non-motor symptoms. The review is centered around the prospective study conducted by Karlsen et al., which assessed 111 patients with Parkinson's disease from Rogaland County, Norway. Health-related quality of life (HRQoL) was measured at two time points—1993 and 1997—using the Nottingham Health Profile (NHP), which evaluates six dimensions: physical mobility, pain, emotional reactions, social isolation, sleep, and energy levels.

In addition to the Karlsen study, relevant peer-reviewed articles were identified through a structured literature search focused on non-motor symptoms of Parkinson's disease. Sources published between 1999 and 2023 were included, with emphasis on studies and reviews discussing pain, sleep disturbances, fatigue, mood disorders, and their influence on daily functioning. Guidelines from major neurological and movement disorder associations were also reviewed.

All sources were categorized by theme and compared with the findings from Karlsen et al. to provide a deeper understanding of the multifactorial burden that non-motor symptoms impose on patients with Parkinson's disease.

DISCUSSION

Studies show that chronic pain is one of the most significant factors affecting the quality of life in patients with Parkinson's disease and other chronic conditions. According to Bouhassira et al. [5], chronic pain can lead to deterioration in mental and physical functioning, especially in patients with neurological disorders. Pain occurs in 67% of patients. Effective pain management, both through medication and non-pharmacological techniques (e.g., physiotherapy), can significantly improve patient comfort. D. Quinn et al. [6] were among the pioneers in developing a detailed pain classification scheme for patients with Parkinson's disease (PD), which considered the level of motor ability. In their study, they described different pain scenarios and were among the first to highlight an important aspect: taking levodopa could partially alleviate pain associated with non-motor symptoms during the "off" phase (such as anxiety or depression), regardless of the patient's motor state [7].

While these findings remain relevant, it is important to consider that more recent studies have emphasized the complex and multifactorial nature of pain in PD, with contributions from central sensitization, musculoskeletal disorders, and medication fluctuations. New approaches, including personalized dosing strategies, mindfulness-based interventions, and targeted physiotherapy, are increasingly being explored as part of comprehensive pain management.

SLEEP

Sleep disorders are frequently reported by patients with Parkinson's disease, leading to increased fatigue, mood deterioration, and reduced energy levels. Sleep problems may be linked to pain and fatigue, creating a vicious cycle that worsens daytime functioning. In Parkinson's disease, sleep disorders are among the most common non-motor symptoms, occurring in about 40-90% of patients. Sleep problems can arise at any stage of the disease, but their severity increases with the progression of motor symptoms [8]. Sleep issues in patients may include excessive daytime sleepiness, insomnia, obstructive sleep apnea, and REM sleep behavior disorder. These are most often associated with the symptoms of the disease but can also result from the side effects of medications such as L-DOPA or dopamine agonists. Sleep quality, circadian rhythm, and wakefulness can also be affected by factors not directly related to the disease, such as other comorbid conditions, the aging process, or poor sleep hygiene [9].

While these associations are well-documented, clinicians still face challenges in accurately diagnosing and treating PD-related sleep disorders. Sleep assessments using wearable actigraphy devices and home-based polysomnography have emerged as valuable tools. Moreover, behavioral interventions such as cognitive-behavioral therapy for insomnia (CBT-I) and sleep hygiene education have shown promise in improving sleep quality among PD patients.

ENERGY

Low energy levels are a common problem for patients with Parkinson's disease. Fatigue in this group of patients may result from a combination of physical symptoms, sleep disorders, and side effects of the therapy used. Fatigue is often associated with damaged structures of the basal ganglia in the brain [3].

Fatigue also correlates with reduced dopamine levels and may reflect broader dysfunctions in motivational systems and reward processing. Despite its high prevalence, fatigue is frequently underassessed in clinical settings. There is a growing consensus on the need for standardized diagnostic tools and personalized fatigue management strategies.

PHYSICAL ACTIVITY

Bradykinesia, or slowness of movement, is one of the main symptoms of Parkinson's disease. It is one of the most disabling conditions characteristic of the basal ganglia [15],[16]. In people with Parkinson's, there is a loss of automatic movements (such as blinking or alternating limb movements while walking). Movements are often delayed, slower, and incomplete [17]. Parkinsonian rigidity is an increased resistance to passive stretching. It affects axial, distal, and proximal muscles. Postural stability disorders are particularly noticeable in patients whose Parkinson's disease develops at an older age or is in an advanced stage.

Current rehabilitation approaches emphasize the importance of early, consistent, and tailored physical activity. Programs that include aerobic exercises, resistance training, and balance-enhancing tasks have demonstrated benefits in mobility, posture, and even mood. Assistive devices and wearable gait monitors are increasingly used to optimize activity patterns and reduce fall risk.

SOCIAL FUNCTIONS

Literature confirms that physical limitations and pain can lead to social isolation and deterioration of mental health in patients with chronic illnesses. Lack of energy and mobility can cause patients to limit social interactions, which in turn affects mood and deepens loneliness [18].

Newer studies suggest that group-based psychosocial interventions, including peer support and structured social activities, significantly enhance social participation and subjective well-being. Moreover, digital platforms and telehealth solutions have shown potential in maintaining social connectivity, especially during periods of limited mobility or isolation.

EMOTIONS

A review of the literature indicates that depression meeting the criteria for "major depression" occurs in 5–25% of patients with Parkinson's disease (PD), with the prevalence of "major depression" being 25% according to DSM-IV criteria [19]. Mild depressive symptoms and dysthymia are much more common, occurring in up to 50% of patients [20]. The causes of depression in Parkinson's disease involve both reactive and endogenous components. Most studies indicate a combination of subjective response to disease progression and objective neurobiological changes affecting dopaminergic, serotonergic, and noradrenergic systems.

Advances in neuroimaging have revealed structural and functional alterations in the limbic and prefrontal areas associated with PD-related depression. Multimodal treatment approaches combining pharmacotherapy, psychotherapy, and exercise are recommended. Special attention should also be given to comorbid conditions such as hypothyroidism, which can exacerbate depressive symptoms and diminish treatment response.

Functional neuroimaging studies reveal significant similarities between depression associated with PD and isolated depression occurring in individuals without Parkinsonian symptoms. Notable observations include significant reductions in regional blood flow in the anterior-medial frontal area and the cingulate gyrus, as well as decreased metabolism in both caudate nuclei in the lower frontal areas [21], [22], [23], [24].

Overall, the complex interplay of non-motor symptoms in PD requires a comprehensive, patient-centered approach. Future research should explore integrated models of care that combine medical, psychological, and social support to improve quality of life in people living with Parkinson's disease.



RESULTS AND THERAPEUTIC APPROACH

Fig. 1. Results obtained from the study by Karlsena et al. [25], presenting the average values in six dimensions of quality of life assessed using the Nottingham Health Profile (NHP) in patients with Parkinson's disease.

Here are the conclusions based on the patient's results, using literature data on health assessment in chronic diseases and the application of the Nottingham Health Profile (NHP):

PAIN AS A MAJOR FACTOR REDUCING QUALITY OF LIFE

A high score (80) suggests that pain is one of the patient's main health issues. Such severe pain can significantly limit functioning, affect daily activities, and reduce quality of life. Effective pain management strategies are necessary to mitigate its impact on the patient's health. This finding supports the growing concept that different doses of levodopa may be necessary to effectively manage both motor and non-motor symptoms that respond to dopamine. Thus, patients experiencing variable pain may benefit from adjusting levodopa doses, even if their motor symptoms are already optimally controlled [26].

Sleep Problems and Health Status: A score of 70 in the sleep range indicates serious issues with sleep quality or quantity. This may be related to pain that interferes with falling or staying asleep leading to increased fatigue, mood deterioration, and worsening physical health. Behavioral interventions, such as relaxation techniques and cognitive-behavioral therapy (CBT) targeted at sleep problems are recommended to improve sleep quality [27].

LOW ENERGY AND DAILY FUNCTIONING

The low energy levels are likely the result of sleep problems and pain, which deprive the patient of the strength needed to perform daily tasks. Lack of energy can also lead to decreased motivation and greater difficulties in daily functioning. Strategies to improve energy levels, including regular physical exercise tailored to the patient's abilities, can support the maintenance of mobility functions and overall well-being. In the treatment of Parkinsonism, bilateral pallidotomy is always used [3],[20].

LIMITATIONS IN PHYSICAL ACTIVITY, MOBILITY, AND INDEPENDENCE

The score in the dimension of physical impairment in the NHP has also increased [3]. The patient reports difficulties with physical activity, which may be due to both pain and low energy levels, hindering movement, walking, or performing tasks independently. Limited mobility increases the risk of further deterioration in physical health. Regular walks lasting 30–45 minutes, covering a distance of at least 2 km, are recommended. This allows the patient to maintain control over their fitness. It is crucial to choose the right time of day, ideally early or late afternoon, as well as to avoid walking during hot weather. Patients should walk at a comfortable pace, avoiding frequent stops to practice movement automation. Walking forces strategic planning of steps, avoiding obstacles, and moving over varied terrain. Comfortable, full footwear and walk in daylight are recommended to help reduce the risk of falls. Although treadmill walking is safer and provides a steady walking rhythm, it does not allow for interaction with the environment, does not encourage natural torso movements, or train balance when the patient holds onto the handrails. Daily walks improve step length and walking speed, with effects lasting for several months after regular exercise ends [28].

SOCIAL ISOLATION AS AN EFFECT OF DISEASE SYMPTOMS

The degree of social interactions can also affect the observed variability in health-related quality of life (HRQL). In the category of social functions, the patient scored 50, indicating moderate difficulties in making or maintaining social contacts. This may be due to fatigue, pain, malaise, or limited mobility, which discourage the patient from engaging in social activities and can lead to isolation [3]. Involving patients in social support programs and support groups is recommended to counteract the feeling of isolation [18].

EMOTIONS

A relatively low score in the category of emotions indicates fewer emotional problems compared to other areas. However, issues such as pain, fatigue, and limited mobility can negatively impact mental health over time, especially if the patient feels lonely or isolated. Psychosocial interventions, including group therapy with psychoeducational elements and cognitive-behavioral techniques can be beneficial. In some cases, improvement can occur when the patient is included in an educational program aimed at facilitating coping with Parkinson's disease symptoms, reducing stress, and improving quality of life through support. Social counseling and physical rehabilitation, including regular exercise, can also yield positive effects. In patients with Parkinson's disease and coexisting mood or cognitive disorders, the increased risk of hormonal disorders, especially hypothyroidism, should always be considered. It has been reported that untreated hypothyroidism can result in poorer response to antidepressant medications. Therefore, regulating potential hormonal disorders is crucial for effective treatment, both in the context of antidepressant therapy and managing Parkinson's disease symptoms [29].

NEW TECHNOLOGIES IN THERAPEUTIC APPROACHES

MEMS accelerometers (Micro-Electro-Mechanical Systems) play a crucial role in monitoring the symptoms of Parkinson's disease, such as tremors, bradykinesia (slowed movements), and freezing of gait (FOG). They are used in wearable devices, such as Stat-On[™], to enable an objective assessment of the patient's

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condition and provide doctors with precise real-time data [30].

The operation of MEMS accelerometers is based on detecting changes in body acceleration along three axes (X, Y, Z), allowing for a detailed analysis of the patient's movement patterns. Thanks to their high sensitivity, these sensors can record the characteristic Parkinsonian tremor at a frequency of 4–6 Hz. Moreover, advanced algorithms analyzing accelerometer data help identify sudden movement arrests, which can assist physicians in adjusting therapy to the patient's individual needs [31].

Deep Brain Stimulation (DBS) has become the preferred surgical treatment for Parkinson's disease due to its high effectiveness in reducing motor symptoms. Among the three primary anatomical targets—the internal segment of the globus pallidus, the ventral intermediate nucleus of the thalamus, and the subthalamic nucleus (STN)—the subthalamic nucleus (STN) is considered the most beneficial. Its stimulation provides the greatest improvement in bradykinesia, muscle rigidity, and tremors, while also enabling a significant reduction in levodopa dosage. Additionally, there is evidence suggesting that STN stimulation may have a neuroprotective effect, slowing the progression of the disease [32].

Studies have shown that STN stimulation in Parkinson's patients, combined with a reduction in levodopa dosage, led to an over 80% increase in glucose oxidation, as measured by calorimetry. This resulted in a beneficial decrease in fasting blood glucose levels. At the same time, resting energy expenditure normalized, and the intensity of protein and fat oxidation decreased. As a consequence, patients experienced weight gain, which varied by sex—in men, the increase was primarily in lean body mass, which is generally acceptable, whereas in women, there was a predominant and unfavorable increase in fat tissue [33].

CONCLUSIONS

Parkinson's disease is a chronic progressive condition that significantly affects patients' physical, emotional, and social well-being. This literature-based review, centered around the findings of Karlsen et al., confirms that non-motor symptoms—such as chronic pain, sleep disturbances, fatigue, depression, and social withdrawal—often have a more profound impact on quality of life than motor symptoms alone.

Despite their clinical relevance, non-motor symptoms remain underrecognized in routine care. This underscores the need for a shift toward a comprehensive, multidisciplinary approach that incorporates not only pharmacological treatment but also psychological support, behavioral interventions, physical rehabilitation, and social integration.

The Nottingham Health Profile (NHP), as used in Karlsen's study, has proven to be a valuable tool for assessing health-related quality of life and guiding tailored care strategies. However, its limitations highlight the importance of using disease-specific tools such as PDQ-39 or MDS-UPDRS in modern practice.

Physical activity interventions—especially those that combine aerobic, balance, and resistance training have demonstrated clear benefits in mobility, emotional well-being, and fall prevention. Group-based psychosocial programs and peer support have also been shown to reduce isolation and enhance perceived quality of life.

Additionally, the growing use of wearable technologies and mobile health applications allows for real-time monitoring of symptoms and treatment effects, providing clinicians with individualized insights to optimize care.

Future research should focus on:

- the integration of digital health tools for real-time symptom monitoring,
- the evaluation of group-based and cognitive-behavioral interventions,
- the role of endocrine factors, such as hypothyroidism, in treatment-resistant depression,
- and the development of targeted fatigue assessment and management strategies.

Ultimately, improving quality of life in PD requires more than symptom control—it demands personalized care plans informed by both clinical evidence and individual patient needs, supported by a coordinated, technology-enhanced, and person-centered approach.

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