LITERATURE REVIEW

Gait in Parkinson's Disease: From Neurophysiology to Rehabilitation Overview

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ABSTRACT

Introduction: Parkinson's disease (PD) is a complex and progressive neurological disorder affecting the elderly. The disease is characterized by the degeneration of striatal dopaminergic neurons and gait disturbances. Therefore, this research aims to provide a variety of gait disturbances in patients with PD. The mechanisms and factors associated with impaired walking activity provides a basic concept for selecting appropriate rehabilitation strategies to improve mobility, overcome restrictions, and enhance life satisfaction.

Methods: Research was conducted using PubMed, Google Scholar, and the Cochrane Library to locate original articles, as well as systematic and narrative reviews, concerning neurophysiology, pathophysiology, clinical features, and rehabilitation of gait.
Result: PD patients may experience a reduction in walking speed and stride length, as well as increased axial rigidity. Early alterations in gait associated with PD include reduced arm swing amplitude, asymmetry between the extremities, and a decline in movement fluidity. Subsequently, freezing of gait (FOG) and festination may lead to increased dependency. This can affect the mobility and participation of patients, with further complications of immobility and isolation. Management of gait in PD consists of a combination of pharmacological and non-pharmacological treatments. A well-structured rehabilitation program should be tailored to meet unique needs considering different steps of the disease and distinct gait alterations. As a non-pharmacological method, a specific rehabilitation program plays an important role in addressing the specific needs of PD patients, particularly in terms of improving ambulation and promoting independence.

Conclusion: By understanding neurophysiology of walking and neuropathology of PD, effective rehabilitation strategies are developed to optimize mobility, efficiency, and independence in daily activities.

Keywords: gait, neurophysiology, Parkinson's Disease, rehabilitation, walking

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INTRODUCTION

Parkinson's disease (PD) is a well-known neurodegenerative disorder in the elderly, characterized by chronic and progressive nature as well as motoric and non-motoric symptoms. In this context, global prevalence of PD ranges from 1 to 2 per 1,000 individuals, setting the disease as the 1st global ranking in most movement disorders. The disease obtains 2nd global ranking in the most prevalent neurogenerative disorder after Alzheimer's disease.[1,2] In line with greater age expectancy in the elderly, the absolute number of people with PD will be increased proportionally and exponentially. In Indonesia, there were approximately 90,000 individuals with PD in 2005, and this number is projected to be 250,000 by 2030.[3]

Based in the description above, the symptoms of PD are connected with the progressive degeneration of striatal dopaminergic neurons. A hallmark histopathological feature is the existence of an accumulation of proteins called Lewy bodies, mostly found in the substantia nigra pars compacta. This leads to a deficiency in dopamine focused on the basal ganglia and the manifestation of motor symptoms.[4]

Motoric symptoms are primarily characterized by cardinal signs, including resting tremor, rigidity, and bradykinesia.[5] Postural instability may occur in the late steps due to these symptoms.[6] The disease leads to gait disturbance, where patients may experience slower walking speed, shorter stride length, increased axial rigidity, and impaired gait rhythm.[7] Early alterations in gait associated with PD include reduced arm swing amplitude, asymmetry between the extremities, and a decline in movement fluidity.[8,9]

As the disease advances, asymmetry decreases, and bradykinesia becomes more pronounced.[10] In later steps, the temporary inability to voluntarily control or initiate walking increased significantly.[11] These gait changes can lead to psychiatric problems such as anxiety and depression due to increased dependency, affecting quality of life.[7,12] The literature review provides a detailed discussion of gait disturbances in patients with PD. Additionally, the mechanisms and factors associated with impaired ambulation forms a solid foundation for selecting appropriate rehabilitation strategies, and optimizing overall daily life activities with independence.

METHODS, INCLUSION CRITERIA, AND EXCLUSION CRITERIA

This narrative review aims to gather current updates on gait disorder, walking limitations, and rehabilitation recommendations. The search was conducted for literature in English using PubMed, Google Scholar, and the Cochrane Library, with the search terms (MeSH) including "gait", "walking", "neurophysiology", "rehabilitation", and "Parkinson's disease. A total of 33 references were selected with 10 reviews, 2 randomized controlled trial articles, 6 observational research, 5 articles discussing mechanism or theoretical frameworks, 3 case studies, as well as 2 textbooks and authoritative resources. However, a systematic analysis of the available databases was not performed.

In the context of inclusion criteria, the publication type must come from peer-reviewed articles, books, and authoritative sources that contain original research, case reports, meta-analyses, and clinical guidelines relevant to the main topics. The trusted sources considered are PubMed/MEDLINE, Cochrane Library, and Google Scholar. The articles are in English with date ranges of 5 years to ensure up-to-date clinical relevance. The papers can include all steps of PD with the appropriate age group. The content of the

articles addresses motor problems as well as the impact on gait and walking alterations. The content also includes the rehabilitation strategies addressing gait and walking problems in PD. These articles are accepted regardless of the settings in low or high-resource settings.

The excluded research do not report the motor problem in gait and walking performance as well as exercise for addressing difficulties. Publications outside the trusted authoritative sources mentioned in inclusion criteria as well as articles over 5 years old and written in non-English are excluded. Similarly, research with significant methodological flaws, small sample size, or lack of clear results on walking prognosis are also excluded.

RESULTS

Neurophysiology of Gait Control System

Walking posture and patterns are closely related to motor control. In adults, walking is typically purposeful and voluntary, but not all aspects are consciously controlled. Basic locomotor patterns are controlled by the spinal cord through central pattern generator (CPG), which allows for the automation of walking. CPG receives stimuli from the periphery, processes the response in the spinal cord, and produces rhythmic stepping movements without any input from the brain.[13]

Stimuli activated in motor control are focused on cortical areas, primary sensorimotor cortex, basal ganglia, and cerebellum as supplementary motor area (SMA) when a certain move set is gained and routinely performed.[14] The intent to induce movement requires input from cognitive association areas, such as the anterior cingulate gyrus, dorsolateral prefrontal cortex (DLPFC), as well as posterior parietal, middle, and superior temporal gyri. DLPFC creates a corresponding movement plan, and SMA determines the sequence after receiving information from the posterior parietal association area and superior temporal gyrus. Hippocampus and parahippocampus are included in spatial planning and working memory related to the incoming sensory information. This plan is processed by the cerebellum and basal ganglia while simultaneously transferred to the primary motor cortex. Signals are further relayed until reaching the spinal cord and the brainstem. Certain emotional factors also influence movement through limbic-hypothalamic projections to the brainstem.[15]

The motor cortex, midbrain, hindbrain, and basal ganglia play crucial roles in making certain decisions and planning during walking. Supraspinal locomotor regulation includes three centers, namely midbrain locomotor region (MLR), subthalamic locomotor region (SLR), and cerebellar locomotor region (CLR) in the mesopontine tegmentum, lateral hypothalamus, and middle of the cerebellum, respectively.[11,15]

The Role of Basal Ganglia in Gait Pattern

The basal ganglia contain several nuclei that are crucial for motor control. These nuclei are spread in many locations within the striatum and globus pallidus of the cerebral cortex, substantia nigra in the mesencephalon and the subthalamic nucleus in the diencephalon. The striatum includes the caudate nucleus and putamen, while the lentiform nucleus comprises putamen and globus pallidus extended into the internal (GPi) and external (GPe) segments.[16]

The nuclei of the basal ganglia are categorized into three groups, namely input, output, and intrinsic nuclei. Input nuclei, such as the putamen and caudate nucleus, collect information from various sources, including the cerebral cortex and thalamus. Output nuclei, such as GPi and substantia nigra pars reticulata (SNpr),

transmit information to thalamus. Intrinsic nuclei, consisting of GPe, subthalamic nucleus (STN), and substantia nigra pars compacta (SNpc), convey information between the input and output nuclei.[16]

The direct pathway starts with the cerebral cortex sending signals to the striatum through glutamatergic neurons. The striatum sends inhibitory signals using neurotransmitter gamma-aminobutyric acid (GABA) to GPi, reducing the activity. Therefore, the inhibitory output from GPi to the thalamus decreases, producing feedback excitatory signals from the thalamus to the cerebral cortex through glutamate.[17] The indirect pathway serves to suppress unwanted motor activity. In this context, stimulatory signals from the cerebral cortex are transferred to the striatum. The suppressive signals are sent as a response through GABA to GPe, reducing the activity. This inhibition blocks any inhibitory signal, allowing STN to activate and send excitatory signals to GPi. Subsequently, GPi sends inhibitory signals to the ventral thalamus, suppressing activation of the cerebral cortex and inhibiting unwanted motor activity.[17]

The pathways are modulated by the dopamine neurons, specifically substantia nigra playing a crucial role. SNpc releases dopamine into the striatum, binding to D1 receptors to enhance the direct pathway and motor activity. Dopamine also binds to D2 receptors, which modulates the indirect pathway, reducing the inhibitory effect and increasing the action potential from the thalamus to the cerebral cortex.[17]

The basal ganglia, mainly the output nuclei project to MLR associated with the subconscious regulation of muscle tone, postural balance, and gait patterns. MLR includes pedunculopontine tegmental (PPN), cuneiform (CN), and sub cuneiform nucleus.

PPN projects to the reticular formation, which sends signals through glutamatergic pathways to the central pattern generator (CPG), responsible for controlling the rhythm of walking.[18] Additionally, SNpr inhibits muscle tone suppression initiated by PPN.[19]

Neuropathology Related to Gait in PD

Degeneration located in substantia nigra pars compacta (SNpc) leads to greater restriction of the external region of the globus pallidus (GPe) and reduced inhibition of the internal segment of globus pallidus (GPi). This results in excessive excitation of GPi and over-inhibition of the thalamus and PPN. The excitatory signals to SMA and the primary motor cortex are reduced, leading to hypokinetic gait and impairments in anticipatory postural adjustments (APA). Furthermore, APA includes involuntary center of pressure (COP) displacement in preparation for voluntary movements, such as the posterior and lateral shifting towards the leg before initiating a step from a resting position.

Dysfunction in locomotor regulatory areas, basal ganglia, thalamus, and cortical system contributes to slower walking in individuals with PD. The main sources of acetylcholine (ACh) in the brain are cholinergic interneurons in the striatum, nucleus basalis of Meynert (nbM) supplying ACh to the cortex, and pedunculopontine nucleus (PPN) of MLR. ACh provided by PPN to the thalamus is included in postural control, while those supplied to the cortex by nbM are associated with walking speed and hypokinesia. Dysfunction in these non-dopaminergic areas of PPN influences postural responses, increasing the likelihood of falls in PD. PPN is connected to the pontomedullary reticular formation (PMRF), regulating the coordination between posture and locomotion.[20]

The cerebellum receives visual, auditory, vestibular, and spinal inputs, interacting with premotor area (PM) to regulate motor function. This is particularly

important in PD since increased cerebellar activity serves as a compensatory mechanism in association with external cues. Therefore, external cues such as visual and auditory are substantial in walking mechanisms of individuals with PD.[20]

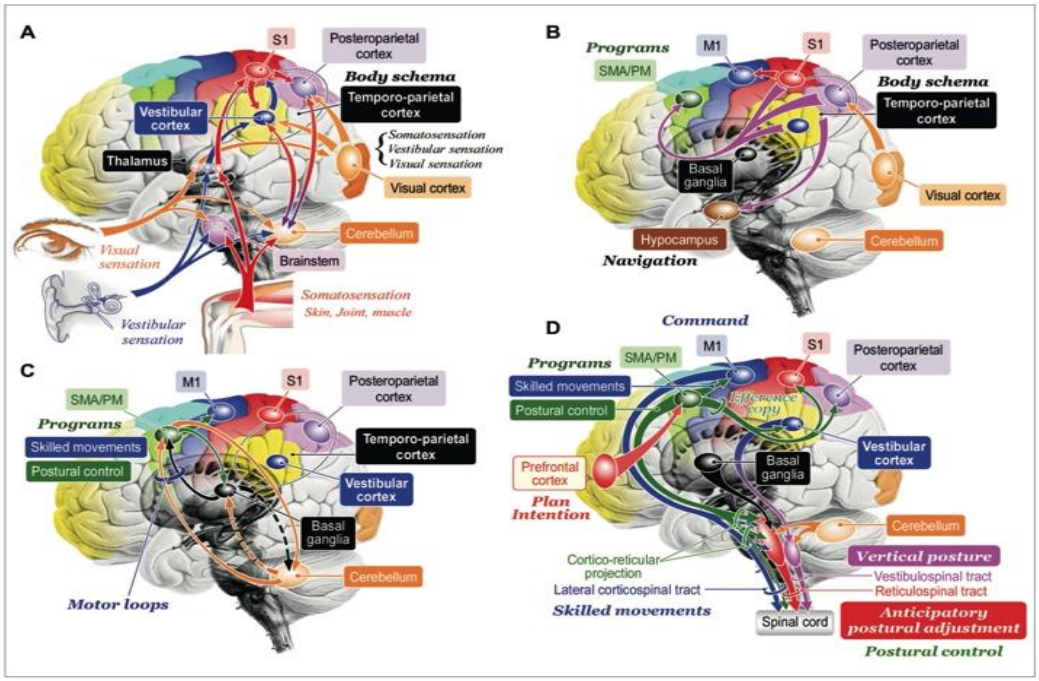

Figure 1. Gait and Posture Control Process Hypothesis[15]

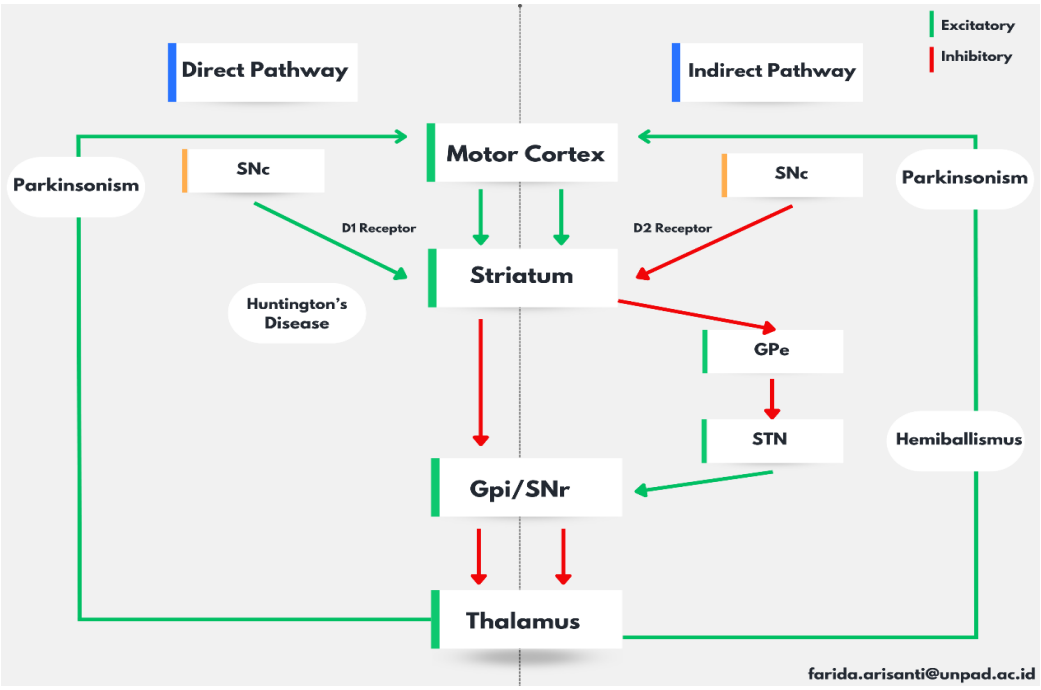

Figure 2. Multiple Pathways of Basal Ganglia

Clinical Features of Gait in PD

Gait abnormalities start with asymmetry in movement between the extremities evident in the arm swing and decreased flexibility of walking movements. Reduced joint range of motion in the pelvis, knees, and ankles results in shorter stride lengths. Movements become less automatic, leading to slower walking. This impaired automaticity is particularly visible when individuals with PD perform tasks.[7] Asymmetry diminishes and movements become more bradykinetic with increased levels of disease. The range of motion in the hip, knee, and ankle joints progressively decreases, accompanied by hypertonia in the flexor muscles. A hunched posture starts to develop, and torsion at the joints of the limbs decreases, causing the center of mass (COM) to shift forward leading to a shuffling gait.[7]

Axial rigidity contributes to turning "en bloc," a pattern where the head, torso, and pelvis rotate simultaneously due to a limited rotational range of motion.[20,21] The double limb support step increases with decreased axial rotation, increasing the rigidity of walking movements.[24] Reduced ankle plantarflexion torque, which affects the primary propulsive force during walking, also contributes to shorter stride lengths.[24] In this context, strides become smaller, and cadence increases.[7]

In more severe cases, freezing of gait (FOG) becomes more frequent. During FOG, there is a certain episode where an individual is unable to take a step effectively. Therefore, the intention to walk may lead to the disturbance in forward progression from light reduction to complete cessation in more severe cases.[26] Wobbling or Trembling of the knee and brief shuffling steps or total akinesia lasting for 1-2 seconds are the common characteristics of the episode.[22] The risk of falls increases due to the deterioration of balance and postural control. Meanwhile, muscle endurance and strength also decline over time, leading to the potential need for assistive devices. Festination is a gait disorder characterized by small and rapid steps to maintain the center of gravity (COG) between the legs due to a forward-leaning trunk in PD.[23]

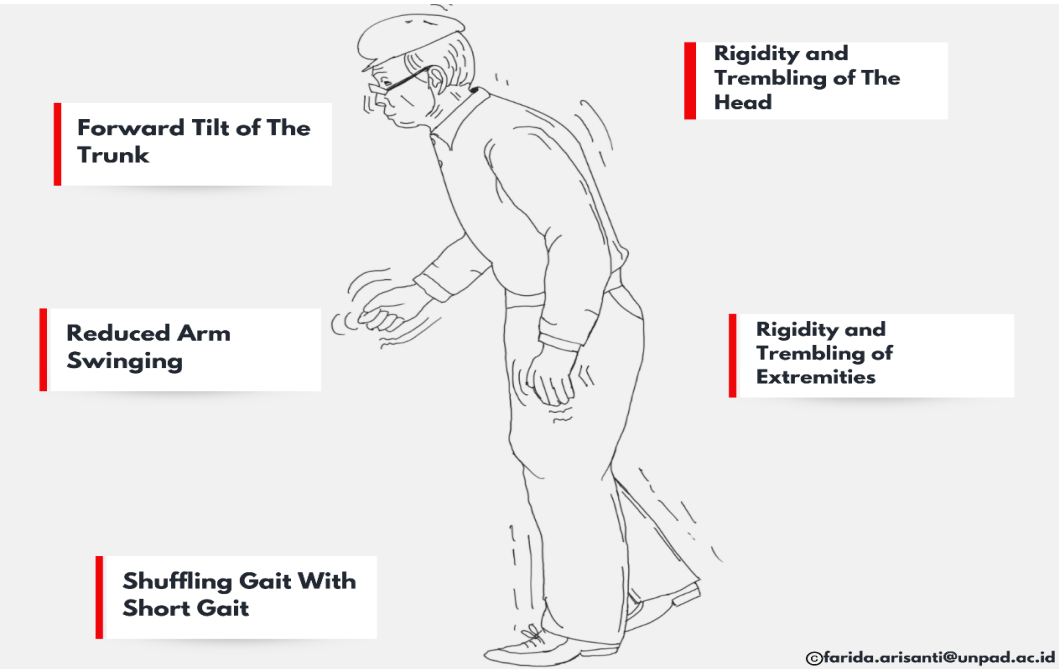

Figure 3 Symptoms of Parkinsonism

There are two forms of festination, namely primary and secondary phenomena. Primary phenomenon includes the shortening of stride length compensated by an increase in cadence. This typically occurs at the start of walking during walk initiation or turning and is associated with FOG.[23] Secondary phenomenon of festination results from postural and balance control deficits, where the forward-leaning body compensates with small steps to maintain balance. The retropulsion test can provoke this phenomenon since patient continues stepping backward due to insufficiently large steps to restore COG.[24]

Gait abnormalities in PD can be influenced by levodopa administration. During the "off" period, gait is characterized by akinesia. However, during the "on" period, there is a positive response to levodopa, choreic, dystonic, or dyskinetic gait. Intermittent stimulation from levodopa administration leads to changes in striatal output and disinhibition of the motoric cortex due to increased pallidothalamocortical pathway activation.[25]

DISCUSSION

Gair Disorder Rehabilitation Plans in PD

Effective management of gait disturbances necessitates a specific treatment plan, combining both pharmacological and non-pharmacological methods. A rehabilitation program designed for PD should be individualized, considering the specific needs of each patient. Several critical factors must be evaluated before initiating gait rehabilitation. These factors include assessing the strengths, obstacles, and expectations of patients about the ability to engage in rehabilitation. According to Nonnekes et al., five key aspects require assessment.[26]

The first aspect concerns the motor symptoms influencing gait of patients. This includes the severity of the disease, impaired balance, and the presence of FOG. The second aspect consists of mainly non-motoric symptoms, such as altered autonomic function, cognitive degeneration, neuropsychiatric challenges, and psychological conditions including mood disorders and anxiety. The third aspect is comorbidity, which comprises orthopedic issues, muscle strength deficits, and cardiorespiratory conditions. The fourth aspect pertains to environmental factors to assess the constraints in the surroundings of patients. Walking patterns of individuals with PD can be affected by turns or narrow pathways, and the placement of furniture in the home and workplace plays a significant role in facilitating smooth movement. The fifth aspect is cultural, including personal goals, preferences, environment, ability to travel, the presence of caregivers, and cultural background.[26]

Following this comprehensive assessment, the rehabilitation program should ideally include a multidisciplinary method after the comprehensive assessment.[27] The rehabilitation team may include physiotherapists, occupational therapists, speech therapists, and psychologists, who can provide various interventions. Furthermore, physical exercise was proven effective in improving physical capacity and cognitive functioning in PD.[28] These interventions may consist of compensatory strategies, such as cueing to overcome FOG.[29] Patients are also given functional gait training on different surfaces and with a treadmill, flexibility exercises to address rigidity, and resistance training to strengthen muscles crucial for walking. Multi-task training that integrates gait, cognitive, and functional exercises is recommended.

A systematical review in 2023 had several conclusions about physical rehabilitation strategies effectiveness for People with Parkinson's disease (PwP). The

initial results regarding the Rehabilitation of PwP with the aid of VR were statistically significant in TUGT, BBS, and FGA (Functional gait analysis) with a p-value of <0.05. The second conclusion showed that using music as therapy was not statistically significant in improving balance, dual tasking, or gait freezing. Motor-dual task training (MDTT) is more efficient in limiting gait difficulties in PwP. Meanwhile, effective enhancement of gait capacity, endurance, and global independence is produced by devices such as G-EO System or a treadmill.[29]

Exercise plans combining both balance and resistance training have given significant improvement in PD rehabilitation on certain aspects, reflected by increasing performance of functional reach, TUG value, and improvement in speed, step length, and more stable gait.[30] A systematic review and meta-analysis in 2018 stated that gait-specific training was selected to improve performance with most of the research subjects containing mild to moderate PD (Hoehn and Yahr I-III).[31] The supervised training session was implemented in gait rehabilitation and semi-supervised home-based treadmill training was not sufficient to improve walking performance in PD.[31]

Environmental modifications, such as reducing obstacles in the surroundings and planning daily activities with scheduled breaks to minimize stress, are important strategies. Cognitive-behavioral therapy may also be used to alleviate anxiety and the fear of falling.[32] The use of walking aids, such as canes and walkers, should be considered for patients at high risk of falls. A Timed Up and Go (TUG) test result exceeding 13 seconds and an Activities-specific Balance Confidence (ABC) score below 75 may indicate the need for a walker. [33]

CONCLUSION

In conclusion, the process of walking in humans could be complex, including numerous structures and controls. Even though walking was fundamentally an automatic function, the role of intentionality in humans required the inclusion of supraspinal structures. In PD, neurodegeneration of the basal ganglia contributed to disturbances in gait and walking ability. Postural instability further increased these impairments and the likelihood of falls. Additionally, disrupted cholinergic activity in PD further impaired walking. The effective rehabilitation strategies of neurophysiology of walking and neuropathology of PD could be developed to address walking limitations in PD patients. Therefore, gait-specific training exercises were crucial for rehabilitation programs addressing gait parameters and walking performance, specifically in mild to moderate steps of PD.

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