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Effectiveness of Body Weight Treadmill Exercise in Gait Rehabilitation for Early Stage Parkinson's Disease: A Systematized Literature Review

AN APPLICATION FOR THE PUBLIC HEALTH CARE SERVICES POHJOIS-HAAGA PALVELUKESKUS

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Abstract

Since Parkinson's disease (PD) has revealed its dreadful nature, notably by affecting a larger morbidity rate in the human's population, plenty of interrogations have been formulated, and some answers suggested. Nonetheless, today, healthcare communities are still seeking to ascertain how to treat the disease at best.

Physiotherapy is a field addressing responsive care for patient with PD. Thereupon, as walking ability is threatened by the disease, and considering that it is one of the main attributes of human function, there are significance reasons of preserving this skill. In fact, the correlation between disability, limitation or participation, quality of life and gait aptitude is evidently highlighted. In this context, relevancy of treadmill exercise efficacy in the objective of improving gait ability in early stage of Parkinson's disease is questioned.

Finding out evidence-based data is the aim of this systematized literature review, which focalized its inquiry in recent publications. The review defined the latest knowledge in PD and provides systematic methodology that illustrates the research process.

Furthermore, by screening through pertinent documentation an outcome has been assembled, which explicitly characterizes treadmill as a beneficial rehabilitation tool in gait therapy, particularly in the purpose of improving stride length and walking speed.

In conclusion, Pohjois-Haaga Palvelukeskus can find interest of utilizing the apparatus in the treatment of gait. Suggestion of outpatient sessions for early stage PD can offer favorable circumstances for the community, moreover for the person affected by this pluri-symptomatic disease, which in this 21st century has no cure yet!

Key words
Parkinson's disease, Gait, Treadmill, Exercise

CONTENTS

1 INTRODUCTION

"A journey of a thousand miles begins with a single step" (Tzu, 4th century B.C.).
It is probable that a person diagnosed with Parkinson's Disease (PD) consider his/ her world collapsing, as he/ she may endure a long road to acceptance. This makes certainly "a single step", challenging for anyone (Website of the Food & Drug Administration 2016).

If the inception of any health condition is the human being, it induces an extended complexity when trying to understand the process of rehabilitation (Website of World Confederation for Physical Therapy, 2011). One' self-motivation has been shown as a milestone approach in physiotherapy (Website of American of Physical Therapy Association 2017).

Interestingly, walking can be identified as one of the most desirable skill to acquire, knowing that it requests a constant demand toward earth's gravity, and that it is also leading to other functional movement abilities (Adolph & Robinson 2013, 1-3).
Therefore, understanding the relationship between treadmill exercises, gait rehabilitation and Parkinson's disease in early stage is relevant in providing cues in physiotherapeutic treatment.

Throughout a systematized literature review of research and publication the author aims to evaluate the background information, and to capture the major element concerning, the efficiency of treadmill apparatus for PD in early stage. There are also objectives, to extract the exercise recommendation demonstrating improvement of gait, that could be implemented in public health care services, at the Pohjois-Haaga Palvelukeskus (PHP). Furthermore, the interest of PHP for this systematized literature review befalls with the idea of supporting their physiotherapists in the plan of care of PD's in-outpatients. In this framework, this study means to look at scientific evidences in gait rehabilitation, and to present opportunities yielded by the effect of treadmill

exercise on early stage of patient with PD. In term of opportunities and development, it will be possible from the results of this review to determine or not, a blueprint of gait rehabilitation with treadmill workout. Thus, the author explores the recommendation that can be exploited by the physiotherapy team at PHP. For later stage, PHP in partnership with the Finnish Parkinson's disease Association would eventually offer treadmill exercise session with the objective to enhance walking. Ultimately, support independency and higher quality of life

2 PARKINSON'S DISEASE

Historically, it is admitted that the piece of writing "an Essay on the Shaking Palsy" published in 1817 and penned by James Parkinson, describes with the most clarity the premises of what will be called by nomenclature; the Parkinson's disease. Another pioneer, and contributor is the French neurologist Jean-Michel Charcot, who provided substantial scientific breakthrough by discriminating PD with other neural disorders (Teive, Munhoz, & Lees 2017). Since then, tremendous amount of research has been conducted and, yet PD has no curable treatment. Nevertheless, research progress and recent therapy have proven to be supportive in the treatment of the disease, but unfortunately, not without side effects (Website of National Institute of Neurological Disorders and Stroke 2019). This progressive disorder is a burden, not only for a person with a conclusive diagnosis and his family, but also for the community. Today, PD is worldwide, the second most common neurodegenerative disease after Alzheimer (Website of Finnish Parkinson Association 2018).

But what exactly is Parkinson's disease? It can be defined as an idiopathic neurodegenerative disorder that affect primarily the brain's cells, and inclined discernible symptoms. Although, signs and symptoms (motor and non-motor) can be affiliated to PD distinctively, affected patient can experience syndromic differences (Mackenzie 2001, 43). Can one die from PD? This will depend on multiple factors, but it is most likely that the disease will not be the direct, or the only cause of death

(Website of European Parkinson's Disease Association, 2017). For information, the author does not address this review to atypical parkinsonian syndrome, which can be differentiated from PD (e.g. the Lewy bodies aggregation in and related dementia).

Pathophysiogically, researchers have demonstrated disruption of dopaminergic cells, predominantly in the substantia nigra, which affects notably motor skill and muscle tone (Postuma, Berg, Adler, Bloem, Chan, & Deuschl 2016, 15). Consequently, a person affected can experience psychosomatic, cognitive, physical, or physiological disorders. Therefore, it can result in feeling pain, loss of memory, dementia, dystonia, sexual disorder, urinatory problems, speech disorder, or/ and dysphagia. Thus, fatigue, sleeping problems or/ and depression are also related signs. Among the manifestations that can be observed, four symptoms characterize primarily Parkinson's disease (PD), tremor at rest, bradykinesia, rigidity and postural instability (Lawton et al. 2018, 89).

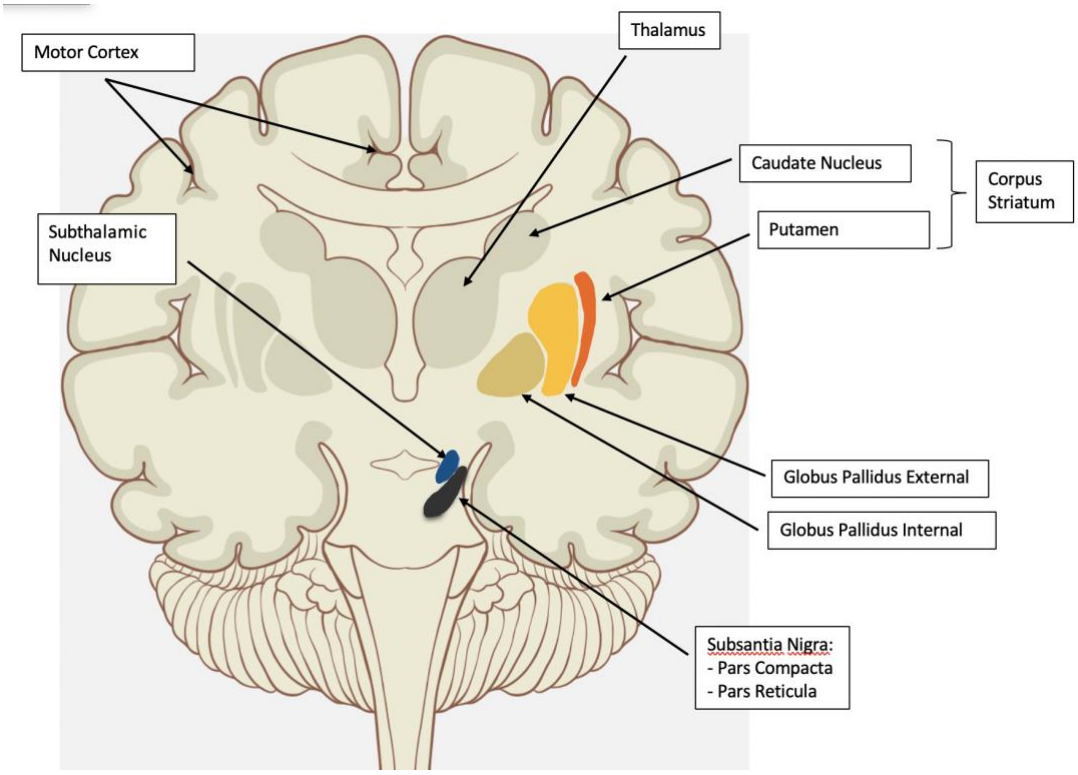
It is in the interest of this report to address current knowledge of PD's physiotherapeutic treatment for gait rehabilitation. The research on the topic demonstrates direct correlation between gait impairment and PD. This phenomenon is described as the freezing of gait; during patient's assessment intermittent pattern of walking can occur, generally at the toes off in the stance phase, but likewise during gait (Website of Physio-Pedia 2018).

2.1 Pathophysiology

By comparing and illustrating the normal physiological activity of the brain in relation to movement and consequently to walking, with the pathophysiology in PD; the author intends to present of how voluntary movement is affected in this health condition. Hereof, the following description can expose the problems that researcher's inquiries has identified in gait disorder (Selzer, Cohen, Duncan & Gage 2006, 24).

2.1.1 A normal brain activity in voluntary movement

Svoboda & Li (2018, 33-41) described what has been demonstrated in the scientific community as evidence for decades; the brain is the central command of initiating voluntary and control movement. It refers to the divisions of the cerebral cortex: frontal cortex, premotor cortex, supplement motor cortex and primary motor cortex, which are hierarchically the primarily initiators (Picture 1). The below picture illustrates some the brain section, where the BG is rather medial.



Picture 1. Brain's description (Leraillez 2020)

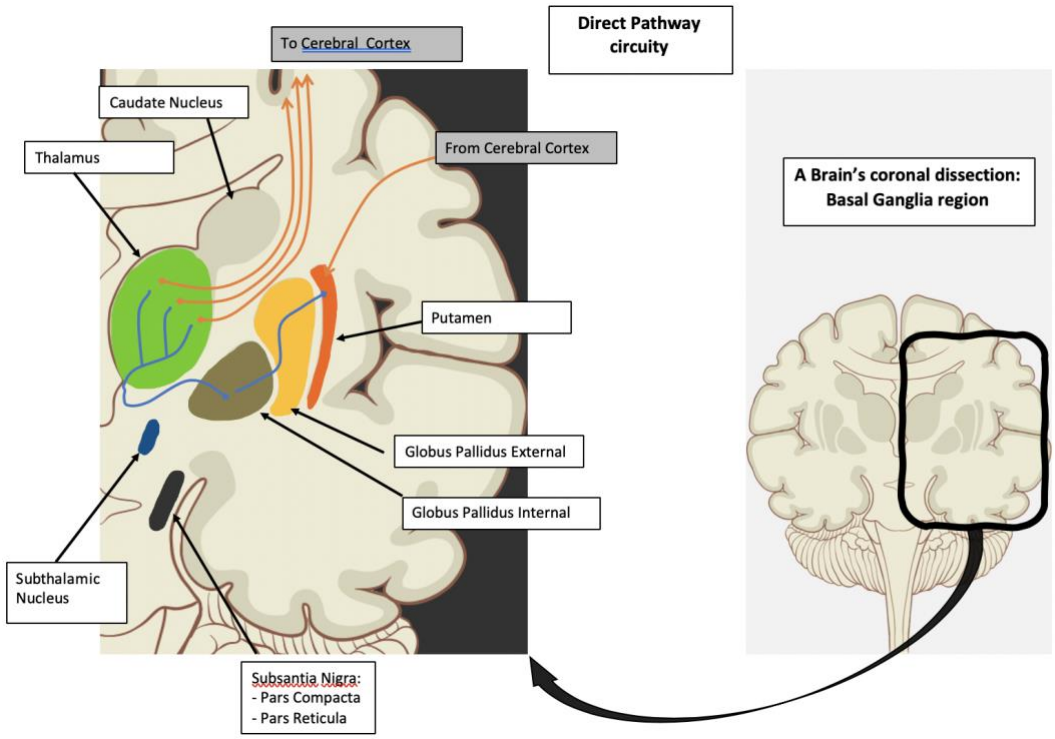
Thereby, it is established that prior a stimulus is sent by the cerebral cortex through the central nervous system (CNS) to the peripheral nervous system (PNS) and finally to the target muscles, direct - indirect stimuli loops occur within the circuitry of voluntary movement which involves the motor cortex, the basal ganglia, the subthalamic nuclei, the thalamus, and the cerebellum notably. In this context, the basal ganglia (BG) or basal nuclei acts as excitatory/ inhibitory regulator at the pre/ post-synaptic potential (PSP), which influences the subthalamic nuclei, the thalamus "the

relay station of the brain" and the cerebral cortex in the planning of engaging movement (Website of University of Texas Mc Govern Medical School 2018, 1).

What is the basal ganglia? This system is a bundle of neurons that operates between the cerebral cortex and the thalamus, throughout different striatal tracts. The role of this collection of nuclei is to ease or to generate smooth movement, to regulate muscle tone and to execute learned pattern of movement (Website of Encyclopaedia Britannica 2018).

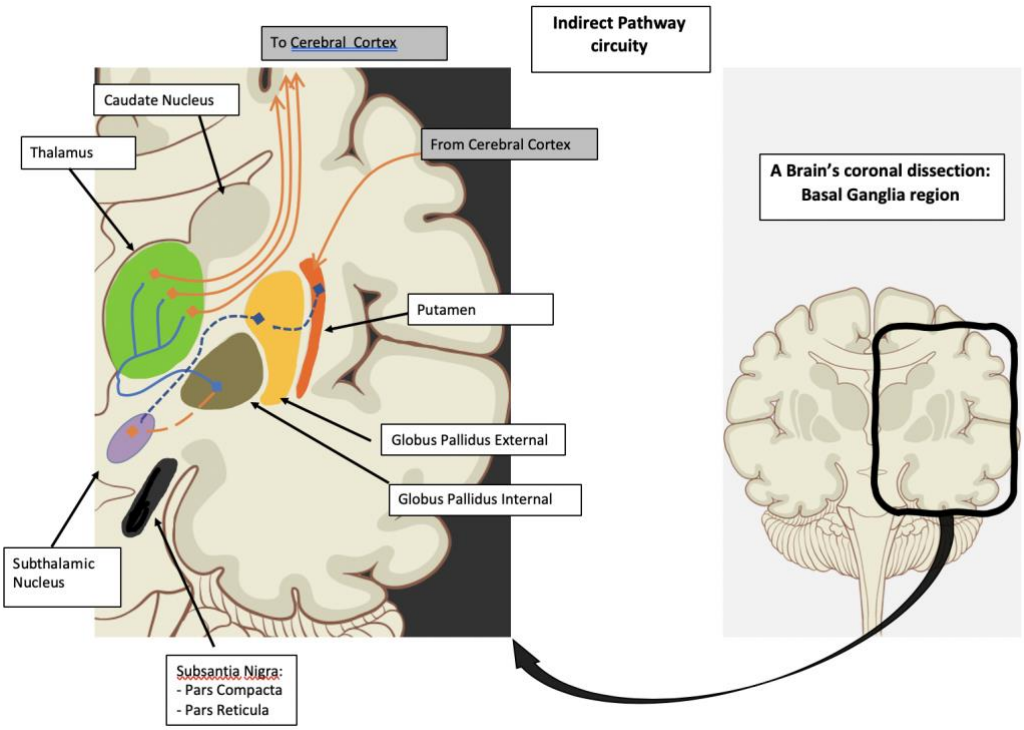
BG consists of several distinct sections interconnected by specific neurons. The caudate nucleus, the nucleus accumbens and the putamen pair-up to constitute the striatum. When the combination of the putamen, the goblus pallidus externus and the globus pallidus internus assemble the lentiform nucleus. In addition, the substantia nigra is also an inclusion of the basal ganglia (Website of Journal of Science Direct 2019). The connections between these different structures array, mainly abundances of glutamate (GluT), which is the neurotransmitter acting as an excitatory substance, and gamma aminobutyric acid (G.A.B.A.), which the neurotransmitter acting as an inhibitory substance. There is a logical aspect in the description of the direct/ indirect pathways, almost mathematical. As, when high level of glutamate is released from the pre-synaptic bulb to the post-synaptic receptors, then neurons get an excitatory response (Website of University of Texas Mc Govern Medical School 2018, 2).

For instance, if an individual wishes to elicit a motion from standing position to walking, a higher level of stimulation is required for the muscle group involved in the intended function. Reminiscently, such processes are initiated by the motor cortex and these carry electrochemical interactions (sequences of excitatory and inhibitory stimulations at the basal ganglia) to notably excite the thalamus throughout the *direct pathway* (picture 2), which consequently modify the balance between the GluT and the G.A.B.A. in favour of glutamate (Website of University of Texas Mc Govern Medical School 2018, 3). The below picture represents the direct pathway of the brain corticostriatal circuitry.



Picture 2. Basal Ganglia direct pathway circuitry (Leraillez 2020).

Finally, these complexes brain's circuitries return emulated to the cerebral cortex, which is governing the efferent neurons and the motor units (nerves and muscles) to fire the required electrical impulse for the walking to occur as planned (Yin 2014). But conversely, if the same individual wishes to decelerate and go from walking to stopping, lesser stimuli are required for the muscle group associated in gait. These activities refer to the *indirect pathway* of the brain corticostriatal circuitry and its involvement of the subthalamic nucleus (Picture 3).



Picture 3. Basal Ganglia indirect pathway circuitry (Leraillez 2020).

Neuron fibres that come from the motor cortex to synapse within the putamen via the corticostriatal pathway and connect to the globus pallidus external passing through the subthalamic nuclei via the pallidosubthalamic nuclei pathway, bond to another neuron at the thalamus (Website of R&D Systems 2019). Hereof, the motor cortex plans notably new actions (contraction of agonist muscles and relaxion of antagonist muscles), and sequences of stimulation are rebalanced to favour an increase of inhibitory stimulus at the end of process. This means that subthalamic nuclei is firstly involved, before the thalamus gets more inhibited, which allows the cerebral cortex to interpret accordingly the inhibitory stimulus. Consequently, the peripheral activity at the lower limb decreases till it stops (Website of University of Texas Mc Govern Medical School 2018, 4).

2.1.2 Essential role of Substantia nigra

Anatomically, the substantia nigra (SN) is located in the midbrain and is distinctly recognizable by the black pigmentation of its cells. Two apparent sections associate the SN: the Subtantia Nigra pars compacta (SNpc) and the Subtantia Nigra pars

reticula (SNpr). Markedly, the pars compacta is understood to gather high concentration of dopaminergic cells in the midbrain (Galvan & Wichmann, 2008, 1459-1474). Depletion of dopamine occurs when α-synuclein (transmembrane protein), which are intrinsically related to dopamine release, are misfolding in this distinct area of the brain. Thereupon, Lewy Bodies will accumulate causing decrease of dopamine (Duda, Lee & Trojanowski 2000, 121-17). Ribot et al. (2019) confirmed in their publication that dopaminergic cells effect greatly the *direct and indirect pathways*.

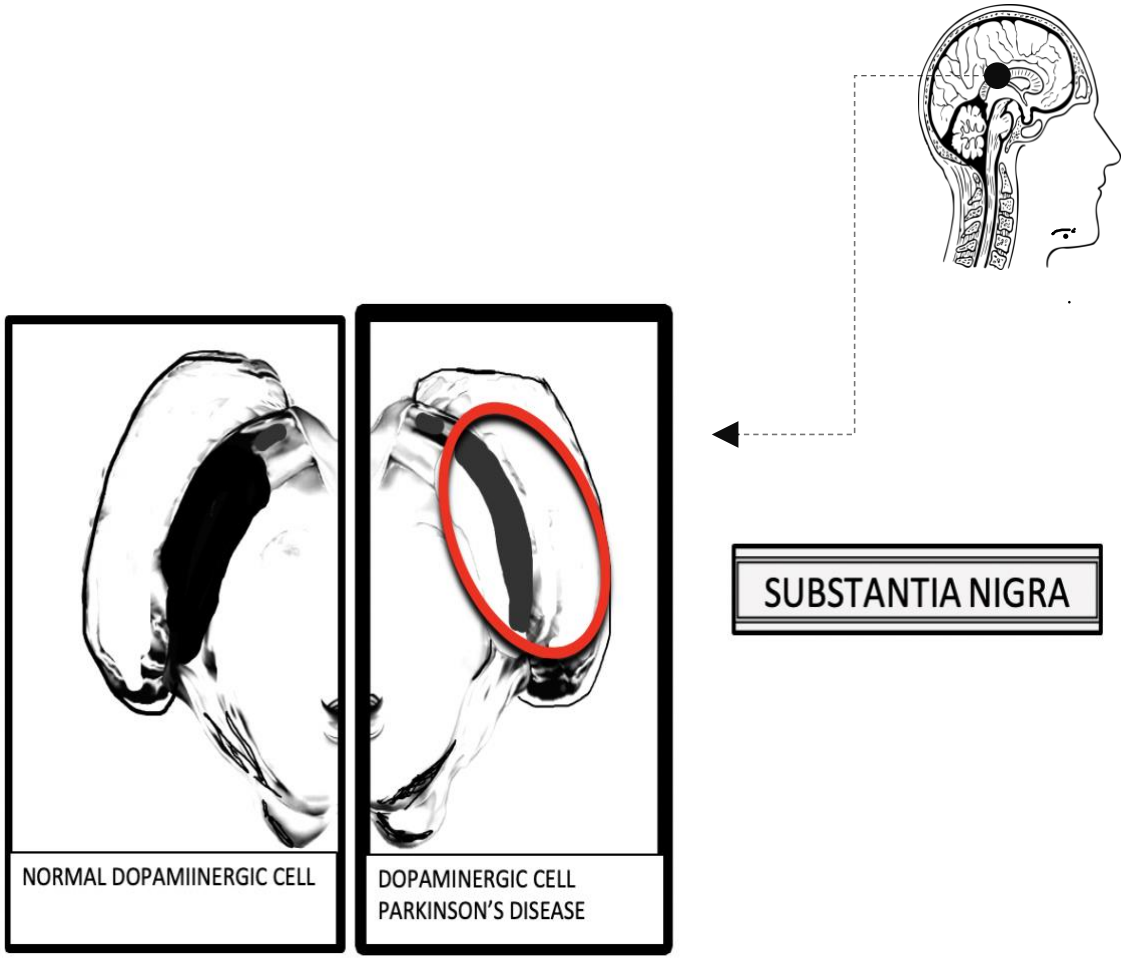
In fact, the neurons release dopamine into the putamen via the nigrostriatal pathway at the specific stimulatory receptor named D1, which causes, when all processes are carried on at the *direct pathway*, a net increase of excitatory activity for the motor cortex (a subject can have more movement). Jointly, when the neuron from the SN synapses at the putamen still via the nigrostriatal pathway but on the *indirect pathway* to the inhibitory receptor named D2, the net stimulus at the motor cortex is less impeded and become more inhibitory. This mechanism can be resumed when maximum contraction of muscle is needed and when movement requires to illicit some inhibitory signal at the muscle group that need to distribute higher muscle strength (Marshall, Ruskin & LaHoste 1997, 193-219). Importantly, in this process the cholinergic cells present in the putamen act oppositely to the dopamine (tends to balance dopamine activities) and negate dopaminergic activator's effect (Masato, Plotegher, Boassa & Bubacco 2019, 35).

2.1.3 An abnormal brain activity in voluntary movement

This is the last section and on these pages the page numbering is not in use.
The current scientific understanding of Parkinson's disease exposes explicitly the *Subtantia Nigra pars compacta* (SNpc) as being the prominent disorder factor. In fact, at a post-mortem brain's dissection the depletion of dopaminergic cells can be physically observed as its segment shows lighter black coloration. Literally, neurons affiliated to the release of dopamine are dying or their normal function is disrupted, which has an impact on the correlated post synaptic tracts, causing decreases of net

excitatory impulse to the motor cortex and then to the motor units (nerves and muscles) (Website of Medicine Plus 2018).

The D1 receptor (*direct pathway*) synapsing through the nigrostriatal pathway within the putamen is no longer receiving excitatory dopamine input. Meanwhile, the D2 receptor (*indirect pathway*) synapsing also within the putamen through the nigrostriatal pathway is no longer stimulated by dopamine, and a net declined of stimuli occur at the motor cortex, causing decrease of muscle activity. This pathophysiological phenomenon describes precisely the symptomatic condition of bradykinesia, akinesia or facial "mask" (Meder, Herz, Rowe, Lehéricy & Siebner 2018, 79-93, 1). Similarly, dopaminergic neuron imbalance and depletion causes cholinergic neuron over activity in the putamen. This is understood to generate over activities at the motor cortex, which can be observed on symptomatic tremors at rest, or on the patient's rigidity (Meder, Herz, Rowe, Lehéricy & Siebner 2018, 79-93, 2).



Picture 4. Disrupted dopaminergic cells in Basal Ganglia (Leraillez 2020).

2.2 Aetiology and risk factors

The order in the body of the text can vary. Discuss your solution with your supervisor. The causes that explain Parkinson's disease are unknown so far. Nevertheless, research have identified probable trends or cues that are recurrently discussed. In fact, genetical and environmental factors, age, gender, ethnicity related, or history of traumatic brain injury are believed to be involved somehow in the disease development (Gasser, Wichmann & DeLong 2014, 281-202; Website of Parkinson's Disease 2019).

There is a level of uncertainty when trying to understand the causality of the disease. For instance, unexpectedly, researches have distinguished cigarettes' consumption and Parkinson's disease. Moreover, long-term or massive smokers appear to be less affected in comparison to a non-smoker population. Similarly, caffeine is another incongruent factor in PD.

Under scrutiny of the researcher, some of the environmental factors are thought to be involved as risk factor, which include pesticides, herbicides and heavy metals. Unfortunately, it is not yet conclusive (Kouli, Torsney & Kuan 2018). Although, according to Gunnarson & Bodin (2017) the interrelation between PD and the exposition to pesticides is measured, withal approximately 50% augmented risks are noted. Hereof, the evidences identify the multifactorial components of the disease.

2.3 Epidemiology, Prevalence and Incidence

Recent studies have presented the Parkinson's diseases' worldwide pandemic mapping, but it remains still a challenge to interpret the values of occurrence. Nevertheless, some valuable information have been extracted from systemic analysis in PD. In this regard, PD's prevalence is predominant in western countries (America, New Zealand, Australia) compared to the eastern ones (Europe, Asia, Russia).

Ethnically, it appears that genetic plays a role and influences the dissemination of PD. Indeed, the researches show higher incidence in Caucasians, Hispanics or Latinos

population compared with Asiatic or Africans. Meanwhile, cross-evaluation on same ethnical groups as Afro-Americans and Africans demonstrated lesser incidence for the Africans. Conclusions, which are fingering a clout on the environmental factors (Abbas, Xu Ba & Tan 2017). Thus, PD is correlated with aging. This autoimmune disorder is in fact more frequent in older population, and it remains seldom health condition for individual being less than 50 years old. Remarkedly, statistics show that PD is also affecting men almost twice more than women (comparably, there is less obvious differences between the gender in Asian countries). In addition, some categorial heredities are aggravating factors as history of PD in the family is detected (Website of Mayo Clinic 2019).

In Finland, about 15,000 people are diagnosed with PD and the estimation of incidence appears higher in the rurality than in the urbanized regions (Isotalo, Vahlberg & Kaasinen 2016, 459; Website of Parkinsonlitto 2015). Hence, advantageously the population is seen still as rather homogenous, and the study conducted by Autere, Moilanen, Myllyla & Majamaa (2000, 107-109) provides interesting results in this regard. The likelihood, indeed, of genetical incidence of the disease within the territory emerges to be mostly a recessive inheritance rather than inheritance factor only.

2.4 Diagnosis and Measurement scale

The disease's medical diagnosis becomes a challenging exercise for health care professionals. The process requests time and numerous tests, which can affect psychologically a patient who needs to wait for his/ her test results (Website of Parkinson ORG- UK 2014). The roadway might feel often too long before a confirmation is given, and the 10% to 30% misdiagnosis are here to remind the difficulties to provide certainty to the examinee.

Several recommendations and diagnostics criteria have been proposed, and if common ground can be found, some distinctions are still brought to light. Among them the publication released by the United Kingdom Parkinson's Disease Society Brain Bank (UKPDSBB), the recommendation published by the American Academy of Neurology (AAN) (Marsili, Rizzo & Colosimo 2018) or the NICE guidance, which provide a

booklet of information (Website of NICE 2005). The European Academy of Neurology is another contributor, and its Task Force released a guideline, which classify the method of detection in three categories; Level A (effective), Level B (probably effective) and level C (possible effective). Their publication introduces clinical diagnosis criteria as genetic testing, autonomic function testing, olfactory tests, drug challenge tests, neurophysiological tests, neuropsychological tests and neuroimaging tests as processes of diagnosis (Berardelli et al. 2012, 16-34).

In practice environment, professionals are commonly adopting the Unified Parkinson's Disease Rating Scale-III (UPDRS-III) or the actualized version MDS- UPDRS, as a tool to control and to appraise the activities of daily living (ADL), the psychological and neuromuscular functions, the degree of severity or other complications (Website of International Parkinson and Movement Disorder Society 2019). The European Physiotherapy Guideline for Parkinson's Disease (2014, 23-25) refers to the common use of the Hoehn & Yahr staging scale in clinical settings. This scale serves to classify patients according to the disease evolution and its motor function disorders. It is important to notice that early stage in PD corresponds to mild symptomatic condition. The Hoehn & Yahr (table 1.) early stage is considered as uncomplicated phase (1 - 2), when the middle stage is recognized as the complicated phase with quality of life's deterioration (3 to 4). The late phase (5) is characterized by restriction to bed or wheelchair.

Table 1. Description of Description of the Hoehn and Yahr staging scale and disease phases (Website of Parkinsonnet 2020)

Scale	Description	Symptoms	Stage
1	One side engaged only; no functional disability or minimal	Mild	Early
2	Two side or axial engaged; No balance impairment	Mild	
3	Two side; mild to moderate activity limitations; reflex of posture impairment; physically autonomous	Moderate	Middle
4	Severe limitations of activity; walk or stand independently	Severe	Advanced
5	Restricted to bed to wheelchair and in need of assistant	Severe	

Moreover, there is an important concept to integrate in the understanding of the Hoehn and Yahr Staging Scale. In fact, if it is widely utilized in the medical assessment it does not resist a fool-proof requirement. The scale is examining the onset of symptoms and the ipsilateral versus the contralateral of occurrence, but researches has shown the complexity of the symptomatic resurgence (Berg & Bandmann 2013), it is not thoroughly accurate. Nonetheless, Hoehn and Yahr' scale provides when combine with other measurement an adequate valuation. Plus, in PD, individual can have same symptomatic disability in assessment although they had been diagnosed since months or years (Goetz, Poewe, Rascol & Sampaio 2004). For instance, two patients can be diagnosed on early stage, but one can have the disease in 2 years when the other one for 8 years.

2.5 Symptoms and cognitive changes in Parkinson's disease

Parkinson's disease affects primarily the central nervous system (CNS), which is a complex matrix of biochemical and physiological circuitry. Five milestones of motor symptoms characterize the disease; tremor at rest, bradykinesia, rigidity, impaired posture, and walking disorders (Website of Parkinson Australia 2019).

Firstly, tremors are external but also internal shaking manifestations. More commonly starting in an asymmetrical manner. This condition can affect head, jaw, upper or lower extremities. Secondly, bradykinesia is defined as a slow movement, which can also be observed with the decreased of facial expression "mask-like face". Thirdly, not only movement can be slow, but in the later stage of PD some or all body parts can present some rigidity. For instance, when a physiotherapist wishes to extend elbow of his patient, the movement is restricted, and greater force needs to be applied, which generate often "cog-wheel" movement type. The fourth's observable condition in PD, is the postural instability, where the patient cannot maintain the ideal steady position in standing. Consequently, this symptom increases the risk of fall as the centre of mass is displace further away to the body's medial line. Lastly, the walking pattern can be impaired with a modified gestural behaviour. In advance cases, it produces a "freezing of gait" phenomenon, where movement flow of action stops like a *"rabbit caught in the headlights"* (Kalia & Lang 2015, 896-912).

In the other side of the symptom's spectrum, the non-motor manifestations, for their parts, alter cognition abilities, vision, smell, bladder or sleep, but also, influence mental status with sensation of fatigue, pain, depression and/ or anxiety (Website of American Parkinson Disease Association 2019; Website of Parkinson's News Today 2019).
In the medical evaluation, the cognitive changes are ranged from mild (MCI) to dementia (PDD). On a related note, The Parkinson's Foundations (2019) identified that about half of the diagnosed patients experience heterogeneous cognitive impairments, as such as keeping their concentration, formulating an intellectual organization, producing and expressing vivid thoughts, or remembering an information (Weil, Constantini & Schrag 2018, 2). Why does it matter? When some activities like reading a book, following a conversation with friends, watching a piece of theatre, planning series of daily living activities become laborious, a person mental health is vulnerable (Rektorova 2019, 65-73).

In this context, the International Classification of Functioning, Disability and Health (ICF) holds a fundamental place within the healthcare's patient management process (Figure 1.). Thus, the disease is also highly rank in term of disability, which causes work ability and activities of daily living (ADL) problems (Schulman 2010).

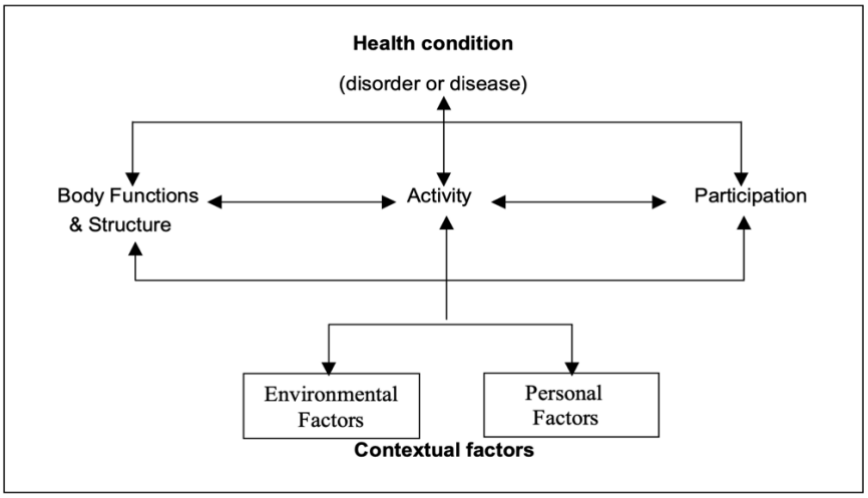


Figure 1. ICF model (World Health Organization 2002, 15).

Indeed, one physiotherapy needs to consider the health condition, body functions and structures, activity, participation, personal and environmental factors in the strategy of

optimizing his patient's outcome (Website of World Confederation for Physical Therapy 2019).

2.6 Pluri-disciplinary approach in treatment

Due to the intricacy of autoimmune diseases, the medical corpus understands nowadays that multidimensional approaches are to be foretokened to reach the optimum prognosis (Okun 2017). Furthermore, the PD's treatment satisfaction's survey published by Jost & Bausch (2017, 7-11), described that 51,3 % of the 4.485 patients have evaluated treatment's successfulness when the aforementioned one is addressing motor symptoms problems, but only 6,5% of them consider primarily the non-motors symptoms. Thus, merely 27,7 % of the subjects questioned have appraised as *good* or *very good* their PD's medication, when 86,7% considered quality of life improvement as valuable benchmark in their therapy. What could explain above appraisal from the patients? The answer can probably be found in the research conducted by Fahn & Jenner (2007), which states that drug's intake implies complication, and in later stage some *resistant symptoms*.

Subsequently, any therapy includes ideally patient education and comprehensive individual plan of care, with multi-disciplinary professionals. In point of fact, today's main treatments consist of medication, surgery, assistive therapies (physiotherapy, occupational therapy, speech and language therapy), nutrition and management of eventual side effects (Website of NSH 2019).

2.6.1 Medical treatment

If there is no cure yet or miraculous medicine available, the actual drugs aim to improve patient's experiences of the disease, to manage day-to-day life, as normal, as safe and as long as possible (Website of American Parkinson Disease Association 2019). Throughout the centuries of medical research in PD, balancing deficiency of brain's dopamine and/ or of acetylcholine have provided significant progresses. For instance, the combination of Levodopa (L-dopa) – Carbidopa has demonstrated great

results in term of decreasing the motor PD's condition as bradykinesia, rigidity and tremors at rest. Unfortunately, it is not without side effects and Carbidopa still can cause nausea or vomiting (Website of WebMD 2020).

Conversely, Deep Brain Stimulation (DBS) is invasive surgical intervention, where an implant (lead/ electrode) is placed deep-seated in the brain (in the thalamus' ventralis intermediate nucleus, in the globus pallidus pars interna, or in the subthalamic nucleus) to transmit electrical stimulation. This lead integrates a wire that receives its signal from a neurotransmitter normally located on the chest. Interestingly, the medical procedure is generally performed when patients are awake and conscious. It is a pain free intervention as brain has not pain sensory input. Furthermore, DBS is considered as an effective method to improve symptomatic occurrence in PD, when the device successfully interferes with the abnormal neuronal circuitry that causes tremors, bradykinesia (slow movement) or rigidity. Then, fluid gestures and diminished dyskinesia (involuntary movement) can be expected (Website of AANS 2019).

To summarize, numerous drugs or invasive treatments are utilized with intention of mitigating the PD' onset symptoms and prolonging the *off period*. But these interventions are implying short/ long-term risks also. Hereof, the scientific investigations have formerly demonstrated that physical activity is a valuable contribution to the therapy (Dietz 2013).

2.6.2 Physical activity

The World Health Organization (2018), defines physical activity (PA) as a generated purposeful action involving human's musculoskeletal system, while dispensing corporal's fuel. In the meantime, overwhelming evidences are available supporting PA in healthy individuals either in term of prevention, lifestyle or rehabilitation. However, with regard to Parkinson's disease, physical activity is generally recommended in consolidation of medical treatment intending to improve quality of life (see Figure 1. ICF model) (Bhalsing, Abbas & Tan 2018, 242-249). Thereby subjects submitted to PA can demonstrate superior endurance, balance, strength, proprioception, coordination, cognition, physiological and psychological functions, which bound back

on motor and non-motor symptoms (Website of Parkinson's News Today 2018). Uhrbrand, Stenager, Sloth Pedersen & Daglas (2015, 9-19) reports that intensive *resistance* and *endurance training* or *other intensive training modalities* results in achievable and reliable therapeutic exercises.

2.7 Physiotherapy

Physiotherapy (Pt) belongs to the multidisciplinary professions (up to 19 professions) involved in PD's intervention (Website of European Parkinson's Disease Association 2019, 1). What role does it plays? What the evidences show?

Firstly, physiotherapists are professionals that undertake ethic, compliance and rehabilitation as working fundamental requirement, as depicted by the World Confederation of Physical Therapy (Website of WCPT 2019). Hence, the professionals are also expected to invoke patient's rights, values and wishes. Secondly, according to Keus et al. (2014, 1) not only Pt is in front line of the Parkinson's burden in term of community's health and welfare, but this line of work also accompanies individuals in needs of care and support. One physiotherapist operates with multiple resources of regimen methods, but these become relevant only when client centeredness is first and foremost acknowledged. In this regard, The European Parkinson's Disease Association listed the different Pt's responsibilities; whereon, in the *Early stage* of the disease, alleviating sedentary behavior, promoting endurance, strength and body maximal function is critical. If the *Mid stage* includes the risk of falls, it also proposes to focus on postural quality, reaching, grasping, balance, transfers and gait; the *Late stage* is rather orientated to prevent any complications as such as breathing or pressure sores (Website of European Parkinson's Disease Association 2019, 2). This concedes on the complexity of establishing guidelines, as yet full understanding has to be found on why some exercises are more effective than others. conclusively, the idea, in which the earlier the subject exercises the better, won't raise much controversy (Schenkman, Hall, Barón, Schwartz, Mettler & Kohrt 2012, 1395-1410).

Thirdly, the goals of physiotherapy in PD is to stabilize or to increase functional capacity, which are allowing the patient to live independently. In this regard, addressing postural and balance impairment while exercising gait, is relevant to limit risk of falls. Activities of Daily Living (ADL) require strength and agility in all limbs but devoting cognitive, breathing and relaxing method is equally important (Website of European Parkinson Disease Association 2019, 3).

Fourthly, as per the nature of the disease, whereon deterioration of function and health condition is inevitably, physiotherapy resources likewise exercises have shown favorable implications in the life of people with PD. The modification can be observed through Unified Parkinson's Disease Rating Scale-III (UPDRS) notably. However, exercises must undoubtfully be individualized, and SMART (Specific, Measurable, Achievable, Realistic, Timely) goals are the opportune approach to be utilized by physiotherapists (Website of Physio-Pedia 2019).

According to the World Health Organization classification (2019), exercise is a subcategory of physical activity and stands as a practical means one physiotherapist can expect accretion. Hereof, questions spring up like mushrooms; can exercises be recommended in PD? If so, which exercises, at what doses and which of those are proven the most beneficial and safe?

Agreeably, "Walking is the best possible exercise. Habituate yourself to walk very far" is not directly extracted from scientific reviews but quoted from a letter written by Thomas Jefferson in August 1785; the text reveals the role of exercise at some point in time. Thus, in his letter addressed to Peter Carr (1770-1815), Jefferson (1743-1826) was recommending as substantial accredit a minimum of 30 minutes' walk on daily basis (Website of Yale Law School 2008).

In present day, guidances are mostly based on research, and an unprecedented amount of literatures present intensive exercise as most profitable for persons with PD. In this context, moderate to vigorous exercises are recognized to improve functions, and therefore quality of life. Nonetheless of the positive results in this matter, some clarifications need to be brought in term of dosage and timing, for instance (Ellis & Rochester 2018, 95-100).

Finally, in their publication Keus, Bloem, Hendriks, Bredero-Cohen & Munneke (2007) recommend six best physical therapy for patient with PD. The guidance encloses transfer, posture, reaching and grasping, balance and falls, gait, physical ability and performance. Hence, in the intention of promoting gait, treadmill appears to be a relevant point of association with the other therapy methods. For a longtime indeed, the apparatus has been used to implement exercises or scientific experiment, meanwhile its characteristic provides valuable sources of treatment according to Mehrholz, Kugler, Storch, Pohl, Hirsch & Elsner (2015).

2.8 Prevention

Patient education remains often the primary source of prevention, when physical activity provides an additional cost-effective approach. Some researchers claim that vigorous exercise is clearly beneficial and preventive for PD's health condition (Ramaswamy, Jones & Carroll 2018, 399-406). The query for a physiotherapist is from what a patient diagnosed with PD needs to be prevented or supported. Is treadmill a preventive and supportive apparatus?

The promotion of healthy lifestyle with integrative and regular exercise are assuredly appropriate resources. If Uehara et al. (2019) have disclosed promising results influencing gene of alpha-synuclein in mouse, their experimentations are still at the embryonic stage. As the health condition PD degrades, it is primordial to delay loss of motor and non-motor functions. Therefore, identifying risks factors that hinder therapy or accommodate symptoms' aggravation is certainly productive in term of prevention (Website of Stanford Medicine 2019).

Furthermore, non-motor disfunctions like low blood pressure, motor functions as postural impairment (center of mass' transition), overall joints mobility or muscle performance can affect the walking pattern's capacity, which increases the risk of fall. When posture is dysfunctional patient with PD are more likely to fall, consequently risking bony injury or trauma (Web site of Parkinson Foundation 2019).

If the risk increases by 50% in the population that have fall once at least, it can further generate more fear of falling. Most publications are recommending not only exercises (treadmill, balance, resistance trainings, stretching), but also advocate for the use of assistive aid, or activities like yoga or tai chi (Website of American Physical Therapy Association 2018). In this regard, treadmill is wildly used in sport, rehabilitation and research settings for performance's evaluation or therapeutic means. Prominently in the scrutiny of science, the device provides interesting characteristic in PD.

3 HEALTHCARE SERVICE: POHJOIS-HAAGA PALVELUKESKUS

Pohjois-Haaga Palvelukeskus (PHP) is an organization located in the north area of Helsinki that provides healthcare service for elderly in-outpatient. Administered by Helsinki City, the Center offers physiotherapy among diverse medical management for aged groups with Alzheimer, Parkinson's disease or other morbid conditions (Website of Helsinki City 2020).

4 THE FINNISH PARKINSON'S DISEASE ASSOCIATION

Since almost 30 years, the association conducts its work throughout more than 100 municipalities around Finland. Their ambition succeeded to assemble a community, gathering people diagnosed with Parkinson, healthcare specialist and public welfare's administrators. One organizer could claim effortlessly "stronger together!" as the association not only offers peer-support, but also provide some information and is central point of the latest discussion in PD (Website of Parkinsonliito 2019).

5 GAIT REHABILITATION

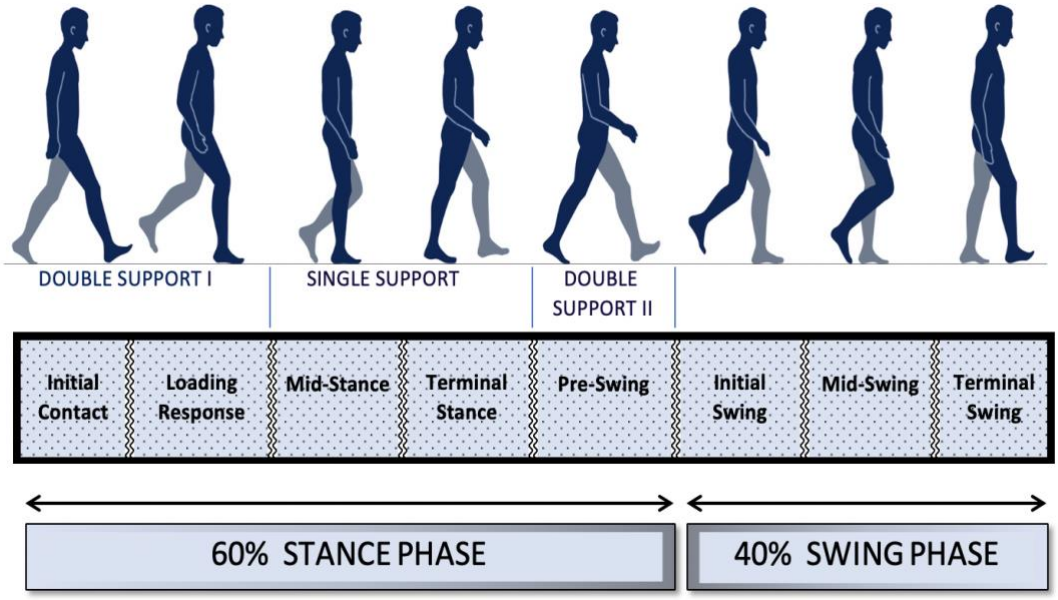
Gait is defined as a particular pattern of walking that engages full body (Website of Medicine Net 2018). Pathological walking patterns are classified as hemiplegic, diplegic, neuropathic, myopathic, choreiform, ataxic, sensory or parkinsonian gait (Website of Stanford Medicine 2020). An ideal walking requires optimal standing position, which is precisely one of the motor function default in PD; inability to maintain good posture (Giroux 2014). In term of rehabilitation, one physiotherapist consolidates his therapy plan by converging maximal function, participation and activity according to health's condition, environmental and personal factors, performance plus capacity (Website of WCPT 2019). When walking is impaired or unsafe, participation or other related functions can be affected (Bouça- Machado, Maetzler & Ferreira 2018, 121-130).

5.1 Gait model

In biomechanics, walking is considered more like a balanced displacement of mass through space defying gravity, than solely a propulsion generated by neuromuscular functions. The motion occurs efficiently with an ideal expectation of body parts sequences. In fact, walking with reciprocal movement in a contra-lateral manner and the overall assignment of motion from a steady position represent the basic movement of walking. Gait analysis allows measurement of stride length, biomechanics, kinematic, movement strategy, body control, and speed, which determine deviation from an ideal walking model (Website of Physio-Pedia 2 2019).

The term gait cycle describes the dicing of human locomotion, which follow a concatenation stimulus from brain to arms and toes. Precisely, a commend sent from the central nervous system is sent to the peripheral nervous system, which generates agonist muscle contraction, and relaxation of the antagonist muscle group. The motion describes a physical energy transmitted throughout the body displacing in sequence corporal segments in two main phases. The stance phase represents 60% of the cycle, when the swing phase serves for 40% of it. Furthermore, during walking the body

alternates between open and close chain (picture 5), which starts with heel strike (or initial contact), loading response, mid-stance, terminal stance, then the phase switches to pre-swing, initial swing, mid-swing and terminal swing (Website of Protokinetics 2018).



Picture 5. Gait Cycle (Leraillez 2020)

5.2 Parkinson' disease specificity

Individuals with PD can demonstrate walking complication already at the disease's onset. It is also an indicator of the disease's progression. The active postural control may be affected when shifting direction. Another recognizable characteristic (shuffling/ festinating gait) is seen when fastening speed but shortening stride length as the feet drag on the ground to gain assuredness. Among these problems the individuals may experience the specific freezing of gait. This syndrome is described as if one would be paralyzed by fear and ergo presents hesitations that temporarily illicit movement. The direct fallout is risk of fall, or risk of crossing a paved boulevard as the pedestrian greenlight as turn to red on the walkaway and vehicles are ready to take off (Website of Parkinsons Disease 2017). In fact, faulty gait places higher risks

at individuals with PD. Additionally these symptoms increase exposure for falls or other secondaries impairments (Piker & Katzenschlager 2016). Conclusively, it occurs that stimulating patient's auditory, ocular systems or corporal senses with respective rhythm, visual or physical cues, help to activate other brain pathways that elicit smooth control gait pattern and therefore by-passing the defected corticostriatal's pathways (Website of Parkinsons Victoria 2019).

6 TREADMILL

In 1952, Dr. Bruce and Dr. Quiton proposed for the first time to assess heart and lung diseases with a "medical" treadmill. Hereof, treadmill (Picture 6.) has proven its utility in countless research's field whereof stand amid the rehabilitation (Van Hooren et al. 2019).

Picture 6. Treadmill (Website of KindPNG. 2020)

The singularity of this machinery allows one to tread water while walking on wide rolling belt. The treadmill is a playmaker in PD's rehabilitation, contributing in exercises program that target gait overhauls, gait disturbances, cardiovascular system, or prevention of fall (Capodaglio et al. 2008). Lastly, as physical activity has been proved to be essential for maintaining or improving health condition, and by all means this thesis exposes the data of if treadmill exercise for gait's restoration in PD can bring *water to the sea* (Pelosin et al. 2017). The following chapters review the literature in a systematized manner and discuss the findings.

7 AIM AND OBJECTIVES

The aim of this thesis is to present the scientific evidence that determines if the treadmill exercises in gait rehabilitation for early stage PD is efficient.

The objective of this thesis is to conduct a systematized literature review, and to focalize to answer the following fundamental questions: if and how treadmill exercises can benefit to gait rehabilitation for Parkinson's diseases in early stage? What are the benefits in term of quality of life, fall prevention, freezing gait? How Pohjois-Haaga Palvelukeskus can interpret the result of the literature review, and implement treadmill exercises guideline or recommendation? In this topic, the objective also includes a discussion on the opportunities for the Pohjois-Haaga Palvelukesus in the use of treadmill exercise

8 TIMEFRAME, METHODOLOGY AND PROCESS OF RESEARH FRAMEWORK

This systematized review collects and reviews the literature applying unequivocal strategy protocol (Grant & Booth 2009, 102-103). The timeframe is represented in the chronological order of the process (table 2.; figure 2).

Table 2. Schedule of the thesis

	SCHEDULING THE THESIS
Week 19 - 39	Researching and defining thesis subject
Week 39 - 45	Building study plan and strategy
Week 47	Seminar presentation
Week 39 - 45	Theorical background research
Week 51 - 15	Writing the background information
Week 02 - 10	Starting the review and selecting the studies
Week 15 - 34	Writing the literature review
Week 36 - 38	Finalization
Week 41	Thesis presentation

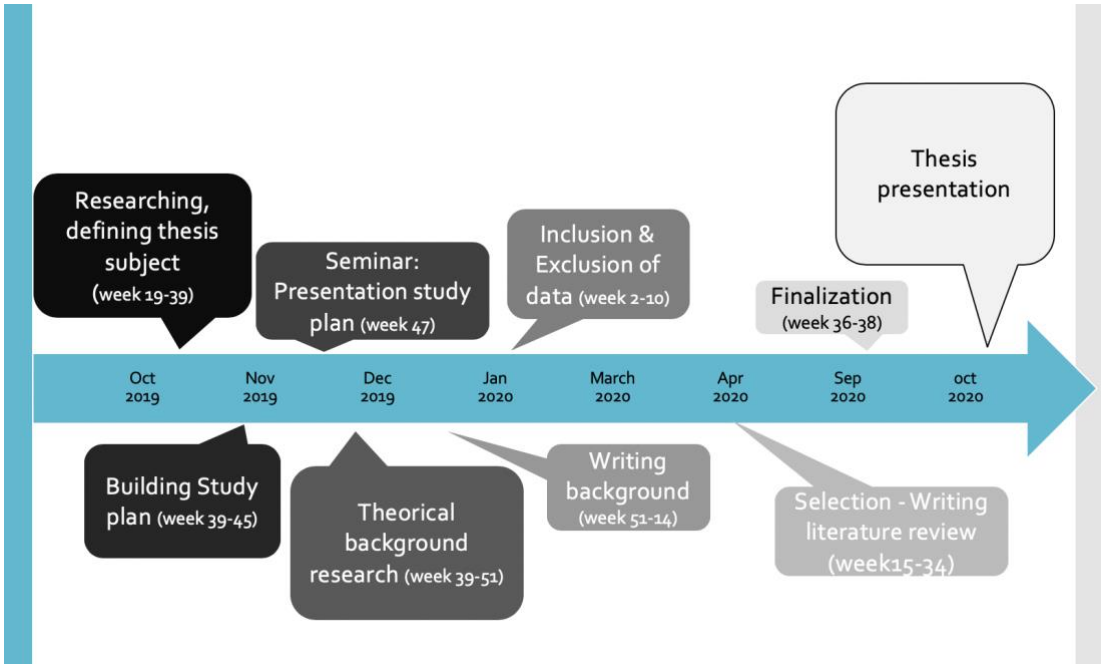


Figure 2. Timeframe of the thesis

The author is describing the process of research framework that can be distinctly verified, and three defined phases are presented as followed; firstly, the literature is extracted from the most selective database available in research (Table 3.) with related preferential keywords based on thesis' inquiry: *Effectiveness of treadmill exercise in*

gait rehabilitation for early stage Parkinson's disease (Table 4.). Secondly, the process circumscribes the research in criteria of inclusion and exclusion, which leads to a circumscribed and pertinent selection process (Table 5.). The collection of publications is based on Prisma 2009 checklist and is presented in the Prisma Flow Diagram (Moher, Liberati, Tetzlaff & Altman 2009). Thirdly, the PICO model (Website of Murdoch University 2020) is providing the resource for synthetization of the documentation that are screened and included in this review (Table 6. and 7.) (Website of EBSCO 2020). Fourthly, the National Institute for Health and Health Care (NICE) checklist model is used to evaluate risk of bias in the appraised scientific studies (Table 8.) (Website of National Institute for Health and Health Care, NICE 2020). Finally, the summery provides a gateway to the discussion that develops critical views on the topic tackled in this review (Adolphus, 2013, 1-10).

9 LITERATURE REVIEW

The purpose of a systematized literature review is to extract clusters and evidences of study questions through a determine process that can reproduce the applied methodology. For recall, the study question proposes to search evidence on *Effectiveness of full body weight treadmill exercise in gait rehabilitation for early stage Parkinson's disease*. The findings allow to picture the current knowledge, hereof, the author researches of if and how treadmill exercises can benefit to gait rehabilitation for Parkinson's diseases in early stage? What are the benefits in term of quality of life, fall prevention, freezing gait? How Pohjois-Haaga Palvelukeskus can interpret the result of the literature review and implement treadmill exercises guideline or recommendation (Xiao & Watson 2017)?

9.1 Review process, Strategy, Database and Inquiry

The review process demonstrates the component phases conducted in this systematized literature review to answer to the study question. Prima facie, the keys

terms formulated within the study question are submitted to research engines. Each of the five databases provided a list of articles that went through the pre-determined selection criteria. The chart flow PRISMA 2009 (Figure 3.) is implemented to refine, to screen, and to extract relevant data. At that point, the selected documentations are synthetized (table 6. and 7.) and evaluated (table 8.) through the NICE methodology checklist. Result and discussion are then presented formerly (Website of Groningen 2020, 1).

The search engines are selected as per their leading resources for medical scientific data. The table beneath names the databases utilized for extracting the scientific publication available in PubMed (Medline), PEDro, Science Direct and EBSCOhost. The number of studies per database is also provided (Paez 2017). To counterbalance eventual non-published articles that could propose divergent perspectives on the study question, the database OpenGrey was included in the search query.

Table 3. Database research tool

Database
PubMed (26 articles), Science Direct (18 articles), PEDro (22 articles)
EBSCOhost (37 articles), OpenGrey (0 article)

The table below introduces the keys words utilized to extract publications related to the query: *(Parkinson* disease) AND treadmill AND (exercise OR training) AND (gait OR walk* OR ambulation OR locomot*) AND (therapy OR therapeutic* OR rehabilitation OR treatment OR disorder OR freezing)*. The precited query is established with the support of the librarian dedicated personal from the University of Satakunta Applied Sciences (SAMK). It provides a wider extension of keys words for the database research. The search query for the OpenGrey database used the terms Parkinson* disease, treadmill, gait, walk*, ambulation, locomote* separately. Finally, the search displayed a total of 103 articles, of what 32 were duplication and therefore removed from the query.

Table 4. Inquiry terminology

Inquiry terminology				
Main Concepts	Treadmill	Parkinson's disease	Gait	Rehabilitation
Other research		Parkinson disease	Walking, ambulation, locomotion, disorder Freezing	Treatment, Therapy
MeSH-Terms		Parkinson disease	Gait Walking	

9.2 Criteria of exclusions and inclusions

The criteria of the exclusions and inclusions are listed in the table 4. The filtration included clinical trials, randomized control trials, grey literature, cohort and pilot studies, published in French and in English from 01.01.2010 to 29.02.2020. The selection incorporated data related to Parkinson's disease, gait or walking with treadmill exercises. All qualitative studies, meta-analysis and systematic reviews were rejected to avoid redundancy. Other limitations included none peer reviewed document and three or more on the Hoehn & Yahr Scale (table 1.).

Table 5. Criteria of exclusions and inclusions

Criteria of exclusions	**Criteria of inclusions**
Systematic literature review, Meta-analysis, Review	Cohort studies, Case & Pilot studies, Randomized Control Trial, clinical trial, grey literature
Articles edited before 01.01.2010	Articles edited till 29.02.2020
Not relevant to study question	Articles in full text or open access
Not Peer reviewed	Articles in English and French
Trials on animals	
Parkinson disease with ≥ stage 3 in Hoehn & Yahr scale	

9.3 Data analysis

The Prisma chart flow (figure 3.) provides information about the data's process conducted to extract documentation. 71 articles were screened and 51 were excluded as per the exclusions criteria, when some studies were not fully accessible, or were performed with animal sample. Hence, meta-analysis and systematic literature review were disregarded. The 20 publications remaining were scanned entirely and other filters were applied for articles out of scope, outside range of the early stage in PD.

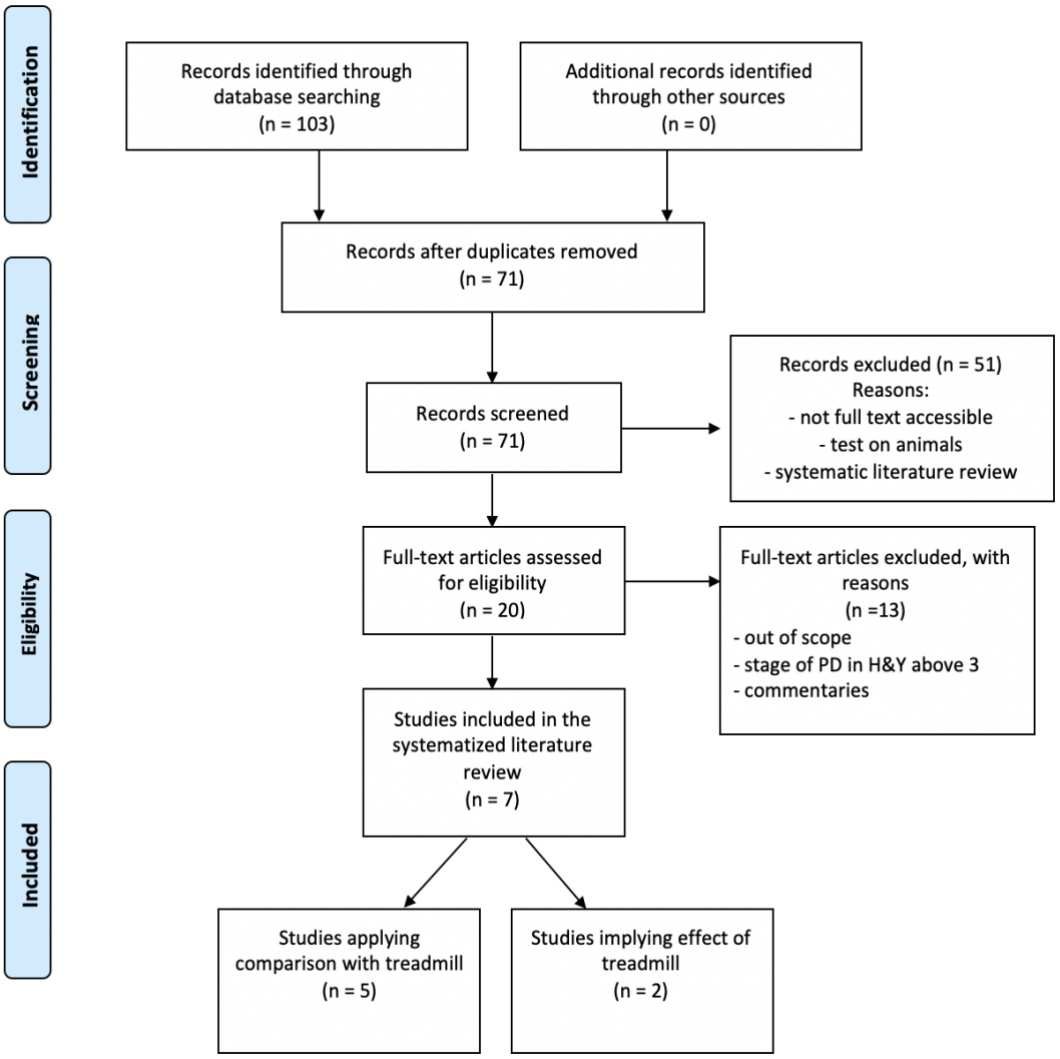


Figure 3. Prisma 2009 flow diagram (Website of Prisma-statement 2019)

The table 5. and 6. synthetize the relevant articles that have been screened for the review. Indeed, the author divided these articles in two distinct tables. The content in table 5. refers to two articles that centralized solely their research on treadmill training's effects in PD (Di Martino et al. 2018; Pelosin et al. 2017). Contrastingly, table 6. correlates documents that were conducted with a comparative mean between treadmill and robotic gait (Carda et al. 2012), treadmill and cycle ergometer (Arcolin et al. 2015), treadmill or overground walking (Fernández-del-Olmo et al. 2014; Fernández-Lago et al. 2015; Fernández-Lago et al. 2019).

Table 6. Synthetized table of articles investigating treadmill effects in PD

AUTHORS, YEAR, STUDY	TITLE, AIMS	POPULATIONAND NUMBERS OF SUBJECT	INTERVENTION	OUTCOMES
Pelosin, E. et al. 2017.	**Treadmill training frequency influences walking improvement in subjects with Parkinson's disease: a randomized pilot study**. Aim= to compare the efficacy of 3 different modalities in Treadmill for gait performance in PD patients.	13 participants with idiopathic PD Hoehn & Yahr 1-2.5-3. without cardiovascular dysfonction or other pathology	Total of 10 sessions of 45-minutes on treadmill walk for each group. Low frequency group trained 2-times/ week. Intermediary frequency group 3-times/ week. High frequency group trained 5-times/week. All participants had identical progressive training program. Starting with 90% speed on treadmill (matching overground comfortable speed). Then increase of 5% every 2 sessions to target objective at 115%.	Low frequency (Lf) training provide same benefits as Intermediary frequency (If), but not with High frequency. Worsening of fEs and 10mWT at 4 months follow-up for high frequency training but not for Lf and If. Lf improved TUG test.
Di Martino, S. et al. 2018.	**Aerobic rehabilitation program for improving muscle function in Parkinson's disease.** Aim= to evaluate the role of an aerobic and intensive rehabili- tation training on skeletal oxidative metabolism and l effects, to evaluate skeletal muscle oxidative efficiency.	60 patients, H&Y mean value 2,72 (+/- 0.89) without cardiovascular dysfonction or other pathology. 32 aged-matched healthy controls group	16 sessions of 1h15 minutes each. 2 phases, phase 1: of active and activie-assisted stretching exercises, posture stabiity and static and dynamic balance. Phase 2 aerobic training on treadmill at 80% of the 10mWT and then increase of 0.2km/h matching participant tolerance (65-80% of calculated maximum heart rate).	Significant high blood lactate levels in PD compare to healthy control group. Improvement of functional sclaes and significant decrease of lactacidemia during aerobic test. Treadmill shows benefits effect on balance and endurance. Measurement: Haematic lactate, cardiac & ventilatory parameters

Table 7. Synthetized table of studies focused of comparing treadmill with other modalities.

AUTHORS, YEAR	TITLE, AIMS	POPULATION	OTHER MODALITY	OUTCOMES
Carda, S. et al. 2012.	**Robotic gait training is not superior to conventional treadmill training in parkinson disease: a single-blind randomized controlled trial.** Aim= to estimate if robotic gait training with Lokomat provides improvement walking compared to treadmill training in PD	Idioapathic PD. 30 patients with no other disease or adverse health condiiton. <75 years old with early-stage PD (Hoehn-Yahr <3)	Treadmill vs. 50% and 30% body weight support on Lokomat	Robotic gait training is not superior to treadmill gait in early stage PD. Treadmill improves the effect of training in term of duration and timing. Improvement of the distance covered in 6MWT, o TUG and 10mWT. Efficacy in long-term results up to 6 months. Safe approaches.
Fernandez-del-Omo, M.A. et al. 2014.	**Treadmill training improves overground walking economy in Parkinson's disease: a randomized, controlled pilot study.** Aim= to find out the walking economy changes in response to a treadmill & overground training session, to compare the differences in the walking economy.	Idiopathic PD, 22 patients (13 males and 9 females). PD with no other disease or adverse health condiiton. range of H&Y from I to II.	Treadmill vs. Overground	Low volume & intensity walking exercise performed on treadmill improve efficiency of PD patients to walk overground at their preferred speed, by reduction in the walking energy expenditure. training on a treadmill is more beneficial than overground. Measurement of energy expendure and metabolic effects.
Fernandez-Lago, H. et al. 2015.	**Gait Pattern and Cognitive Performance During Treadmill Walking in Parkinson Disease.** Aim= to evaluate if attentional demand is involved in treadmill gait improvements in PD	Idioapathic PD. 19 patients (11 males adn 8 females) and 19 age-matched healthy control group. PD with no other disease or adverse health condiiton. range of H&Y from I to II	Treadmill vs. Treadmill dual task + Overground + Overground dual task	Gait improvement are not disturbed by attentional resources when patient with PD walks on treadmill. Treadmill can normalize the temporal variability and the spacial gait variability in PD. Treadmill improve gait. Measurement: Unified Parkinson Disease Rating Scale (UPDRS)
Arcolin, I. et al 2015.	**Intensive cycle ergometer training improves gait speed and endurance in patients with Parkinson's disease: A comparison with treadmill training.** Aim= if cycle ergometer training improve gait speed & endurance and comparing the effects between both training.	Idiopathic PD. 33 patients (15 males and 14 females) Hoehn-Yahr stage between 1.5 and 3. No other neurologic health condition and cardiological greenlight.	Treadmill vs Cycle ergometer	at 3 weeks treadmill can improve in short term walking tasks, balance and functional abilities Measurement: 6 Minutes Walking Test (6MWT), Time and Go (TUG), Mini.BEST, UPDRS, Wilcoxon signed rank test
Fernandez-Lago, H. et al. 2019	**Acute kinematic and neurophysiological effects of treadmill and overground walking in Parkinson's disease.** Aim= to explore short-term effects of a single session of treadmill & overground walking on gait, spinal and corticospinal context in PD.	Idiopathic PD. 15 patients (9 males and 6 females). Hoehn and Yahr 1.5-2	Treadmill vs. Overground	Treadmill walking single session improved short-term gait but not overground walking. Gait stride length and speed improved in 20 minutes session. Measurement Electromyography,Hmax/Vmax ratio, transcranial magnetic stimulation

9.3.1 Participants

The selected articles' population were diagnosed within less than three in the scale of Hoehn & Yahr (Website of European Parkinson Disease Association 2019), which correspond to early stage PD. Health conditions of the participants were assessed and their ability to perform different programs were also pre-tested. Hence, males and females represent a total number of 192 subjects, who carried on the disease for a various period of time. Totality of the studies performed their experimentation during the "on-state" curve. If most programs started between 45-minutes to 2-hours after medication intake, two studies did not specify the timing (Fernández-del-Olmo et al. 2014; Pelosin et al. 2017). The baselines were homogenic and did not present significant differences indeed.

9.3.2 Interest of intervention

All studies produced intervention model testing effects of treadmill. Among these, two of the seven research papers were evaluating treadmill physiological efficacy without comparison with other modalities. In the other hand, five publications measured the differences between treadmill effects and robotic gait (Carda et al. 2012), cycle ergometer (Arcolin, et al. 2015), treadmill and overground walking (Fernández-del-Olmo et al. 2014; Fernández-Lago et al. 2015; Fernández-Lago et al. 2019) cycle ergometer. Furthermore, Fernández-Lago et al. (2015) and Di Martino et al. (2018) selected healthy aged-match control group as referential.

9.3.3 Risk of bias

In the Guidelines of evaluation published by the OECD (2007), the term is defined as a concept assessing research, project, policy or organization in a methodical and equitable manner. Hence, *accountability* and *learning* principles are regarded as important in this review to correlate the review's findings with the study question.
On the grounds, relevancy, feasibility, reliability and validity are shaping the framework in term of data evaluation (Website of Société Suisse d'Évaluation 2019).

In this context, a critical appraisal checklist for randomized control trials is evidently appropriate, as to detect eventual risk of bias (Website of University of Groningen 2020, 2). Hereof, the selected studies are assessed through a methodological assessment tool that provides rigorous standard of evaluation. The below table presents the NICE methodology checklist (table 7.) for control trials, which is available on the Social care Guidance Manual (Website of NICE 2016, 1).

Table 8. Checklist risk of Bias (NICE 2016, 2)

	Carda 2012	**Fernández del-Olmo 2014**	**Fernández-Lago 2015**	**Arcolin 2015**	**Pelosin 2017**	**Di Martino 2018**	**Fernández-Lago 2019**
	RCT	Randomized Control Pilot study	Control trial	Randomized Control Trial	Randomized Control pilot study	Control trial	Pilot study quasi-experiment
An appropriate method of randomization was used to allocate participants to treatment groups	Yes	Unclear	N/a	Yes	Yes	N/a	Unclear
State method of randomization	Single Blinded, Computerized randomization	No	N/a	Yes	Yes	N/a	N/a
There was adequate concealment of allocation	Yes	Unclear	N/a	Yes	Yes	N/a	N/a
State method of allocation concealment	Yes	No	N/a	Yes			No
The groups were comparable at baseline including all major confounding and prognostic factors	Yes	Unclear	N/a	Yes	Yes	No	N/a
Based on your answers, in your opinion was selection bias present?	Low risk of bias	Moderate risk of bias	Low risk of bias	No	Low risk of bias	Low risk of bias	Low risk of bias
If so what was the likely direction of effect?		No baseline analysis accuracy					
The comparison groups received the same care apart from the	Yes	Unclear	N/a	Yes	Yes	Yes	N/a

intervention(s) studied							
Participants receiving care were kept 'blind' to treatment allocation	No	Unclear	N/a	Yes	Yes	Unclear	N/a
Individuals administering care were kept 'blind' to treatment allocation	Yes	Yes	N/a	Yes	Unclear	Unclear	N/a
Based on your answers, in your opinion was performance bias present?	Unclear	Yes	No	No	No	Unclear	No
If so, what was the likely direction of effect?	Groups were treated at different hours of the day; can it affect performance? (nutrition, sleeping condition, hydration)	Baseline differential statistic is not analyzed and there are significant differences in disease duration p-value 0.91					
All groups were followed up for an equal length of time (or analysis was adjusted to allow for differences)	Yes	Yes	N/a	Yes	Yes	Yes	Yes
How many participants did not complete treatment in each group?	2 (1 each group)	Unclear	0	0	0	Unclear	0
The groups were comparable for treatment completion	Yes	Yes	Yes	Yes	Yes	Unclear	Yes
For how many participants in each group were no outcome data available?	2	Unclear	0	0	0	Unclear	0
The groups were comparable with respect to the availability of outcome data	Yes	Unclear	Yes	Yes	Yes	Unclear	Yes
Based on your answers, in your	No	Yes	No	No	No	Unclear	No

opinion was attrition bias present? If so, what is the probable direction of its effect?		11 participants per group and if 1 drop out it is significant				60 participants with PD and 32 healthy control group but the study elude the completion of participation.	
The study had an appropriate length of follow-up	Yes	No	No	Yes	Yes	No	N/a
The study used a precise definition of outcome	Yes	Yes	Yes	Yes	Unclear	Yes	Yes
A valid and reliable method was used to determine the outcome	Yes	Unclear	Yes	Yes	Yes	Yes	Yes
Investigators were kept 'blind' to participants' exposure to the intervention	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear
Investigators were kept 'blind' to other important confounding and prognostic factors	Yes	Yes	Unclear	Yes	Yes	Unclear	Unclear
In your opinion, was detection bias present?	No	Unclear	Unclear	No	Unclear	Unclear	No
If so, what is the likely direction of its effect		How the turning OG was excluded?					
Comments	The research did not specify time of training this is generally questionable for consistence of results. measured at t0 but not after intervention	The research eludes several critical points. Is a Single session reliable?	The research is lacking detail of procedure	15 participants can be considerate as a small number	Interpreting recruits HY scale 1-2,5 as mild to moderate stages when allocating an early stage in the study by Pohl et al (HY scale from 1 to 3)	BMI is measured at t0 but not after intervention	15 participants can be considerate as a small number

Overall assessment	Low risk of bias	Moderate risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Unclear	Low risk of bias
Checker/ Re-checker	GM/ GM	GM/ GM	GM/ GM	GM/ GM	GM/GM	GM/ GM	GM/ GM

Note: 1. N/A, not applicable, RCT: Randomized Control trials. BMI: Body Mass Index. OG: Overground

9.4 Evaluation of outcome

It can be concluded that Fernández-del-Olmo et al. (2014) and Di Martino's et al. (2018) publication lacks information to estimate precisely the risk of bias, for instance there no clear data concerning if all participants completed the test or how many are included in the outcome measurement. Therefore, the overall assessment views these researches as moderate and unclear risk of bias respectively.

The study released by Pelosin et al. (2017) that introduced low frequency program as being more beneficial than high frequency program presents a confusing argumentation. In fact, in a chapter of the discussion, it is mentioned that the team's finding disputes the study by Pohl et al. (2017) claiming that highly intensive training affects stride length and speed (Pohl, Rockstroh, Rückriem & Mrass 2003). One of the reasons invoked by Pelosin et al. (2017) is the disparity between the stage of their respective PD population, which in the case of Pelosin et al. (2017) is mild to moderate (1 to 2,5) and early stage (1 to 3) in Pohl' study. There is clearly a misinterpretation of the Hoehn and Yahr Scale (both can be classified in the early stage range), which challenge the argumentation of outcome. Nonetheless, the publications from Carda et al., Arcolin et al. and Fernández-Lago et al. (2015) et Fernández-Lago et al. (2019) present low risk of bias, and their result provides analogous trends concerning effectiveness of treadmill in gait rehabilitation for early stage Parkinson's disease.

10 RESULTS

According to Carda et al.'s (2012) publication, robotic gait program is equivalent to treadmill but only this last provides substantial amelioration on 10-meter Walking Test. Fernández-del-Olmo et al. (2014) argued that 5 weeks low intensity treadmill exercise decreases energy expenditure remarkedly, compared to overground walking program. Posteriorly, Arcolin et al. (2015) juxtaposed intensive cycle ergometer and treadmill training. The outcome alleged that both modus operandum benefits gait skills, notably distance performance and balance. Similarly, Fernández-Lago et al. (2015) and her team investigated cognitive performance on treadmill, and the results disclosed that dual tasks exercise do not depresses treadmill walking efficiency.

More recently, Di Martino et al. (2018) measured the haematic lactate to scale the oxidative musculoskeletal metabolism, cardiac and ventilatory parameters along with intensive rehabilitation training. The aim was to evaluate aerobic stress during walking on treadmill. Indeed, Berg Balance Test (BBS) and the 6-minutes Walking Test improved after 4-weeks (16 sessions). Meanwhile, the researcher Fernández-Lago et al. (2019) in his investigation on acute kinematics and neurophysiological impact of treadmill compared to overground walking, came into conclusion that single treadmill exercise generates ambulation therapeutic effects.

Without exception, the seven reviewed trials assert in their findings that treadmill is developing ambulatory skills. Interestingly, Pelosin et al. (2017) focused on intensity of training by comparing low frequency (2-time per week) training to intermediate frequency (3-time per week) and high frequency (5-time per week). The results provide distinction that only low frequency and intermediary program significantly improve speed and risk of fall in a short and long-term.

11 CONCLUSION

Each of the studies argued that treadmill provides beneficial outcome, and rather in the speed, stride length, cardio-pulmonary system, distance or balance. Low or moderate intensity implies greater improvement that high intensity walking demand according to the analysis. Nevertheless, more research can be conducted to confirm this trend.

12 DISCUSSION

If all the studies concluded that treadmill exercises are beneficial and favors gait rehabilitation in early stage of PD, although different methods and aims were applied; a discussion need to be brought on the preceding results. In fact, only Fernández-Lago et al.'s (2019) primary findings are in concordance with Mehrholz, Kugler, Storch, Pohl, Elsner & Hirsch 2015's report that demonstrated speed and stride length improvement (Mehrholz Kugler, Storch, Pohl, Elsner & Hirsch 2015). Furthermore, the apparatus appears to have a good acceptance among the subjects in PD. Statement that can be correlated to Carda et al. (2012) publication as the patient's feedback. Treadmill can be used as a rehabilitation with the mean to improve gait pattern, but the potential population with dementia, heart disease, and other health condition should not be included in the target pool of participants. The conclusion postulated by Di Martino et al. (2018) is arguable as in inclusion of the treadmill program in understanding aerobic treatment for muscular system, stretching, dynamic and static postural control or balance were implemented. Hence, Rosenthal & Dorsey (2014, 156-157) demonstrated the effect of balance exercise in patient with PD. In this context, how much of the balance, strength, stretching training have had an influence on the result presented? This question remains on the work published by Di Martino et al. (2018) and his team.

There are still questions standing, as most of the studies displayed a rather small number of participants, which request to relativize the discovery (Martinez-Mesa,

González-Chica, Bastos & Bonamigo 2014). Additionally, all researches were performed within the medication window's effect, which may also influence measurement and therefore outcome. For this reason, the scientific papers that included healthy aged-match control group or treadmill training intensity comparison contributed to higher reliability when interpreting prevailing results.

Finally, based on evidence screened and presented the author can defend the concept that treadmill is efficient in gait rehabilitation to increase speed and stride length for Parkinson's disease in early stage, especially compared to overground workout. But, the specificity in which this equipment acts seems so far to be limited to stride length, speed of gait as strong evidence, when balance and endurance are apparently weaker ones. To conclude this discourse, treadmill physiological impact in PD is still under scrutiny of researchers, as all phenomenon are probably not yet exposed, and the one that have been theorized, are not explained yet in their exhaustive significance. Nevertheless, the concept depicted above is so far discussed consensually in the scientific community. Treadmill is efficient in gait rehabilitation.

12.1 From key questions to recommendation

How treadmill exercises can benefit to gait rehabilitation for Parkinson's diseases in early stage? According to the outcomes, it is obvious that neuroplasticity profits from treadmill training but there are no clear views on how long it can last. The cardiopulmonary system is challenged, and it allows the subjects to gain in endurance. Stride length increases also, and gait motor skill abilities promotes the transfer on overground walking (Mehrholz, Friis, Krugler & Twork S., Storch, A. & Pohl 2010, 1-28).

What are the benefits in term of quality of life, fall prevention, freezing of gait?
Physical activity is certainly a generator of life's quality improvement, but it has not yet been proved that the *ambulatory device* directly influences it. Nevertheless, it is possible to suggest that if one with PD profits in walking faster and with longer stride, it can contribute in his/ her activity, for instance, being able of crossing the road with a safer fashion. If such activity is important for the patient, then his/ her quality of life

can be induced. Freezing of gait is a phenomenon that can be by-passed when using auditory, or visual cues. In the study published by Frazzitta, Maestri, Uccellini, Bertotti & Abelli (2009, 1139-1143) it is advocating that combination of treadmill and visual or auditory cues affect positively the freezing of gait occurrence.

How Pohjois-Haaga Palvelukeskus can interpret the result of the literature review, and can implement treadmill exercises guideline or recommendation? The health centre can implement session for in/out-patient. Additionally, it is appropriated to introduce physical activity with treadmill as it is considered safe and cost effective, knowing that a physiotherapist can conduct sessions with several patients simultaneously (Earhart & Williams 2012).

PD provokes polysymptomatic resurgences, which requires multi-interventional therapies (e.g. postural control, balance, mood, smooth voluntary movement). The ICF model (Figure1.) is predominant in the patient management and physiotherapist need to consider the differential between performance and capacity characteristics (incidence in participation) within the environmental factors. Behaviour alterations are another facet of the disease and medication's side effects can trigger change in the state of mind, which consequently modify a patient's motivation. In this aspect, physical activity can actually influence advantageously a state of mind (Website of NHS 2019).

The guidance developed by the KNGF's task force proposes evidence-based management of patient with PD. Certainly, not only the questionnaire annexed in this guide support coverage ICF fields of action, but also measurement tools as the Berg Balance Test (BBS), the Modified Parkinson Activity Scale (M-PAS) and the Timed up and Go (TUG), the Mini-BEST test. For gait assessment, the Dynamic Gait Test Index (DGI) or the Functional Gait Assessment (FGA), the Six-Minute Walk Test (6-mWT), the 10 Meter Walk Test (10mWT). Interestingly, those evaluation tool have various sensitivity depending on the stage of PD determined by the Hoehn & Yahr scale (Keus et al. 2014, 39-74).

Currently, the evidence arbitrates strongly in favour of treadmill for improvement of stride length, gait speed, postural instability and freezing gait, but there are less

certitudes on balance, walking distance, movement functions (UPDRS), or cadence. Meanwhile, the machinery is considered safe especially when used with harness or automatic switch-off twine. This is a critical matter when utilizing treadmill in the treatment plan as home-based exercises, although risk of fall is seldom according to the ground rule. Authors recommend in their guideline, at least four weeks training three times a week for 30-minutes, at the overground preferred pace in the first week and then gradually increasing intensity. The use of the Borg scale at 13 out of 20 for the exertion perception, (14/20 with beta-blockers intake). Heart rate measurement can be applied, and moderate intensity is estimated from 40 to 60 % during the workout. Thus, physiotherapy can support the activity by introducing cognitive cues (Website of KNGF 2019).

Finally, there is case to be made as this literature review have not been able to resolve the relation between treadmill, cardiovascular system, and boost of dopamine released in the substantia nigra (Hou, Chen, Liu, Qiao & Zhou 2017; Knab & Lightfoot 2010, 133-150). In fact, dopamine is known as being a neurotransmitter for voluntary movement, examining the phenomenon further is surely a necessity (Petzinger et al. 2015, 29-39; Petzinger et al. 2007).

12.2 Actualizing methods and creating opportunity for community

Risk of fall, sedentary behavior or walking capacity are problematic in PD. There is also the performance (exercise executed in a clinical setting) versus the capacity (ability for a patient to apply the exercise in his personal environment) that need to be considered in the prognosis. Treadmill session is a complementary regimen to conventional physiotherapy, as recommended in the systematic review and meta-analysis by Ni, Hazzard, Signorile & Luca (2018).

Finally, the Founding Father John Adams (Website of Library of Liberty 2020) wrote a long-lasting statement, which point out that *"every problem is an opportunity in disguise"*. It makes sense in this circumstance to seek for solutions, as the world is currently facing a vile crisis, inflicted by the Corona virus (CO-VID19) since end of 2019 (Website of Finnish Government 2020; Website of Wealth Health Organization

2020). Many European countries have imposed or recommended confinement as safety measures, and in Finland, the capital Helsinki is under a total lockdown (Website of Iltasanoma 2020). Interestingly, a correlation can be made with research published by Canning, Allen, Dean, Goh & Fung (2012) concluding that semi-supervised home- based treadmill exercises are safe and provide improvement in walking skills, as the 6-MWT was measure as primary outcome. Those results are supported by the systematic review released by Flynn, Allen, Dennis, Canning & Preston (2019), which confirmed that home-based exercises are beneficial in PD and treadmill is indicating good outcome in a home-based environment. Therefore, there are possibilities to consider the treadmill for home exercises, if population at risk can gain from this approach, not only in case of a pandemic but also in the larger aspect too.

13 LIMITATIONS

The literature review's limitation is enclosed in the shortcoming of capturing contradictory data that could have been included in the research articles. The OpenGrey database did not provided any information on this matter.

14 DEVELOPMENT

The review demonstrated effectiveness of treadmill exercise in gait rehabilitation for Parkinson's disease in early stage. However, the results need to be interpreted with cautious as studies present low to moderate risk of bias. Nonetheless, empirical studies are univocal that the apparatus transfer neurophysiological component is patient with Parkinson's disease, and in this regard, it provides valuable treatment opportunities.

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