Wearable Health Technology

Subjects: Automation & Control Systems

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The occurrence of peripheral neuropathy (PNP) is often observed in Parkinson's disease (PD) patients with a prevalence up to 55%, leading to more prominent functional deficits. Motor assessment with mobile health technologies allows high sensitivity and accuracy and is widely adopted in PD, but scarcely used for PNP assessments. This entry provides a comprehensive overview of the methodologies and the most relevant features to investigate PNP and PD motor deficits with wearables. Because of the lack of studies investigating motor impairments in this specific subset of PNP-PD patients, Pubmed, Scopus, and Web of Science electronic databases were used to summarize the state of the art on PNP motor assessment with wearable technology and compare it with the existing evidence on PD.

Keywords: Parkinson's disease ; peripheral neuropathy ; Wearable technology

1. Introduction

Parkinson’s disease (PD) is a chronic and progressive neurodegenerative disorder, clinically defined by the presence of resting tremor, rigidity, and bradykinesia [1]. These features are collectively referred to as motor symptoms and mostly related to loss of dopaminergic neurons in the pars compacta of midbrain substantia nigra. Alpha-synuclein-positive intracytoplasmatic inclusions, known as Lewy bodies, are the pathological hallmark of the disease [2]. As the disease progresses, motor disturbances represent considerable illness burdens. Deficits in balance and gait are common and disabling features that significantly increase the patient’s risk of falling [3] and the managing of daily living activities [4].

PD is also characterized by strong clinical and neuropathological evidence of systemic involvement. The presence of Lewy bodies in several other nervous structures, such as the nervous fibers in the skin, indicate that peripheral nervous system (PNS) involvement may be an intrinsic part in the PD pathological process [5][6]. Since the PNS is a target of alpha-synuclein deposition, it is plausible that intrinsic pathogenic features of PD may predispose to peripheral neuropathy (PNP).

PNP refers to any disorder of the PNS including single and multiple mononeuropathies, symmetrical involvement of nerves (polyneuropathies), or isolated involvement of sensory ganglia (ganglionopathies) [7]. It usually starts gradually and presents in the most common types a distal-proximal gradient, affecting first the feet and later the hands [8].

The occurrence of PNP in PD (PNP-PD) has been shown to be present in up to 55%, compared to 8% in the general population with comparable age [9][10][11]. Typical features of PNP include postural instability, muscle cramps, and numbness, of which the latter two are more prominent at distal part of the legs. As both PD and PNP pathologies are associated with these symptoms, the concurrence of peripheral involvement could be considered as an additional cause of motor deficits and general worsening in PD [12].

PNP can worsen the global functional mobility of patients, since neuromuscular factors (hip strength, ankle proprioception, and decreased peripheral sensation) have been linked to gait and balance difficulties [13]. It is, therefore, plausible to hypothesize that PD patients with PNP (PNP-PD) may develop more prominent gait and balance deficits and, consequently, be at risk of falling, injuries, and reduced quality of life [14].

Wearables are constituted of all mobile devices worn on the body (also called on-body sensors), such as inertial measurement units (IMUs), smartwatches, or Holter electrocardiogram monitors [15]. They provide objective and quantitative measures from controlled and unsupervised environments, allowing the development of accurate treatment plans and disease monitoring. In particular, data obtained from IMUs can successfully estimate spatial-temporal parameters and provide sensitive and objective information about motor deficits of various neurological pathologies, which nontechnological motor assessments often cannot identify. Mobility assessment with wearable health technologies are widely investigated in a variety of illnesses, particularly in PD, and allows high sensitivity, accuracy, and reproducibility [16]. However, these methodologies are scarcely studied and have yet to be explored in PNP [17], although a small number of previous works using wearable sensors have successfully demonstrated motor and physical activity characteristics in PNP compared to controls [18][19]. Since the presence of PNP has only recently been considered related to PD, we were interested in understanding whether PNP-PD patients showed specific motor deficits, which can be measured with the use of wearable health technology. For such purpose, a preliminary review of literature performed by the authors showed no studies evaluating the functional impact of PNP in PD on mobility using wearables. Identifying specific gait and balance patterns in this specific subset of PNP-PD patients could provide additional information about gait and balance problems, which can be used to monitor and stratify patients, optimize treatment, prevent falls, and increase quality of life.

2. Sensor Type and Placement

2.1. PNP

Multiple wearable sensor types were used within the included articles to assess measures of gait and postural stability in PNP patients. Among the 24 included articles, the most commonly used inertial sensors included a tri-axial accelerometer and a tri-axial gyroscope (83.3% of the studies): LegSys™ and BalanSens™ (BioSensics), used, respectively, for gait and balance assessment; the Opal v1 (APDM) and the Physilog® (BioAGM) for balance assessment; the GaitMeter™ for gait assessment; and the mHT (mHealth Tecnologies) for both gait and balance assessment. Accelerometers only were used in two studies: PAMSys™ (BioSensics) and DynaPort Mini-Mod (McRoberts BV). One study used a gyroscope-based sensor (SwayStar device, Balance International Innovations GmbH) for balance assessment [20]. Sampling frequencies between 50 and 200 Hz were used to acquire the signals. The most commonly used sampling frequency was 100 Hz.

Several sensor placements and numbers of wearable sensors were used, depending on the task and on the type of assessment. Among the 16 included studies analyzing gait in PNP, four papers (25%) used one sensor, four studies (25%) analyzed gait with sensors on both shanks (two sensors), one paper (6.25%) used four sensors, and six studies (37.5%) assessed gait with five wearable sensors placed on thighs, shanks, and lower back. One study did not report sensor placement (6.25%).

Postural stability was assessed in 13 studies: Three studies (23%) used one sensor on the lower back, five studies (38.6%) used two sensors, and two studies (15.4%) used three sensors on both shanks and lower back. The remaining three studies (23%) utilized five sensors (Figure 1, Table 1).

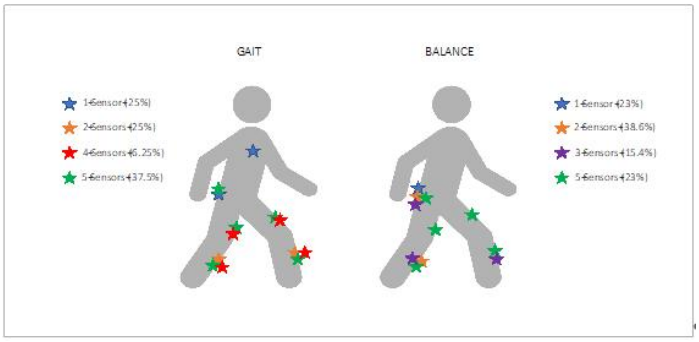

Figure 1. Anatomical representation of sensor placement for gait and balance assessment in patients with polyneuropathy (PNP).

2.2. PD

There is currently no consensus available on the optimum number and placement of sensors to measure PD symptoms. All reviews included that evaluated sensor number and placement showed that the majority of the studies used one sensor placed on the lower back (at lumbar vertebrae level L3, L4–L5, sacrum, or waist) or on the dominant lower limb (thigh, shank, ankle, or foot). Single sensors seemed sufficiently robust for all applications: For gait assessment at home, one sensor was used in 28% to 47% of the studies [21][22][23], while for gait evaluation in the laboratory it ranged from 44% to 69% [24][25]. Not surprisingly, for balance assessment the use of one sensor, and specifically on the lower back, was preferred in 77% to 100% of the studies included in the reviews [25][26][27]. Other most commonly used sensor placements for PD were on both wrists or lower limbs (in 30% of studies) or on lower back and both lower limbs (in 14% of studies) for the home assessment and at both lower limbs (8% of the studies) for laboratory assessment (Table 2).

3. Parameters and Main Outcomes

3.1. PNP

We included 24 original full-text manuscripts: Eleven studies (45.8%) investigated gait, eight (33.4%) analyzed balance, and five (20.8%) evaluated both gait and balance in PNP patients.

Gait was assessed mainly during a straight walking task at preferred gait speed, with a distance varying from 7 to 50 m. In two studies patients were asked to perform a 90° turn during walking [28][29]. Several parameters were calculated from the signals acquired through the wearable sensors. The most commonly reported parameters computed from the filtered signals were spatiotemporal gait parameters: gait speed (m/s), stride and step length (m), stride and step time (sec), number of steps, double limb support time (%), and cadence (steps/min). Coefficient of variation (CV) of gait speed and stride length and time (%) was calculated in eight studies [28][29][30][31][32][33][34][35]. Gait speed initiation, number of steps, and total distance required to reach steady-state walking were studied in four papers [33][34][36][37]. Duration (%) and number of walking bouts were extracted in one study [18].

Clinical trials among the included papers did not show any statistically significant changes in the gait parameters when comparing pre- and post-intervention. Najafi [38] analyzed gait differences between intervention and control groups after plantar electrical stimulation in DPN patients and Schwenk et al. [32] evaluated gait after a new interactive training in CIPN subjects. Nevertheless, the effect size of these studies suggested the presence of a moderate to large improvement of cadence and gait speed post-treatment. In contrast, Caronni [39] compared the responsiveness to rehabilitation in a group of PNP patients and found a statistically significant difference in gait speed between groups (p = 0.001, Table 1). Spatiotemporal parameters were significantly different between PNP patients and healthy controls only in studies investigating gait under more challenging conditions. Kang et al. [31] described a statistically significant difference between DPN and healthy participants in the coefficient of variation of gait speed and stride length during dual-task gait. De Bruin et al. [40] found significant differences in speed, step length, and cadence when comparing DPN patients during dual-task walking on paved trajectories compared to single-task. Another study by Kang [41] showed improvement in stride velocity, stride length, and double limb support (%) during dual-task and fast walking, compared to single-task, after plantar mechanical stimulation. Differences from controls were found in step time, cadence, and gait speed but not in stride length in a study by Esser et al. [17], and gait speed was also 10% decreased in DPN group compared to controls in a study by Ling et al. [30]. Another important result was pointed out by Najafi et al. [33], who found differences in spatiotemporal parameters only during long distances, especially in gait variability and in double support time, when comparing DPN patients with controls. These differences were more pronounced during barefoot walking.

Balance and postural stability were investigated through numerous tasks. The most frequently used task in all 13 studies was the double leg stance performed in different conditions:

- Position of feet: Standing balance was assessed with feet together in eight (61.5%) studies, feet apart (spaced shoulder width) in two studies (15.3%), and both feet positions in one paper (7.6%), while two papers (15.3%) did not specify the position of the feet. In two studies patients were also asked to perform a semi-tandem position [32][42], while one other study introduced a detailed balance test protocol with single leg stance [20].
- Open and closed eyes: Twelve studies (92.3%) analyzed balance with both open and closed eyes, and one study only used eyes-open condition [43].
- Foam: Two studies used a foam surface (height 10 cm, density 25 kg/m3) to analyze balance [20][42]. The other papers only performed balance tasks on firm surfaces.

Other tools to assess postural stability were clinical tests such as the functional reach test [44]. Functional tests (to investigate functional mobility, addressing both gait and balance characteristics) were performed in three selected studies [39][41][44]. They applied the timed up-and-go (TUG) test. This test was split by Caronni et al. [39] into five subphases, and the duration of each phase was measured, as well as the total TUG test duration.

The included studies reported multiple outcomes of standing balance and postural stability that were calculated from the signals provided by the wearable sensors (Table 1). Of these outcomes, the most commonly reported measures included center of mass (COM) sway (cm^2), defined as total sway (in seven studies, 53.8%), and related parameters (anterior-posterior (AP) and medio-lateral (ML) sway (cm)). These parameters were also reported in three studies analyzing gait to investigate balance control during walking and gait initiation [33][34][37]. In addition, ankle sway (deg^2), hip sway (deg^2), and COM sway area (m^2) were calculated in six papers (46.1%). Center of gravity (COG) sway (cm^2), COG AP, and COG ML (expressed in cm) were calculated in one paper [45]. Other parameters were root mean square (RMS, m/s^2), trunk acceleration, and trunk jerk (m^2/s^3) [39][46]; postural coordination of upper and lower body (defined as the reciprocal coordination between hip and ankle motions) [36]; roll and pitch velocity (deg/sec) and roll and pitch angle (deg) [20]. Further parameters were local (in short time intervals, sec) and central (in long time intervals) control balance strategies [45], and cross-correlation function (CCF) of angular velocity to investigate the coordination of human movements [46].

A significant reduction in COM sway area (a parameter of postural sway) was shown by Schwenk et al. [32] and Grewal et al. [47] after an interactive sensor-based balance training and by Yalla et al. [44] after an intervention on postural stability with an ankle foot orthosis. These results were found during balance tasks with open eyes, while, interestingly, no significant reduction was found during closed-eyes condition. In contrast, changes of the parameters COM sway area and ML sway area were significant after a virtual reality intervention with eyes-closed and -open conditions [35].

3.2. PD

In PD, a multiplicity of parameters derived from inertial sensors could be described. For the purpose of this review, parameters from the upper part of the body (upper limb) were not considered. The included reviews listed a series of most relevant spatiotemporal parameters representative of five domains (pace, variability, rhythm, asymmetry, and postural control), which included stride length, stride velocity, cadence, double support time [48][49], and turning velocity [50] followed by step time variability [25][48] and step height, reaction time, and gait cycle duration [51]. Frequency-based measures were dynamics in trunk movement during gait, turning and smoothness [52], harmonic ratio, amplitude, slope and width of dominant frequency, peak trunk horizontal velocity, and phase coordination index of gait cycle [25]. Number of steps, single versus multiple step response, turning duration, turn-to-sit duration, and sit-to-stand and stand-to-sit time- and amplitude-based measures were reported to be important features to determine gait impairment [51]. In more detail, PD patients have been shown to have slower gait, less foot clearance, smaller step lengths, lower turning velocity, lower cadence, and lower peak trunk rotation compared to controls [48][50]. Turning velocity, cadence, and peak trunk rotation were associated

with disease progression [53]. Another important parameter in PD is gait variability, also referred to as unsteadiness and arrhythmicity of stepping [54]. Increased gait variability can be seen throughout the disease, and the magnitude of the variability tends to increase with disease severity [48].

Home assessment may have greater ecological validity and gives a true picture of the burden of disease [15]. Parameters that may be particularly relevant for this assessment type are walking bouts (total number of walking bouts, median number of steps per bout, bout duration), turns per hour during the day, duration of each turn, number of steps per turn, peak and average rotational turning rate, and variability of these measures throughout the day and week [22][23].

Regarding standing balance and postural stability, often used parameters were postural sway velocity, RMS accelerations, and jerk [27]. Parameters that may discriminate most effectively between PD and controls are sway area, sway velocity, jerk index, sway amplitude and range of acceleration signals (time domain), and frequency dispersion and centroidal frequency [26][48] (Table 2).

All these features are able to differentiate between PD and healthy controls (HC) at early stage [25][48], different PD stages [27], different medication states in advanced PD, and PD progression (in particular sway dispersion and sway velocity) [48]. Postural sway is also a good measure of balance control to be used as a primary outcome for interventions [48].

Table 1. Summary of the major characteristics of the research design, analyses, and outcomes for the studies on PNP that met the inclusion criteria.

REFERENCE	POPULATION (Mean Age ± SD)	SENSORS (Number and Type)	SENSOR PLACEMENT	ASSESSMENT PROTOCOL	PARAMETERS EXTRACTED/INVESTIGATED/C
Ling et al., 2020 [30]	· 12 DPN + DFU (55.6 ± 3) · 27 DPN (64.3 ± 1) · 47 Healthy controls (62.9 ± 2)	5 Inertial sensors (ACC, GYR and MAG) (LegSys™, BioSensics) Freq: 100 Hz	· Thighs · Shanks · Lower back	Straight walking test at preferred speed for 10 m on a flat floor	· Gait speed and gait s unsteadiness, stride length and s unsteadiness, gait cycle time, dou support and double support limp, limp, gait symmetry

Kang et al., 2020 [36]	· 38 DPN (72.6 ±5) · 33 Healthy controls (77.9 ± 8)	5 Inertial sensors (ACC, GYR and MAG) (LegSys™, BioSensics) Freq: 100 Hz	. Thighs . Shanks . Lower back	Straight walking test at preferred speed for 12 m on a flat floor at two conditions: during single and dual (cognitive) task	· Number of steps and reach steady-state gait · Gait speed and body mediolateral direction in the gait i phase and steady-state gait spee
Kang et al., 2020 [31]	44 DPN + CIPN: · 25 PNP without cognitive impairment (66.5 ± 9) · 19 PNP with cognitive impairment (68.5 ± 9)	2 Inertial sensors (ACC, GYR and MAG) (LegSys™, BioSensics) Freq: 100 Hz	. Shanks	Straight walking test at preferred speed for 12 m on a flat floor at two conditions: during single and dual (cognitive) task	· Coefficient of variatio gait speed, stride length and strid · Spatio-temporal gait parameters: gait speed, stride ler stride time

Kang and Najafi, 2020 [18]	· 49 PNP (DPN+ CIPN) (68.5 ± 7)	1 accelerometer (ACC) (PAMSys™, BioSensics LLC) Freq: 50 Hz	· Chest	48-h period recording	· Durations of standing · Sedentary posture · Total number of walki · Number of total steps

Zahiri et al., 2019 [55]	· 84 subjects with cancer (CIPN+ and CIPN-) (71.1 ± 9) · 57 Healthy controls (69.5 ± 9)	5 Inertial sensors (ACC, GYR and MAG) (LEGSys™and BalanSens™; Biosensics LLC) Freq: not reported	· Shanks · Thighs · Lower back	· Gait assessment: single-task (no cognitive distraction) over 15 m at a self-selected speed. · Balance: double leg stance 30 s with feet close together during eyes-open and eyes-closed situations.	· Gait parameters: stric stride length, stride time and dou time. · Balance parameters: ankle sway, area of hip sway, are of mass (CoM) sway, and CoM s medial- lateral (ML) direction.

Kang et al., 2019 [41]	• 30 DPN (68.1 ± 9)	• Gait assessment: 5 Inertial sensors (ACC, GYR and MAG) (LEGSys™, Biosensics) • Balance assessment: 2 Inertial sensors (ACC and GYR) (BalanSens™, Biosensics) Freq: not reported	Gait assessment: · Shanks · Thighs · Lower back Balance assessment: · Dominant leg · Lower back	• Gait: 10 m walking test at normal and fast pace, and at two conditions: single and dual tasks. • Static balance: (i) double leg stance for 30 s with feet together with eyes open and eyes closed (EC). (ii) semi-tandem stance for 30 s • Global functional mobility: TUG test	• Gait parameters: stride velocity, length, stride time and double su time. Balance parameters: area of ank area of hip sway, area of center o (CoM) sway, and CoM sway in th lateral (ML) direction.

Fino et al., 2019 [43]	• 216 CIPN+ (63.0 ± 6) • 218 CIPN- (62.2 ± 6) •49 Healthy controls (63.3 ± 6)	1 Inertial sensor (ACC and GYR) (Opal v1, APDM) Freq: 128 Hz.	• Lower back	Double leg stance test with eyes open for 30 feet apart	AP-sway, ML-sway, or resultant s

Caronni et al., 2019 [39]	• 25 PNP-LL (76.5 ± 6)	1 Inertial sensor (ACC and GYR) (mHT, mHealth Technologies) Freq: 100 Hz	• Lower back	• Gait: 10 m walking test and TUG test repeated five times each. • Static balance: double leg stance for 30 s with (i) feet apart (FA) and eyes open (EO), (ii) feet apart and eyes closed (EC), (iii) feet together (FT) and eyes open an (iv) feet together and eyes closed.	• Gait: 5 subsequent phases of T to stand (STS), walk 1 (W1), turn walk 2 (W2) and turn and sit (TAS of each phase and total TUG dur (TTD); mean vertical angular velc turn 1 and during TAS • Root mean square (RMS), trunk acceleration (Trunk acc) and trun (Trunk jerk).
Findling et al., 2018 [20]	• 11 CIDN (chronic inflammatory demyelinating polyneuropathy) (61.1 ± 11) • 10 not inflammatory PNP (68.5 ± 11)	1 gyroscope SwayStar device (GYR) (Balance International Innovations GmbH) Freq: 100 Hz	• Lower back	12 stance tasks: • 4 double leg tests with the feet spaced shoulder width apart; • 4 tasks with eyes open on a normal surface and on a foam surface (height 10 cm, density 25 kg/m3)± and eyes closed. • 3 single leg stance tasks with eyes open, 2 on a normal surface (right and left leg) and 1 on the foam surface. • 1 task with single leg standing. 5 tasks for dynamic balance: • 8 steps tandem gait • 3 m walking on heels • 3 m walking pitching the head up and down • 3 m walking with eyes closed and 8 m walking with eyes open	Global balance control index (BC sway and trunk velocity

Esser et al., 2018 [17]	• 17 DPN (63 ± 9) • 42 Healthy controls (61 ± 4)	1 inertial sensor (ACC and GYR). Freq: 100 HZ	• Lower back	• Gait: 10 m at normal and fast pace	Step time, cadence, stride length speed
Najafi et al., 2017 [38]	• 28 DPN: 17 intervention group (56 ± 5) • 11 Healthy controls (64 ± 10)	• Gait assessment: 2 Inertial sensors (ACC, GYR and MAG) (LEGSys™, Biosensics) • Balance assessment: 2 Inertial sensors (ACC and GYR) (BalanSens™, Biosensics) Freq: not reported	Gait assessment: • Shanks Balance assessment: • Dominant leg • Lower back	• Gait: 10 m at normal and fast pace • Balance: double stance for 30 s with feet close together (without touching), with eyes open (EO), and eyes closed (EC).	• Gait: Stride velocity, stride time, length and cadence. • Balance: COM anterior-posterio sway, medial-lateral (ML) sway, a sway area

Schwenk et al., 2016 [32]	• 22 CIPN (70.3 ± 8)	• Gait assessment: 4 Inertial sensors (ACC, GYR and MAG) (LEGSys™, Biosensics) • Balance assessment: 3 Inertial sensors (ACC and GYR) (BalanSens™, Biosensics) Freq: not reported	Gait assessment: • Shanks •Thighs Balance assessment: • Shanks • Lower back	• Gait: 10 m at normal pace • Balance: double stance 30 s with feet close together (without touching), with eyes open (EO), and eyes closed (EC), and semi-tandem position with EO.	• Gait: gait speed and variability • Balance: COM AP sway and ML sway and ankle sway

Toosizadeh et al., 2015 [45]	• 18 DPN (65 ± 8) • 18 Healthy controls (69 ± 3)	2 Inertial sensors (ACC and GYR) (BalanSens™, Biosensics) Freq: not reported	• Ankle • Hip	2 Romberg balance trials (with open and closed eyes) for 15 s	Center of gravity (COG) sway (to and COG (AP) sway, COG (ML) s (in short time-intervals) and centr time intervals) control balance str

Grewal et al., 2015 [47]	• 35 DPN: 19 intervention group (62.5 ± 7) • 16 Healthy controls (64.9 ± 8)	5 Inertial sensors (ACC, GYR and MAG) (LEGSys™, Biosensics LLC) Freq: 100 HZ	•Shanks •Thighs • Lower back	Double leg stance for 30 s with open and closed eyes and feet together	COM sway, COM AP, COM ML sv sway.

Yalla et al., 2014 [44]	• 30 DPN (73 ± 6)	5 Inertial sensors (ACC and GYR) (BalanSens™, BioSensics LLC) Freq:100 Hz	•Shanks •Thighs • Lower back	• 6 double stance of 30 s trials (2 for each footwear condition during eyes-open and eyes-closed) with their arms crossed, feet positioned closeto each other without being in contact. • Dynamic balance: Functional reach task • Global functional mobility: TUG test	Ankle, hip, and COM sway

Karmakar et al., 2014 [28]	• 19 NeP-DPN (65.7 ± 10)	2 Inertial sensors (ACC and GYR) (GaitMeter™) Freq: not reported	•Shanks	Straight walking test at preferred speed for 50 m on a flat floor and a 90° turn without rest time.	Step length, step velocity, gait va

Najafi et al., 2013 [33]	• 12 DPN (60 ± 12) • 8 Healthy controls (60 ± 6)	5 Inertial sensors (ACC and GYR) (LEGSys™, Biosensics LLC) Freq: not reported	•Shanks •Thighs • Lower back	Straight walking test at preferred speed for 7 m (short distance) and 20 m (long distance) at two conditions: barefoot and with regular shoes.	Gait initiation velocity, stride velo variability, average range of moti and AP- CoM during each stride, support time, stride time, stride le number of steps.

Lalli et al., 2013 [29]	• 20 DM (60.2 ± 13) • 20 DPN (62.6 ± 9) • 22 NeP-DPN (63.9 ± 9) • 24 Healthy controls (58.8 ± 11)	2 Inertial sensors (ACC and GYR) (GaitMeter™) Freq: not reported	• Shanks	Straight walking test at preferred speed for 50 m on a flat floor and a 90° turn without rest time.	Gait variability, cadence, step len velocity and total duration of walk

Kelly et al., 2013 [34]	• 16 DPN (73 ± 8) • 18 DM (62 ± 8)	5 Inertial sensors (ACC, GYR and MAG) (LEGSys™, Biosensics LLC) Freq: not reported	•Shanks •Thighs • Lower back	Straight walking test at preferred speed for 20 m on a flat floor	• Gait: stride velocity, stride lengtl time, double support time, gait sp variability, steps required to reacl state walking, AP and ML COM s walking
Grewal et al., 2013 [35]	• 29 DPN (57 ± 10)	2 Inertial sensors (ACC and GYR) (BalanSens™, BioSensics LLC) Freq: 100 Hz	• 1 Shank • Lower back	Double stance position for 30 s at open and closed eyes (width not specified)	COM sway (AP and ML) and swa Postural coordination between th and lower body (in the mediolate anteroposterior directions)

Grewal et al., 2013 [37]	• 16 DPN + DFU (58.3 ± 4) • 15 DPN (54.2 ± 11) • 8 Healthy controls (59.6 ± 6)	A set of Inertial sensors (LEGSys™, Biosensics LLC) (ACC and GYR) Freq: not reported	Not reported	Not reported	Stride velocity, stride length, gait double support time, AP- and ML sway area, knee range of motion variability, number of steps and to distance required to achieve gait state

Turcot et al., 2012 [46]	• 25 DPN (63.5 ± 7)	3 Inertial sensors (ACC and GYR) (Physilog®, BioAGM). Freq: 200 Hz	• Shanks • Lower back	Double leg stance for 30 s with open and closed eyes (width not specified)	Angular velocity at trunk and ank two terms: RMS and with cross-c function (CCF), to investigate the coordination of human movemen control. CFF was calculated betw and right ankle, trunk and left ank and left ankle.

de Bruin et al., 2012 [40]	• 29 DPN (with and without PNP) (61.9 ± 5)	1 accelerometer (DynaPort Mini-Mod, McRoberts BV) (ACC) Freq: not reported	• Lower back	Walking at preferred velocity under two conditions. Single task: walking on the walkway; dual task: walking on the walkway with a counting task. The walkway contained a paved trajectory, cobble stones, and gravel rocks	Step time, step length, velocity, c

Najafi et al., 2010 [42]	• 17 DPN (59.2 ± 8) • 21 Healthy controls (24.4 ± 1)	2 Inertial sensors (ACC, GYR and MAG) (BalanSens™, Biosensics) Freq: not reported	• 1 Shank • Lower back	Double leg stance for 30 s with open (EO) and closed eyes (EC) and feet together, with firm and foam surfaces.	COM sway area, hip and ankle m

ACC: accelerometer; AP: anterior-posterior; CIDN**:** chronic inflammatory demyelinating polyneuropathy; CIPN: chemotherapy-induced peripheral neuropathy; COG: center of gravity; COM: center of mass; DFU: diabetic foot ulcer; DM: diabetes mellitus; DPN: diabetic peripheral neuropathy; **Freq**: sample frequency; GYR: gyroscope; MAG: magnetometer; ML: medio-lateral; NeP-DPN: neuropathic pain diabetic neuropathy; PNP-LL: peripheral neuropathy of the lower limbs; TUG: timed up-and-go test.

Table 2. Summary of the major characteristics of the PD reviews that met the inclusion criteria.

REFERENCE	REVIEW CHARACTERISTICS	NUMBER OF STUDIES INVESTIGATING PD	SAMPLE SIZE (H&Y Stage)	SENSORS (Number and Type)	EXTRACTED PARAMETERS
Morgan et al., 2020 [21]	Analysis of gait during home assessment	65 papers	Almost half of the studies used between 10 and 49 PD participants. 12 studies used fewer than 10 and 8 more than 100 participants.	45.5% of the studies used 1 sensor at the lower back; 2 studies used 3 sensors at lower back and feet; 1 paper used 1 sensor on the chest, 1 used 1 sensor on the wrist. 2 papers do not discribe the position	Features not specified.
Ghislieri et al., 2019 [26]	Analysis of standing balance	14 papers	From 10 to 58 PD patients (and one study with 104 patients)	The 93% of studies used 1 sensors on the lower back. 1 study used 3 sensors: 1 on the lower back and 2 on lower limbs	Jerk index, sway amplitude, range of acceleration signals, frequency dispersion and centroidal frequency.
Rovini et al., 2018 [22]	Analysis of gait during home assessment	30 papers	Ranging from 1 to 75 PD patients	6 papers (28.2%) used 1 sensor: 4 on the waist and 2 on the lower back. 10 (33.3%) papers used 2 sensors: 5 on the wrists, 1 on the feet, 3 on the ankles, one on ankle and dominant leg. 6 studies used 3 sensors on the waist and feet. 2 papers used 5 sensors (on wrists, ankles and trunk; on shanks, wrists and sternum). The last 3 papers used more than 6 sensors.	Average time and distance walked, cadence, gait speed, step length, swing time, double support time; stride time and stride time variability. Inter-trial variability, inter-subject variability; inter-task variability. Number of turns per hour, turn angle amplitude, turn duration, turn mean velocity, number of steps per turn, hourly frequency of turning, duration of each turn, number of steps per turn, peak and average rotational turning rate, jerk, variability of these measures throughout the day and week.

Merola et al., 2018 [51]	Analysis of gait and balance	6 papers	From 6 to 40 (and 2 studies with 190 and 139 PD patients)	Not reported	**Gait:** temporal (reaction time, gait cycle duration), spatial (step length, step height) and biomechanical (ankle torque, vertical landing force) variables, and gait strategies (i.e., number of steps, single versus multiple step response). **Balance and postural instability:** trajectory of the center of pressure (COP) and center of mass (COM) misplacement, trunk acceleration and postural sway
Vienne et al., 2017 [24]	General analysis of gait	16 papers	Not reported	11 studies (68.7%) described the assessment of PD with 1 sensor at the lower back. one paper used one sensor at one ankle, one at one shank and one at one foot. One paper used 2 sensors (upper and lower back), and one paper utilized 3 sensors at lower back and shanks	Features not specified.
Rovini et al., 2017 [52]	Analysis of wearable sensors on support of PD treatment and diagnosis	80 papers	From 5 to 47 (and 1 study of 75 PD patients)	Not reported	Statistical (e.g., mean, variance, skewness, kurtosis), frequency (e.g., energy, power spectral density, fundamental frequency), and spatiotemporal/kinematic (e.g., stride length, TUG time, stride velocity) features; step or stride segmentation.

Godinho et al., 2016 [16]	Mobile health technology characteristics	76 papers	Not reported	Not reported	ISway measures (jerk, RMS amplitude and mean velocity from the time-domain measures, and centroidal frequency); gait parameters with a high degree of accuracy; total number of walking bouts, the percent of time spent walking, the total number of steps, median walking bout duration, median number of steps, and median cadence per bout. Quality-related sensor derived measures included: frequency measures, regularity measures and the harmonic ratio.
Del Din et al., 2016 [23]	Analysis of gait during home assessment	19 papers	From 2 to 169 PD participants (and one study of 467 patients)	9 studies (47.3%) used 1 sensor on lower back; 3 used 2 sensors on thighs; 2 papers used 2 sensors on feet; 1 on both shanks and 1 used 1 sensor on the chest; the other papers used more than 4 sensors.	Number of walking bouts, walking duration, total number of steps, median number of steps per bout, bout duration, cadence, step and stride regularity, frequency domain measures (harmonic ratio, amplitude, slope and width of dominant frequency), step duration, step symmetry, acceleration range and dynamic stability
Oung et al., 2015 [49]	Assessment of motor disorders in PD	Not reported	Not reported	Not reported	Step frequency, stride length, entropy and arm swing
Hubble et al., 2015 [27]	Analysis of standing balance and walking stability	26 papers	From 5 to 67 PD patients	20 studies (76.9%) used 1 sensor on the lower back (sacrum/L3/L4/L5); 2 studies used 2 sensors on the shanks; 2 studies used 1 sensor on sternum/chest; 1 study utilized one sensor on the wrist; and another one on the lateral side of the pelvis.	Sway velocity (23% of studies), RMS accelerations (19% of studies) and jerk (19% of studies). Harmonic ratio (31% of studies) and stride time variability (27% of studies).

Steins et al., 2014 [50]	Assessment of functional activities with wearable devices	6 papers	Not reported	Not reported	Stride length, stride velocity, cadence, and turning velocity
Maetzler et al., 2013 [25]	Quantitative objective assessment of gait and balance	16 papers	Not reported	**Gait**: 4 papers used one sensor on the lower back (44.4%). 2 papers utilized 1 sensor on the shank and 2 papers 2 sensors on both feet. 1 paper used 1 sensor on the forearm and two studies used more than 5 sensors. **Balance**: 5 papers used 1 sensor on lower back **(**100%).	**Gait:** Phase coordination index of gait cycle; stride length; frequency-based measures of gait (harmonic ratio, amplitude, slope and width of dominant frequency); cadence, step time variability; peak trunk horizontal velocity, turning duration, turn-to-sit duration; time- and amplitude-based measures of sit-to-stand and stand-to-sit; peak trunk rotation velocity and rotation range of motion, turning velocity; Walk peak roll velocity, total turning duration, turn peak yaw and roll velocity. **Balance**: Velocity, jerk, acceleration, frequency-based measures; displacement, velocity; Peak trunk acceleration during anticipatory postural adjustments towards the stance leg; Hilbert-Huang transformation of postural parameters
Horak et al., 2013 [48]	Biomarkers of gait and balance	Not reported	Not reported	Not reported	**Gait**: Stride Time Variability, double support time, peak arm velocity, trunk rotation, gait velocity, cadence, stride length. Balance: Postural sway (area, velocity, frequency) and jerk.

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