Muscle Strength and Power in People With Parkinson Disease: A Systematic Review and Meta-analysis

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Background and Purpose: No studies have synthesized the literature regarding mechanical muscle function (ie, strength, power, rate of force development [RFD]) in people with Parkinson disease (PD). Here, we aimed to expand our understanding of mechanical muscle function in people with PD (PwPD) by systematically reviewing (1) the psychometric properties of isokinetic/isometric dynamometry in PD, (2) the literature comparing mechanical muscle function in PwPD with healthy controls (HC), and (3) reported associations between muscle mechanical muscle function and functional capacity and/or disease severity.

Methods: Systematic literature search in 6 databases. Included studies had to (1) enroll and report data on PwPD, (2) include assessment(s) of psychometric properties (ie, validity, reliability, responsiveness) of isokinetic/isometric dynamometry in PD, and/or (3) assess mechanical muscle function in both PwPD and HC using isokinetic/isometric dynamometry.

Results: A total of 40 studies were included. Aim 1 studies (n = 2) showed high reliability for isometric dynamometry (hip-abductor/dorsiflexor/trunk flexor-extensor/handgrip: intraclass correlations coefficients range = 0.92-0.98). Aim 2 studies (n = 40) showed impaired mechanical muscle function (ie, strength, power, RFD) in PwPD compared with HC (effect sizes range = 0.52-1.89). Aim 3 studies (n = 11) showed weak-to-strong associations between overall and lower extremities muscle strength and functional capacity and/or disease severity outcomes (ie, Unified Parkinson Disease Rating Scale).

Discussion and Conclusions: Sparse methodological evidence suggests high reliability when using dynamometry in PwPD. Muscle strength, power, and RFD are impaired in PwPD compared with HC. Muscle strength is associated with functional capacity and disease severity.

Video Abstract available for more insights from the authors (see the Video, Supplemental Digital Content 1, available at: http://links.lww.com/JNPT/A403).

Key words: *clinical exercise physiology, exercise therapy, kinesiology, physical activity, training*

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INTRODUCTION

Parkinson disease (PD) is a chronic, progressive, and neurodegenerative disorder.[1] Muscle weakness is a frequent symptom of PD[2,3] thought to have critical implications in people with PD (PwPD) as it contributes to postural instability and gait difficulties.[2,4] Muscle weakness has also been identified as a secondary cause of bradykinesia,[2] while improvements in muscle strength and power can alleviate bradykinesia.[5] Furthermore, muscle weakness may lead to falls among PwPD.[6] Isokinetic dynamometry is considered the gold standard when assessing muscle strength.[7] However, since isokinetic muscle strength is reduced as the movement speed of muscle contraction increases,[8] isometric dynamometry has been suggested as a more valid measure of muscle strength. The inclusion of both isokinetic and isometric dynamometry (including strain gauge devices and/or custom-made dynamometers) therefore seems relevant when assessing muscle strength. Despite the importance of muscle strength in PwPD and the widespread use of dynamometry when testing PwPD in research studies, no previous review has evaluated the psychometric properties (ie, validity,

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On request, data on original analyses can be accessed if determined of sufficient relevance by the authors.

The present study does not require any ethics approval, but is preregistered in the Prospero database (identifier: CRD42021236791).

All authors have consented to publish the present work.

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reliability, and responsiveness) of muscle testing performed using dynamometry in PwPD. This is problematic since the psychometric properties of muscle strength testing may differ substantially PwPD versus healthy people or other populations, due to greater day-to-day variation caused by the multiple symptoms of PD, drug exposure, or other PD-related aspects. Understanding the psychometric properties of this test is essential for the interpretation of test results, highlighted by the presence of related systematic reviews in other neurological disorders such as stroke[9] and multiple sclerosis.[10]

Another underinvestigated area is the level of muscle strength impairment in PwPD when compared with healthy controls (HC), with only one previous review from 2010[11] addressing this matter. However, the number of studies on mechanical muscle function (MMF) has more than doubled since then, calling for an update of the literature. Furthermore, the review by De-la-Cuerda et al[11] did not perform quantitative comparative analyses (ie, PwPD vs HC), report study eligibility criteria, or analyze separate MMF parameters (ie, strength, rate of force development [RFD], and power). Consequently, no reviews could be identified that have synthesized the current knowledge on muscle strength across different contraction types (ie, eccentric, isometric, and concentric), contraction velocities (ie, fast vs slow), muscle groups (eg, upper vs lower extremities), and muscle strength parameters (ie, peak torque, power, and RFD) in PwPD. Such an overview may help optimize restoration and/or preservation of muscle strength in PwPD.

Finally, an important aspect of MMF is whether muscle characteristics are associated with physical function and/or disease severity. Such analyses could advance our understanding of the functional transfer from MMF to functional capacity in PD and potentially guide the design of effective (exercise) interventions. In addition, central PD symptoms are beneficially affected by progressive resistance training,[12] which may mean that MMF is associated with measures of PD progression, which could further reinforce this mode of exercise as an important component of PD rehabilitation. However, no reviews have so far evaluated the associations between MMF and functional capacity and/or disease severity in PD.

Collectively, the aims of the present review were to systematically review (1) the psychometric properties of isokinetic/isometric dynamometry (including strain gauge and/or custom-made dynamometers) in PwPD, (2) the literature comparing MMF in PwPD with HC, and (3) the associations between muscle strength, muscle power or RFD, and functional capacity or disease severity in PwPD.

METHODS

The present study was conducted in accordance with the PRISMA guidelines for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions.[13]

Search Strategy

Six databases (PubMed, EMBASE, Cochrane Library, PEDro, SPORTDiscus, and CINAHL) were searched for relevant publications. In addition, the reference lists of identified articles were screened for potential publications that were not captured by the search. The search was performed on October 14, 2020. Details on specific and combined search terms in the search string are presented in the Supplemental Digital Content 2 Table 1a, available at: http://links.lww.com/JNPT/A404.

Eligibility Criteria

All included studies had to be peer-reviewed, be in English, Danish, Swedish, or Norwegian and had to enroll people with idiopathic PD according to established criteria.[14,15] Case reports were excluded. Additional inclusion criteria were specific for each study aim and should include the following:

Aim 1: Include assessment of psychometric properties (ie, validity, reliability, and/or responsiveness) related to isokinetic/isometric dynamometry in PwPD.

Aim 2: Include isokinetic/isometric dynamometry (including strain gauge and/or custom-made dynamometers) assessment of muscle strength (maximum force [F_{max}]), muscle power, or RFD in both PwPD and HC reported as body weight–adjusted or absolute values from upper and/or lower extremities (studies applying manual muscle testing, handheld dynamometry, or one-repetition maximum testing were excluded).

Aim 3: Report associations between muscle strength and functional capacity/disease severity in PwPD.

Quality Assessment

The quality and risk of bias in included studies were assessed by 2 reviewers using the Quality Assessment Tool for observational cohort and cross-sectional studies (National Institutes of Health, Bethesda, Maryland). A rating scale of yes = 1, no = 0, and not reported = 0 was applied for the 14 questions of the checklist, and the final study quality was rated as good, fair, or poor, based on individual scores and the severity of the risk of bias. The quality assessment rate for each study is reported in the Supplemental Digital Content 2 Table 1b, available at: http://links.lww.com/JNPT/A404.

Data Extraction and Analysis

Search results were exported to Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia) in which duplicates were removed. Following initial screening of titles and abstracts of all identified studies, full-text articles were retrieved, and finally data were extracted from eligible studies (Figure 1). These procedures were performed separately by 2 authors. Any discrepancies were resolved by consensus, in some cases after consulting a third author. Extracted data categories are similar to those by Jørgensen et al[10] including general study information (author(s), publication year), study characteristics (sample size, age, gender), PD duration and severity (The Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale [MDS-UPDRS], UPDRS, Hoehn and Yahr [H&Y] stage), medication status ("ON"/"OFF"), test methodology (limb tested, contraction type, joint, movement) and study outcome(s) (measures of F_{max}, RFD, and Power). Of note, since the reviewed articles cover a wide range of years, both the older UPDRS[16] and the newer MDS-UPDRS[17] were

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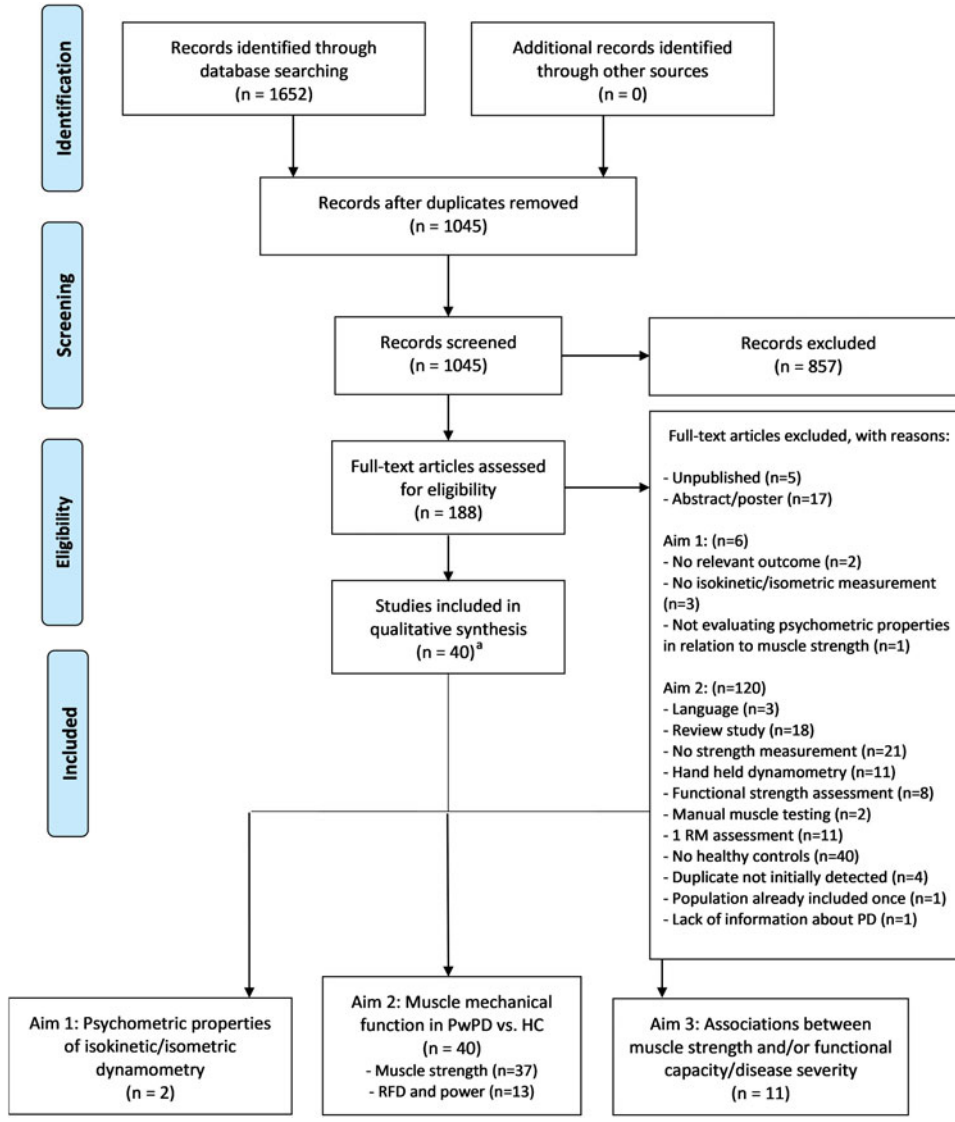

Figure 1. Flowchart. PRISMA flowchart of search strategy and study selection. The included studies could serve multiple objectives that explain the difference between 40 studies included in qualitative synthesis and 54 studies included in aims 1, 2, and 3 all together.[a] For aim 1, 2 of 40 studies were used. For aim 2, all 40 studies were used, a total of 37 for analyses of muscle strength and 13 studies for analysis of RFD and power. For aim 3, 11 studies were used for analyses of associations. HC indicates healthy controls; 1 RM, one-repetition maximum; PD, Parkinson disease; PwPD, people with Parkinson disease; RFD, rate of force development. This figure is available in color online (www.jnpt.org).

extracted, and though there are shortcomings of the original UPDRS,[18] both are regarded as measures of disease severity. The following extractions and data analyses were unique for the different aims.

Aim 1: Psychometric Properties

The definition of the psychometric properties of isokinetic/isometric dynamometry testing was similar to that applied by Jørgensen et al[10] (ie, evaluated with respect to validity, reliability, and responsiveness according to the COSMIN taxonomy[19]). For further specification of validity, reliability and responsiveness, see the study by Mokkink et al.[19]

Aim 2: Comparison of MMF in PwPD Versus HC

Absolute values of muscle strength (N or Nm), RFD (N/s or Nm/s), or muscle power (W) were normalized to body mass reported by the respective studies. If body mass was not reported, absolute values were reported. Mechanical muscle function (ie, isometric strength, dynamic strength, explosive strength [RFD], and muscle power) of PwPD was expressed as a percentage of what was observed in HC.

Aim 3: Associations Between Muscle Strength and Functional Capacity and/or Disease Severity

Included studies were reviewed for associations between muscle strength and functional capacity (ie, balance,

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gait ability, chair-rise time, and Timed Up and Go [TUG] performance) and/or disease severity (ie, MDS-UPDRS scores). Of note, both total score and subscores of the MDS-UPDRS were extracted to investigate potential associations covering both nonmotor and motor symptoms. Both simple linear regression/correlations and multiple regression analyses were extracted. Associations reported as Pearson correlation coefficients (R values)/Spearman's rank correlation coefficients (R_s) were converted to R^2 values when summarizing findings. The analysis of average association patterns across studies was performed on the basis of coefficients obtained in simple linear regression.

Statistical Analysis

Recollecting that F_{max}, RFD, and power can be derived and expressed in several different ways, all reported measures were included and summarized to represent 1 value across lower extremity, trunk, or upper extremity, respectively, from each study. Specifically, if studies reported data on more than 1 muscle group or action (such as extension and flexion) across lower extremity, trunk, or upper extremity, data were summarized (average of reported values) to represent 1 value, respectively, from each study. In addition to the qualitative analysis (summary of identified studies and data), quantitative "PwPD versus HC" analyses were performed by calculating sample-size weighted average differences across lower/upper extremity or trunk of the selected studies. Also, subanalyses were performed between "ON"/"OFF" medication state in PwPD and between contraction types (ISO = isometric; CON = concentric; CON_{slow} = 0-90°/s; $CON_{fast} \geq 100°/s$; ECC = eccentric; ECC_{slow} = 0-90°/s; $ECC_{fast} \geq 100°/s$). These data are presented as mean ± 95% confidence interval (CI). Studies that did not report on medication state were excluded from these analyses, given the expected effect of dopamine replacement medications on force production. Also, between-extremity analyses were carried out using linear mixed models, with study set as random effect and outcome (lower/upper extremity or trunk MMF) as fixed effect. Moreover, sample-size weighted mean effect sizes (Hedges' g) were calculated and illustrated in Figures 2 and 3. Effect sizes are interpreted as follows: small: 0.2 to 0.5, moderate: 0.51 to 0.8, large: greater than 0.8.[20]

As with MMF, the extracted associations between muscle strength and functional capacity or disease severity were analyzed by calculating sample-size weighted average differences across lower/upper extremity using the reported association values (R^2/R or Spearman's correlation coefficient converted to R^2) of the included studies. A correlation above 0.90 was interpreted as very strong (corresponding to $R^2 > 0.81$), 0.70 to 0.89 as strong (corresponding to R^2 between 0.49-0.79), 0.50 to 0.69 as moderate (corresponding to R^2 between 0.25-0.48), 0.30 to 0.49 as weak (corresponding to R^2 between 0.09 and 0.24), and less than 0.29 as little, if any (corresponding to $R^2 < 0.08$), relation.[21] All statistical analyses were conducted using STATA 16 software (StataCorp 2019; StataCorp LLC, College Station, Texas), while graphical illustrations were created using GraphPad Prism 7.0 (GraphPad Software, La Jolla, California; www.graphpad.com). WebPlotDigitizer software version 4.4 (https://automeris.io/WebPlotDigitizer) was used to extract numerical data in studies in which only graphical plots were published.

RESULTS

Eligible Studies

The search yielded a total of 1652 hits, and 1045 hits after removal of duplicates (Figure 1). After initial screening, 188 articles remained for full-text assessment. Ultimately, 40 studies fulfilled the inclusion criteria and were subdivided into aims 1 (n = 2), 2 (n = 40), and 3 (n = 11), respectively. Two studies[22,23] reported relevant outcomes for both aim 1 and aim 2, while 11 studies[6,24-34] reported relevant outcomes for both aim 2 and aim 3. The quality assessment of individual studies is reported in Supplemental Digital Content 2, Table 1b, available at: http://links.lww.com/JNPT/A404.

Aim 1: Psychometric Properties

Two studies[22,23] assessed intersession reliability (ie, variation between trials performed on separate days) of isometric dynamometry in PwPD. Study sample sizes ranged from 15 to 43 PwPD, summing to a total of 58 PwPD. More males than females were enrolled (mean gender ratio [men:women] of 3.8:1). Mean age was 69.5 years. A PD duration of 7.2 years was reported in one of the studies.[23] Both studies included PwPD with H&Y stages of 3 and less. One study[23] conducted the assessments in the "ON" medication state while 1 study[22] did not report on this.

Purser et al[22] reported high reliability when performing isometric contractions during hip abduction and ankle dorsiflexion (ie, intraclass correlation coefficient = 0.92-0.93). Pang and Mak[23] showed excellent reliability of isometric contractions during trunk flexion and extension (ie, intraclass correlation coefficient model 3.1 = 0.97-0.98) as well as handgrip strength of the dominant side (ie, intraclass correlation coefficient = 0.97).[23] None of the included studies evaluated validity or responsiveness of isometric dynamometry and no studies evaluated the psychometric properties of RFD or muscle power. Additional study details are presented in Supplemental Digital Content 2 Table 1c, available at: http://links.lww.com/JNPT/A404.

Aim 2: Comparison of Mechanical Muscle Function in PwPD Versus HC

Forty studies[6,7,22-59] assessed MMF in PwPD versus HC (study characteristics are available in Supplemental Digital Content 2 Table 1d, available at: http://links.lww.com/JNPT/A404). Muscle strength was assessed in 37 studies[6,7,22-37,39-43,45-47,49-59] (see Table, Supplemental Digital Content 3, available at: http://links.lww.com/JNPT/A406) while 12 studies reported RFD[25,26,29(p),31,38,43,44,46,50,54,57,58] and 1 study[48] reported power outcomes (Table 1). Study sample sizes ranged from 6 to 61 PwPD and from 6 to 37 HC, summing to a total of 718 PwPD and 633 HC. All but 1 study[40] reported gender distribution. More males than females were enrolled (mean gender ratio [men:women] of 2.4:1, and 1.5:1 for PwPD and HC, respectively). Mean age was 64.2 years (64.5 and 63.9 years

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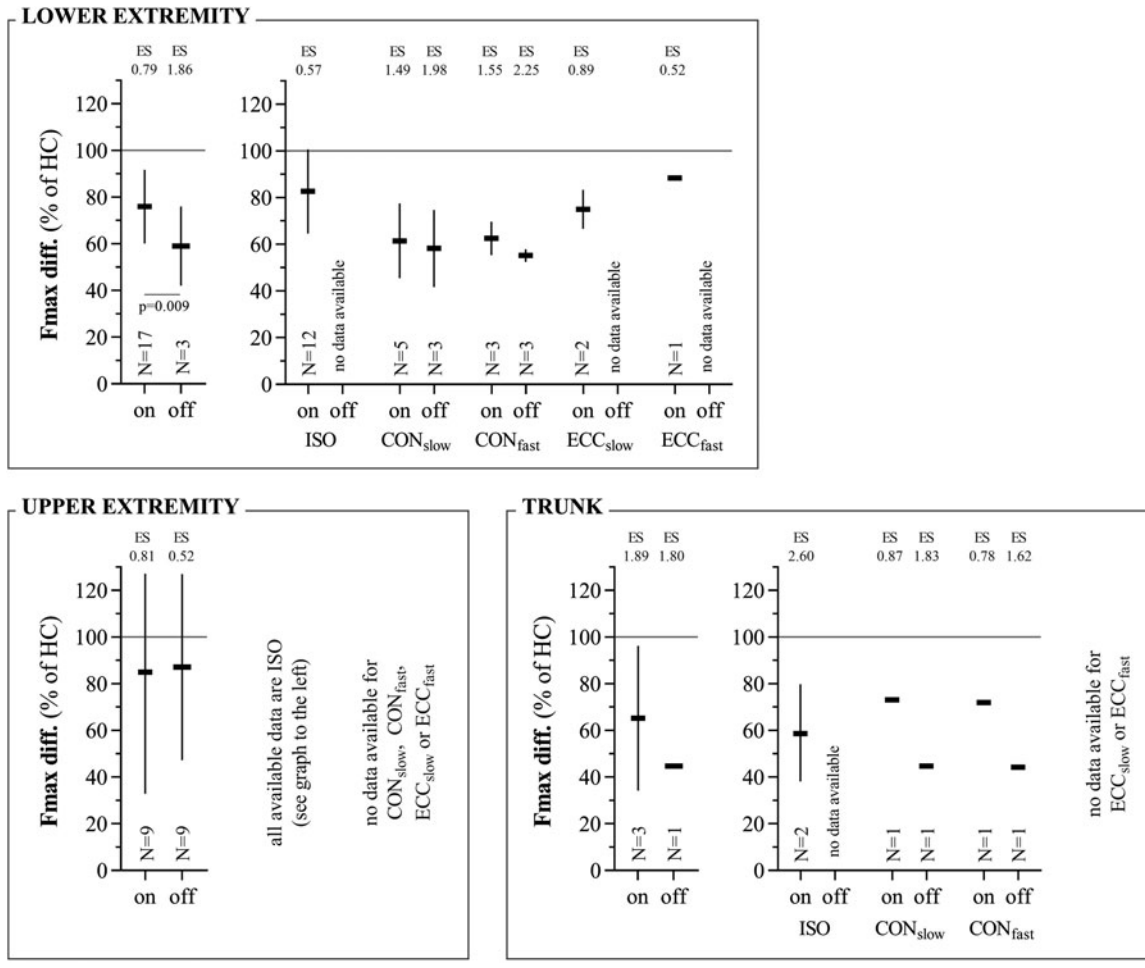

Figure 2. Mean differences from studies (n = 37) comparing lower extremity, upper extremity, and trunk muscle strength, assessed by isokinetic/isometric dynamometry between PwPD and HC. Data are displayed across all contraction types as well as separately for isometric (ISO), concentric (CON_{slow} = 0-90°/s, $CON_{fast} \geq$ 100°/s), and eccentric (ECC_{slow} = 0-90°/s, $ECC_{fast} \geq$ 100°/s). The bold black horizontal lines represent total mean differences across all studies for each category. Statistical significance is based on 95% confidence interval values. The difference in the total number of included studies from the table in Supplemental Digital Content 3, available at: http://links.lww.com/JNPT/A406, and "N" presented in the Figure is due to several studies reporting both "ON" and "OFF"-medication values. ES indicates effect size; HC, healthy controls; N, number of studies.

for PwPD and HC, respectively), and mean duration of PD was 7.3 years. Ten studies[7,22,33,35,36,38,39,43,52,56] did not report on time since PD diagnosis. All studies but 1 included PwPD with H&Y stages of 3 and less; 1 study[34] included PwPD with H&Y stage 4. The majority of studies conducted the intervention and assessments in the "ON" medication state.[7,23-26,28,29(p),31-33,35,36,39,40,42,44,46,49,53,56,59] However, eight studies[27,30,37,41,48,50,51,57] conducted the intervention and assessments in the "ON" and "OFF" medication state, 7 studies[6,38,47,52,54,55,58] in the "OFF" medication state, while 4 studies[22,34,43,45] did not report on this.

Muscle Strength

Supplemental Digital Content 3, available at: http://links.lww.com/JNPT/A406, shows the normalized muscle strength in PwPD compared with HC. Some of the included studies[22,27,28,34,36,37,41,42,46,47,50,51,53-58] did not report on body mass (absolute values are reported for these). In addition, 12 studies[26,29(p),31,32,35,37,39,43,50,51,53,57] allowed only absolute values to be determined from figures.

Muscle strength of the upper and lower extremities as well as trunk muscle strength was analyzed to illustrate the difference (adjusted for sample size) between PwPD and HC (Figure 2). When muscle strength of lower extremities was divided into "ON" and "OFF" medication states, it corresponded to 75% and 59% of muscle strength in HC, respectively, with a more pronounced difference observed in the "OFF" medication state. Similarly, muscle strength of upper extremities showed marked differences (85% ["ON"] and 87% ["OFF"]) in PwPD versus HC. Finally, marked differences were observed "ON" (65%) and "OFF" (45%) medication in trunk strength in PwPD compared with HC. Also, across contraction types, concentric muscle strength of lower extremities showed more pronounced differences (62%-63% ["ON"] and 55%-58% ["OFF"]) in PwPD versus HC compared with isometric (83% ["ON"]; no data for "OFF") and eccentric

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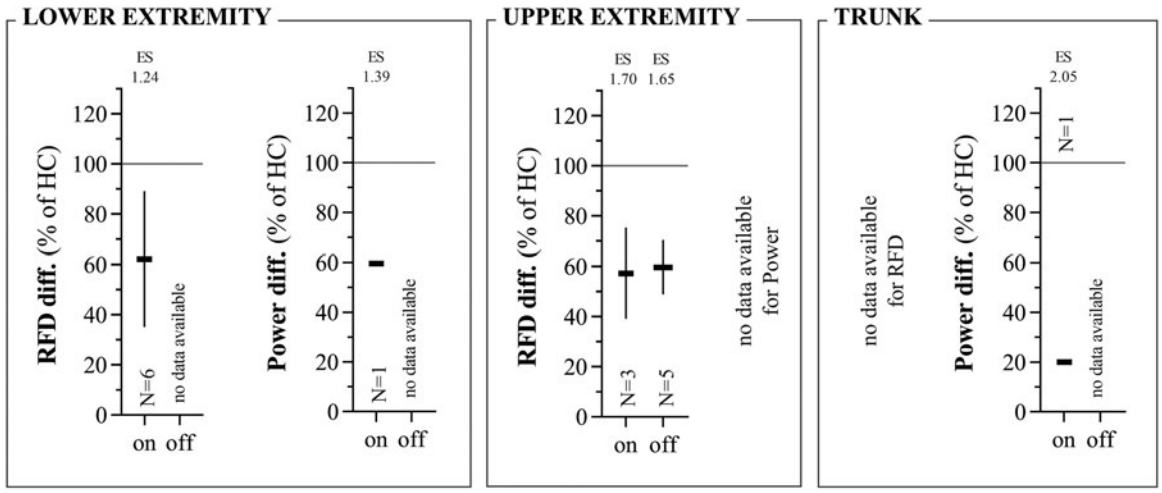

Figure 3. Mean differences summarized from studies (n = 13) comparing lower extremity, upper extremity, and trunk RFD or power, assessed by isokinetic/isometric dynamometry, between PwPD and HC. The bold black horizontal lines represent total mean difference across all studies for each category. Statistical significance is based on 95% confidence interval values. ES indicates effect size; HC, healthy controls; N, number of studies; RFD, rate of force development.

muscle strength (75%-88% ["ON"]; no data for "OFF") of lower extremities in PwPD versus HC (Figure 2). The sparsity of data reported on isometric, concentric, and eccentric muscle strength of upper extremities and trunk left us unable to summarize these data.

Rate of Force Development and Power

Table 1 summarizes the 13 studies reporting RFD (n = 12) or power (n = 1) in PwPD compared with HC. Six studies[38,46,50,54,57,58] did not report on body mass (absolute values are reported for these). In addition, 8 studies[26,29,31,38,43,44,50,58] allowed only absolute values to be determined from figures.

Figure 3 presents mean differences for RFD and power of the upper and lower extremities as well as trunk. Rate of force development of the lower extremities was reported only in the "ON" state (62% of HC), while RFD of upper extremities showed comparable deficits in the "ON" (57%) and "OFF" (60%) state in PwPD versus HC. Finally, isokinetic power, assessed in the "ON" medication state showed marked deficits of trunk and lower extremity muscle power (ie, 20%-60%) at different angular velocities (120°/s, 30°/s, and 90°/s) in PwPD versus HC.

Aim 3: Associations Between Muscle Strength and Functional Capacity or Disease Severity

Table 2 and Figure 4 summarize the 11 studies[6,24-28,29(p),30-33] reporting associations between muscle strength/RFD and functional capacity parameters (ie, balance, gait ability, chair-rise time, and TUG performance) in PwPD. Study sample sizes ranged from 10 to 59 PwPD, summing to a total of 223 PwPD. More males than females were enrolled (mean gender ratio [men:women] of 2.3:1). Mean age was 65 years and mean PD duration was 7.2 years. All studies included PwPD with H&Y stages of 3 and less. The majority of studies conducted the assessments in the "ON" medication state.[7,22-26,28,29,31,32-59] However, 2 studies[27,30] conducted the assessments in the "ON" and "OFF" medication state, and 1 study[6] in the "OFF" medication state.

Two studies[29,31] adjusted for body mass (multiple regression), while the remaining 9 studies reported associations using simple linear regression. The parameter most frequently associated with muscle strength was disease severity in terms of the different variations of the MDS-UPDRS.[6,25,26,32] These 4 studies[6,25,26,32] showed weak-to-strong negative associations (range $R^2 = -0.19$ to -0.58). Other parameters associated with muscle strength were balance performance (assessed in 4 studies), gait ability (assessed in 2 studies), chair-rise time (assessed in 3 studies), and TUG performance (assessed in 1 study). Similarly, these parameters showed associations ranging from no associations to strong associations (range $R^2 = 0.00$ to -0.64). Only lower extremity muscle strength associations were reported.

Figure 4 presents the mean associations (adjusted for sample size) from studies reporting associations between muscle strength/RFD and functional capacity outcomes and/or disease severity.

When analyzed separated by medication states, lower extremity muscle strength and functional capacity showed associations of $R^2 = 0.24$, 95% CI: 0.17 to 0.31 ("ON") versus $R^2 = 0.18$, 95% CI: −0.020 to 0.37 ("OFF"). Furthermore, muscle strength of lower extremities and UPDRS-total showed an association of $R^2 = 0.39$, 95% CI: 0.11 to 0.68 ("ON"), while muscle strength of lower extremities and UPDRS-III yielded an association of $R^2 = 0.40$, 95% CI: 0.22 to 0.58 ("ON") versus $R^2 = 0.34$ ("OFF"). Finally, muscle strength of lower extremities and UPDRS-II showed an association of $R^2 = 0.34$.

DISCUSSION

The present review provides a comprehensive overview of MMF (muscle strength, RFD, power) in PwPD. The main

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Table 1. Results From Studies (n = 13) Comparing RFD and Power, Assessed By Isokinetic/Isometric Dynamometry, Between PwPD and HC[a]

Author	PD (n)	HC (n)	Total (n)	Muscle Group(s), Measurement, Velocity, and Unit		Normalized Power, RFD		Difference (%) PwPD vs HC
						PwPD	HC	
Stelmach and Worringham[46] (1988)[b,c]	7	7	14	EF, RFD, N/s		77.5	222.5	35
Jordan et al[57] (1992)[b,d]	61	24	85	HGS, RFD, N/s		PD-de novo: 406.8 ± 239.77	610.2 ± 177.3	67
	61	24				PD: 440.3 ± 195.3		72
Pääsuke et al[31] (2002)[d,e]	14	12	26	KE, RFD, N•s-1/kg		Left: 13.75 ± 6.1	22.30 ± 9.5	62
	14	12				Right: 14.23 ± 6.6	23.04 ± 10.2	62
Pääsuke et al[29] (2004)[e]	12	16	28	KE, RFD, N/s/kg		40.42 ± 23.26	62.63 ± 26.78	65
Noorvee et al[26] (2006)[d,e]	12	12	24	KE, RFD, N/s/kg		12.01 ± 4.6	16.28 ± 4.5	74
Park and Stelmach[38] (2007)[b,e]	8	8	16	EF, RFD, N/s		15% MVC: 680.27 ± 60.10	1950.11 ± 156.89	35
						35% MVC: 1473.92 ± 109.22	3049.89 ± 173.34	48
						55% MVC: 1814.06 ± 133.55	4160.99 ± 178.42	44
Anzak et al[50] (2011)[b,e]	9	9	18	HGS, pRFD, Kg/s	on	105.4 ± 11.5	162.6 ± 9.7	65
					off	106.5 ± 15.7		65
Neely et al[58] (2013)[b,d,e]	12	12	24	HGS, RFDi, N/s		10.4 ± 10.0	21.2 ± 16.6	49
Pradhan et al[54] (2015)[b]	14	14	28	HGS, RFD, N/s		3.73 ± 1.52	5.0 ± 1.76	75
Lima et al[48] (2016)	10	10	20	TRex, IP, 120°/s, W/kg		27.4 ± 29.8	141.0 ± 105.8	19
				TRflx, IP, 120°/s, W/kg		18.7 ± 18.0	88.3 ± 39.6	21
				KE, IP, 30°/s, W/kg		M-affected: 36.6 ± 11.5	N-dom: 47.2 ± 12.1	78
						L-affected: 39.7 ± 7.0	Dom: 48.1 ± 12.6	83
				KE, IP, 90°/s, W/kg		M-affected: 64.8 ± 27.4	N-dom: 102.4 ± 30.2	63
						L-affected: 76.1 ± 18.4	Dom: 104.8 ± 33.8	73
				KF, IP, 30°/s, W/kg		M-affected: 20.2 ± 7.8	N-dom: 31.9 ± 8.4	63
						L-affected: 20.9 ± 8.0	Dom: 31.9 ± 9.5	66
				KF, IP, 90°/s, W/kg		M-affected: 27.5 ± 14.1	N-dom: 66.4 ± 25.1	41
						L-affected: 31.9 ± 17.8	Dom: 70.2 ± 29.5	45
				HE, IP, 30°/s, W/kg		M-affected: 24.0 ± 8.9	N-dom: 42.0 ± 13.5	57
						L-affected: 22.4 ± 5.7	Dom: 41.4 ± 10.2	54
				HE, IP, 90°/s, W/kg		M-affected: 31.9 ± 17.7	N-dom: 73.7 ± 37.3	43
						L-affected: 35.4 ± 18.8	Dom: 79.4 ± 31.3	45
				HF, IP, 30°/s, W/kg		M-affected: 20.2 ± 7.8	N-dom: 31.9 ± 8.4	63
						L-affected: 20.9 ± 8.0	Dom: 31.9 ± 9.5	66
				HF, IP, 90°/s, W/kg		M-affected: 27.5 ± 14.1	N-dom: 66.4 ± 25.1	41
						L-affected: 31.9 ± 17.8	Dom: 70.2 ± 29.5	45
				DF, IP, 30°/s, W/kg		M-affected: 7.1 ± 2.7	N-dom: 8.6 ± 3.1	83
						L-affected: 8.0 ± 3.6	Dom: 9.4 ± 2.9	85
				DF, IP, 90°/s, W/kg		M-affected: 8.7 ± 4.0	N-dom: 10.3 ± 3.8	84
						L-affected: 10.3 ± 3.7	Dom: 12.6 ± 5.1	82
				PF, IP, 30°/s, W/kg		M-affected: 11.5 ± 4.6	N-dom: 29.0 ± 11.1	40
						L-affected: 14.8 ± 5.1	Dom: 30.4 ± 9.5	49
				PF, IP, 90°/s, W/kg		M-affected: 11.4 ± 8.6	N-dom: 33.2 ± 15.7	34
						L-affected: 18.5 ± 11.0	Dom: 37.8 ± 19.7	49
Krumpolec et al[25] (2017)[d]	11	11	22	Leg press, RFD, N/s/kg		0.31 ± 0.6	0.26 ± 0.5	119
Hammond et al[44] (2017)[e]	7	6	13	KE, RFD, N/s/kg		26.96 ± 16.99	56.63 ± 13.38	48
Alota Ignacio Pereira et al[43] (2018)[e]	19	20	39	Leg press, RFD-50 ms, N/s/kg		1.28 ± 0.52	15.97 ± 8.8	8
				Leg press, RFD-100 ms, N/s/kg		0.68 ± 0.26	15.95 ± 10.8	4
				Leg press, RFD-200 ms, N/s/kg		0.41 ± 0.14	13.23 ± 25.9	3

Abbreviations: DF, dorsal flexion; Dom, dominant; EF, elbow flexion; HC, healthy controls; HE, hip extension; HF, hip flexion; HGS, handgrip strength; IP, isokinetic power; KE, knee extension; KF, knee flexion; L-affected, least affected side; M-affected, most affected side; MVC, muscle voluntary contraction; N-dom, nondominant; PD, Parkinson disease; PF, plantar flexion; pRFD, peak rate of force development; PwPD, people with Parkinson disease; RFD, rate of force development; RFDi, rate of force increase; TR, trunk; TRex, trunk extension; TRflx, trunk flexion.

[a] Data were normalized to body mass when possible and expressed as a percentage of muscle strength in HC.

[b] Body mass not reported.

[c] SD not available.

[d] SD determined from SE/SEM.

[e] Absolute values are determined from figures.

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Table 2. Summary of Studies (n = 11) Reporting Associations Between Isometric/Isokinetic Muscle Strength or RFD of Lower Extremities and Objective Functional Capacity Outcomes or Disease Severity in PwPD[a]

Authors	PD, n	Variable	Muscle Group	Notes	Medication	R^2/R^2_S	P
Pääsuke et al[31] (2002)	14	Chair-rise time	KE	Right	ON	$R^2 = -0.41$[b]	<0.05
		Chair-rise time	KE	Left	ON	$R^2 = -0.27$[b]	<0.05
		Chair-rise time	KE	Right/BW	ON	$R^2 = -0.20$	>0.05
		Chair-rise time	KE	Left/BW	ON	$R^2 = -0.18$	>0.05
		Chair-rise time	KE RFD	Right	ON	$R^2 = -0.08$	>0.05
		Chair-rise time	KE RFD	Left	ON	$R^2 = -0.10$	>0.05
Inkster et al[30] (2003)	10	Chair-rise time	HE		ON	$R^2 = -0.50$[b]	<0.05
		Chair-rise time	HE		OFF	$R^2 = -0.64$[b]	<0.05
		Chair-rise time	KE		ON	NR	>0.05
		Chair-rise time	KE		OFF	NR	>0.05
Pääsuke et al[29] (2004)	12	Chair-rise time	KE		ON	$R^2 = -0.40$[b]	<0.05
			KE	/BM	ON	$R^2 = -0.22$	>0.05
			KE RFD		ON	$R^2 = -0.09$[b]	>0.05
Nallegowda et al[27] (2004)	30	Gait velocity	Ankle, hip, trunk		ON	$R^2 = 0.14$[b]	<0.05
			Ankle, hip, trunk		OFF	$R^2 = 0.31$[b]	<0.05
		Dynamic balance (movement velocity)	Ankle, hip, trunk		ON	$R^2 = 0.15$[b]	<0.05
			Ankle, hip, trunk		OFF	$R^2 = 0.00$	>0.05
		Dynamic balance (reaction time)	Ankle, hip, trunk		ON	$R^2 = 0.03$	>0.05
			Ankle, hip, trunk		OFF	$R^2 = 0.01$	>0.05
		Gait velocity	Ankle		ON	$R^2 = 0.15$[b]	<0.05
			Ankle		OFF	$R^2 = 0.16$[b]	<0.05
		Static balance (ankle strategy)	Ankle		ON	$R^2 = 0.13$	>0.05
			Ankle		OFF	$R^2 = 0.00$	>0.05
Noorvee et al[26] (2006)	12	UPDRS-Total	KE		ON	$R^2_S = -0.58$[b]	<0.01
		UPDRS-III	KE		ON	$R^2_S = -0.32$[b]	<0.05
Canning et al[28] (2006)	16	6MWD	KE		ON	$R^2 = 0.30$[b]	0.03
Schilling et al[33] (2009)	17	TUG	Leg press		ON	$R^2 = -0.46$[b]	0.003
		Postural sway	Leg press		ON	NR	>0.05
Durmus et al[6] (2010)	25	UPDRS-III	KF	90°/s	OFF	$R^2_S = -0.41$[b]	<0.01
		UPDRS-III	KE	90°/s	OFF	$R^2_S = -0.27$[b]	<0.01
		UPDRS-III	KF	120°/s	OFF	$R^2_S = -0.46$[b]	<0.01
		UPDRS-III	KE	120°/s	OFF	$R^2_S = -0.31$[b]	<0.01
		UPDRS-III	KF	150°/s	OFF	$R^2_S = -0.41$[b]	<0.01
		UPDRS-III	KE	150°/s	OFF	$R^2_S = -0.23$	>0.05
		UPDRS-II	KF	90°/s	OFF	$R^2_S = -0.36$[b]	<0.01
		UPDRS-II	KE	90°/s	OFF	$R^2_S = -0.49$[b]	<0.01
		UPDRS-II	KF	120°/s	OFF	$R^2_S = -0.31$[b]	<0.01
		UPDRS-II	KE	120°/s	OFF	$R^2_S = -0.32$[b]	<0.01
		UPDRS-II	KF	150°/s	OFF	$R^2_S = -0.29$[b]	<0.01
		UPDRS-II	KE	150°/s	OFF	$R^2_S = -0.28$[b]	<0.01
Pang and Mak[24] (2012)	59	Balance (OLS)	Ankle PF		ON	$R^2 = 0.09$[b]	0.022
		Balance (LOS)	Ankle PF		ON	$R^2 = 0.15$[b]	0.003
Stevens-Lapsley et al[32] (2012)	17	UPDRS-III	KE		ON	$R^2 = -0.45$[b]	0.003
Krumpolec et al[25] (2017)	11	Balance (BBS)	KE/KF/leg press		ON	$R^2 = 0.29$[b]	0.0036
		MDS-UPDRS total	KE/KF/leg press		ON	$R^2 = -0.19$[b]	0.043

Abbreviations: /, adjusted for BM, body mass; BBS, Berg balance scale; BW, body weight; DF, dorsal flexion; Dom, dominant; EF, elbow flexion; HC, healthy controls; HE, hip extension; HGS, handgrip strength; IP, isokinetic power; KE, knee extension; KF, knee flexion; LOS, limit of stability; MDS-UPDRS, (The Movement Disorder Society-Sponsored Revision of the)-Unified Parkinson disease rating scale; MVC, muscle voluntary contraction; N-dom, nondominant; NR, not reported; OLS, one-leg standing test; PD, Parkinson disease; PF, plantar flexion; pRFD, peak rate of force development; PwPD, people with Parkinson disease; *R*, Pearson correlation coefficient; R^2, coefficient of determination; R^2_S, coefficient of determination based on Spearman rank correlation coefficient; RFD, rate of force development; RFDi, rate of force increase; 6MWD, 6-minute walking distance; TRex, trunk extension; TRflx, trunk flexion; TUG, Timed Up and Go.

[a]Studies reporting associations as R/R_S values were subsequently converted to R^2 values prior to summarizing findings on associations.

[b]Significant association.

findings were that in PwPD (1) few studies have evaluated psychometrics of dynamometry testing of maximal isometric contractions, but these studies showed high reliability suggesting that this method is a reliable tool for assessing muscle strength, (2) MMF was impaired when compared with HC (medium-to-large effect sizes ranging from 0.52 to 1.89 across all contraction types and medication status), and (3) muscle strength of the lower extremities was moderately associated with physical functional capacity and UPDRS scores (MDS-UPDRS-total, UPDRS-III, and UPDRS-II). Moreover, the quality underlying this evidence was rated as fair (ie, studies met 5-9 out of the 14 questions) with no blinding of outcome assessors (except for 1 study[48]), no correction of potential confounders (except for 3 studies[23,44,56]), no and/or short follow-up time, and only few studies[24,32,33,39] providing sample size justification. These general shortcomings in study design should be kept in mind when interpreting the findings of the present study.

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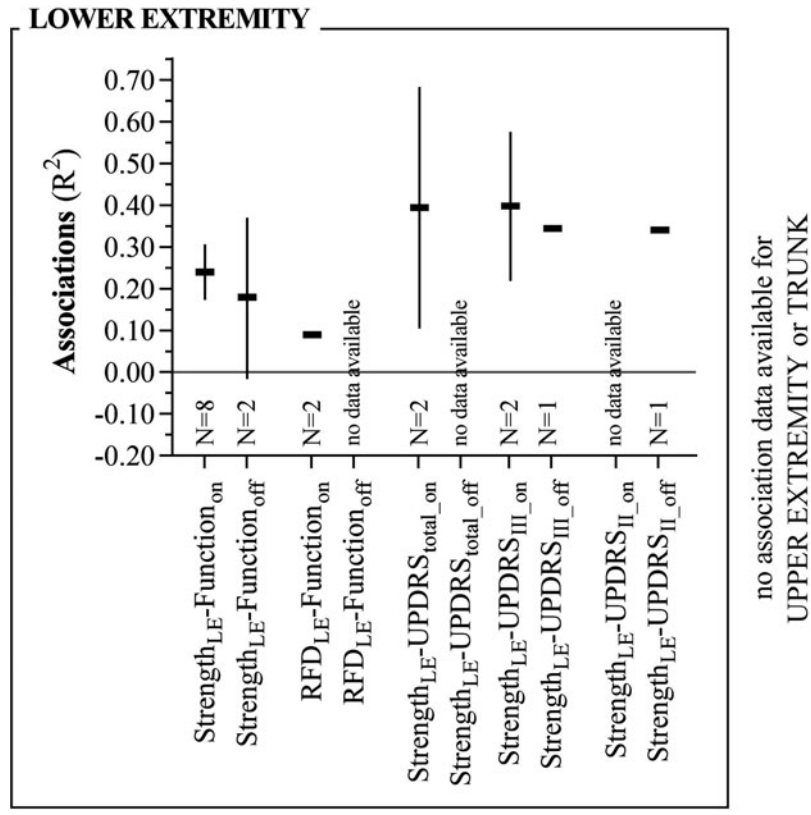

Figure 4. Mean associations between lower extremity muscle strength (across all contraction types) and objective functional capacity outcomes or disease severity in PwPD. The bold black horizontal lines represent total mean associations across all studies for each category. Statistical significance is based on 95% confidence interval values. The difference in the total number of included studies from Table 2 and "N" presented in the Figure is due to several studies reporting both "ON" and "OFF"-medication values. If a study reported left- and right-side values and/or different velocities (ie, 90, 120, and 150°/s), the mean was used. LE indicates lower extremities; N, number of studies; RFD, rate of force development; UPDRS, Unified Parkinson's Disease Rating Scale.

Aim 1: Psychometric Properties

Only 2 studies[22,23] assessed the reliability of dynamometry in PwPD—in the mild to moderate stages of PD—showing excellent test-retest reliability,[60] while no studies assessed validity and responsiveness. None of the studies reported on familiarization thus neglecting the potential for learning effects.[9] Similarly, Jørgensen et al[10] reviewed the psychometric properties of isokinetic dynamometer testing in people with multiple sclerosis, with 4 studies reporting high intraclass and intersession reliability. Thus, future studies on all psychometric properties of isokinetic/isometric dynamometry in PwPD in all stages of the disease, and other neurodegenerative disorders, are therefore highly warranted as the method is widely used and insights into these properties are essential for interpretation of study results.

Aim 2: Comparison of Mechanical Muscle Function in PwPD Versus HC

A consistent finding of the present review was that MMF was impaired—across muscle groups, contraction velocities and modes, and medication state—in PwPD when compared with HC. However, a trend toward a larger deficit in lower extremity and trunk muscle strength was observed when compared with upper extremities (Figure 2). This notion is supported by animal study findings showing greater proximal versus distal motor impairments in PD models.[30,42] Moreover, upper limb muscles are activated more often than lower limb muscles during everyday activities in humans, potentially leading to less inactivity-related decline in physical function.[61] As expected, the largest deficits in mean lower extremity and trunk muscle strength were observed in the "OFF" medication state, thus complying with previous results showing decreased isometric strength of the knee extensors (7%) and flexors (11%) in the "OFF" versus "ON" medication state.[62] Moreover, irrespective of "ON" and "OFF" medication state, contraction type seemed of importance, as we observed greater deficits in lower extremity concentric muscle strength (at slow-to-fast contraction velocities) than in lower extremity isometric as well as eccentric muscle strength (at slow-to-fast contraction velocities). Interestingly, the decrease in knee extension strength in the "OFF" medication state was caused by reduced activation of the agonist muscle, rather than any change in antagonist coactivation, and these changes were associated with reduced locomotory performance.[62] The latter

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may be especially important for long-term (ie, >5 years) users of dopaminergic medication experiencing reduced sensitivity and fluctuations in motor disability and drug-induced dyskinesias,[62] as resistance training may hold the potential to defer or reduce drug use by maintaining MMF in the absence of medication.

Nine studies[24,35,37,40,46,49,51,53,58] reported MMF outcomes for the most affected body parts, while only 1 study[48] reported values of both the most and least affected limbs, making the amount of data too limited for separate analyses of this parameter. Previous studies, however, have suggested torque deficits between the most and least affected side of the lower extremities in early PD[8] or only at a faster speed.[63]

At a mechanistic level, central and peripheral mechanisms may contribute to impaired MMF in PwPD. A decrease in muscle activation and altered motor unit behavior have been demonstrated.[64] Also, peripheral morphological mechanism seems involved, including potential hypertrophy of type I muscle fibers and atrophy of type II muscle fibers.[65,66] In addition, Chiang et al[67] found decreased muscle quality (ie, higher fat infiltration), which correlated with increased disease severity and frailty. However, these morphological changes may be caused by physical inactivity and/or reduced mobility rather than by the disease per se. A recent study by Martignon et al[68] investigated the role of physical activity against the neuromuscular deterioration in PD and found no difference between physically active PwPD and HC in lower limb muscle voluntary contraction (142 ± 85 vs 142 ± 47 Nm). This interesting finding further supports the possible effectiveness of exercise in PwPD potentially counterbalancing neuromuscular deterioration despite PD pathology.[68] Moreover, physical inactivity may thus be an important confounder when examining MMF in PwPD[69] and may lead to exacerbated symptomatology in these persons.

Other factors such as the time since diagnosis and sex differences may influence MMF in PwPD. In this review, studies included PwPD with an average time since diagnosis between 1.2 and 15.6 years (10 studies[7,22,33,35,36,38,39,43,52,56] did not report on this). However, studies that included newly diagnosed PwPD with a short time since diagnosis[27,30,41,48,57] still showed relatively large deficits when compared with HC. This supports the general view that time since diagnosis is a rough measure that often says little about actual disease onset (which potentially occurred several years earlier). Based on this, deficits in MMF may already exist at the early stages of the disease suggesting early interventions to be highly important in PD. Moreover, increasing experimental and clinical evidence supports the notion that PD differs between women and men as they experience the disease differently and different mechanisms seem to be involved in the pathogenesis of the disease.[70] Although only 2 of the identified studies reported on MMF sex differences, 1 reported greater numerical deficits in isometric, concentric, and eccentric dorsal flexion muscle strength of men compared with women,[36] whereas another reported greater deficits in handgrip muscle strength of women compared with men.[59] Altogether, studies in the area of sex differences in MMF and its clinical implications are currently underinvestigated.

Parkinson disease rehabilitation should target the strength deficits identified in the present review. It is therefore uplifting that studies have shown that different (exercise) interventions, progressive resistance training in particular, effectively improve muscle strength in PwPD. A systematic review and meta-analysis by Gamborg et al[71] examined the effects of strength training in PwPD and reported improvements in muscle strength (15%-30%), functional capacity (TUG), and quality of life (39-item Parkinson's Disease questionnaire). Similarly, a recent systematic review and meta-analysis by Gollan et al[72] showed significant large effects on muscle strength following resistance training (standardized mean difference: = –0.84, 95% CI: –1.29 to –0.39). Of note, all the included strength training protocols in the study by Gollan et al were effective in improving muscle strength despite variety in session duration, frequency, intensity, and length. However, most trials recruited PwPD with mild to moderate disability and provided information about only short-term effects. Consequently, future studies are needed to further elucidate how to optimize exercise interventions that improve MMF in PwPD, while taking into account parameters such as medication state, strength training protocol parameters (ie, muscle groups, session duration, frequency, intensity, and length), long-term effects, the level of disability, and potential sex differences.

The present review shows that MMF is impaired in PwPD when compared with HC (with the largest deficits in lower extremity and trunk muscle strength), which likely exists already at the early stages of the disease. Although isokinetic/isometric dynamometry is not available to most clinicians, they should be aware of these impairments and emphasize to all PwPD the importance of implementing strength training/physical activities in their daily lives in order to counteract muscle weakness and potential adverse consequences.

Aim 3: Associations Between Muscle Strength and Functional Capacity or Disease Severity

This is the first study to synthesize the current body of literature on the associations between muscle strength and functional capacity and/or disease severity in PwPD. Although purely speculative due to unknown causation, the reported associations between muscle strength and objective functional capacity outcomes, although only moderate in magnitude, suggest that PwPD may attain improvements in such PD-related symptoms by improving muscle strength. This is somewhat supported by findings across studies showing that lower extremity muscle strength explained a moderate part of the variance (18%-24%) in lower limb functional capacity tests (ie, balance, gait ability, chair-rise time, and TUG performance) while lower extremity muscle strength explained 34% to 40% of the variance in UPDRS scores (ie, MDS-UPDRS-total, UPDRS-III, UPDRS-II). Weak associations were reported between RFD and functional capacity outcomes (ie, chair-rise time). However, only 2 studies from the same group (Pääsuke et al 2002[31] + 2004[29]) reported on RFD hindering solid conclusions on the importance of this outcome at present.

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Despite the large number of studies (n = 40) evaluating MMF in PwPD, only a subset of these (n = 11) reported associations between MMF (predominantly muscle strength) and functional capacity and/or disease severity thus limiting relevant association patterns. Future studies in MMF are therefore encouraged to report on relevant associations with all MMF parameters (ie, muscle strength, power and RFD), while also taking into consideration the influence of relevant covariables.

As always, correlation does not imply causation. However, the present associations between muscle strength and functional capacity or disease severity can provide a useful springboard to further research. In this context, the role of muscle strength/strength training in the causation of PD progression (ie, MDS-UPDRS score) or functional capacity deterioration should be further investigated in both the short- and long-term perspectives. Finally, given the associations presented in this review, clinicians should consider "prescribing" strength training to all PwPD and especially those with functional capacity impairments (ie, balance, gait ability).

Methodological Limitations

Some methodological considerations have to be kept in mind when interpreting the results of the present review. First, the reported associations do not allow conclusions on causality. Second, the heterogeneity of studies in terms of study design, PD populations, gender classification, applied strength testing devices, applied strength (eg, peak torque, RFD, and muscle power), and functional capacity outcomes limits direct comparison across the included studies. Finally, the functional capacity results of the present review referred to physical function and not to other functions of importance for functioning, and, further, the recommendations generated in the results may not be transferable to PwPD with higher disease severity (ie, H&Y 4).

CONCLUSION

In PwPD, the limited existing evidence suggests that a reliable test of muscle strength can be performed using dynamometry during isometric contractions, but further studies on psychometric properties are needed. Mechanical muscle function (ie, muscle strength, power, and RFD) in PwPD is impaired compared with HC, with the largest deficits observed in the lower extremity in the "OFF" medication state and of concentric contractions. The current literature shows that muscle strength is associated with objective functional capacity outcomes as well as disease severity/level of disability, measured by MDS-UPDRS scores.

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