Review

Factors related to functional independence in females with Parkinson's disease: A systematic review

Kaitlyn P. Roland\textsuperscript{a}, Jennifer M. Jakobi\textsuperscript{b,1}, Colin Powell\textsuperscript{c,2}, Gareth R. Jones\textsuperscript{b,∗}

\textsuperscript{a} Interdisciplinary Graduate Studies, Health and Exercise Sciences, University of British Columbia Okanagan, 3333 University Way Kelowna, British Columbia, Canada V1V 1V7
\textsuperscript{b} School of Health and Exercise Sciences, Faculty of Health and Social Development, University of British Columbia Okanagan, 3333 University Way Kelowna, British Columbia, Canada V1V 1V7
\textsuperscript{c} University of Calgary, 2500 University Dr. NW, Calgary, Alberta, Canada T2N 1N4

\textbf{A R T I C L E  I N F O}

Article history:
Received 5 May 2011
Accepted 22 May 2011

Keywords:
Parkinson's disease
Female
Functional abilities
Exercise
Therapy
Movement

\textbf{A B S T R A C T}

Males and females may exhibit diverse expressions of Parkinson’s disease (PD) as a result of biological and social differences. In general, a higher incidence of PD is found among males (RR = 1.5) compared to females. However, rigidity, postural instability and levodopa-induced dyskinesia are more prevalent in females with PD. These fluctuations affect motor performance and impact functional ability. This systematic review suggests that there is minimal research literature with respect to females living with PD. Specifically, the influence of physical ability in females with PD is underemphasized, considering its contribution to functional daily living and quality of life. Three intervention and nine functional assessment studies met inclusion criteria (n = 302; mean age = 65.5 ± 8.3 years, 44% female). Reports suggest that females with PD have different gait patterns compared to ‘healthy’ age-matched females and males with PD. Females with PD experience increased freezing of gait as compared to males with PD. Dynamic balance was reduced in females compared to males with PD. Differences in cardiorespiratory fitness compared to healthy age-matched females was inconclusive. Studies were rated to be of moderate quality (20 ± 5.4/32) and future studies should focus on improving sex-matched recruitment, randomized group allocation, and binding of evaluators to ensure unbiased results. Regardless, the specific impact of PD on females warrants further investigation.

Crown Copyright © 2011 Published by Elsevier Ireland Ltd. All rights reserved.

\textbf{Contents}

1. Introduction ........................................................................................................................................................................ 305
2. Methods .................................................................................................................................................................................. 305
2.1. Literature search strategy .................................................................................................................................................. 305
2.2. Data extraction and quality analysis .................................................................................................................................. 305
3. Results ...................................................................................................................................................................................... 306
3.1. Literature search .................................................................................................................................................................. 306
3.2. Participants ........................................................................................................................................................................... 306
3.3. Study design ........................................................................................................................................................................ 306
3.4. Quality analysis ................................................................................................................................................................... 306
3.5. Outcome measures ............................................................................................................................................................ 308
3.5.1. Functional capabilities .................................................................................................................................................... 308
3.5.2. Intervention studies ........................................................................................................................................................ 309
4. Discussion ................................................................................................................................................................................ 309
4.1. Recommendations ............................................................................................................................................................. 310

\textsuperscript{*} Corresponding author. Tel.: +1 250 807 8102.
E-mail addresses: rolandka@interchange.ubc.ca (K.P. Roland), jennifer.jakobi@ubc.ca (J.M. Jakobi), ccpowell@ucalgary.ca (C. Powell), gareth.jones@ubc.ca (G.R. Jones).
\textsuperscript{1} Tel.: +1 250 807 9884.
\textsuperscript{2} Tel.: +1 403 943 8650.

0378-5122/– see front matter. Crown Copyright © 2011 Published by Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.maturitas.2011.05.009
1. Introduction

Parkinson’s disease (PD) is a progressive neurological disease affecting 1% of North American’s 65 years and older [1]. A unifying PD mechanism has yet to emerge [2]. The cardinal pathological feature of PD is dopamine neuron degeneration in the substantia nigra pars compacta and subsequent striatal dopamine loss, associated with primary motor features [3]. Combined genetic, cellular and environmental factors may contribute to cell death and disease pathogenesis [2]. In Europe and North America the incidence of PD is 1.5–2 times lower and symptom onset is two-years later in females than males [3–7]. Conversely, in Yamagata Japan PD incidence is reported to be greater in females (91.0/100,000) compared to males (61.3/100,000) [8]. Reasons for this diversity have yet to be determined. Evidence suggests that clinical presentation of PD may differ between males and females [9].

Symptom expression differs between males and females with PD (Table 1). Females with PD seek hospital care 1.3 times more than males, likely from a debilitating fall [10,11]. Females experience greater fluctuations in PD motor symptoms specifically; pain, tremor, rigidity, dyskinesia, and instability [12]. These affect motor performance and impact functional ability [5]. Existing reviews address greater disability and reduced quality of life in women with PD [13]. Differences in cognition and resulting clinical characteristics (e.g. sleep, behaviour, depression, visuo–spatial) are attributed to the underlying effect of estrogen on dopamine metabolism [14]. Pavon and colleagues review motor and neuropsychiatric symptoms, disability, behaviour, management and social outcomes in women with PD. These authors recommend further investigation into impact of estrogen on pathology, symptoms, and treatment [15]. However, few studies emphasize the influence of sex-related differences for physical ability, considering its importance to daily independent function.

Reviews present PD characteristics, yet there is a paucity of evidence on how biological differences affect day-to-day function in females with PD. Successful PD management should support performance of activities of daily living (ADL) to the best of one’s ability, defined as functional capacity [16]. Growing evidence indicates that exercise and physical therapy interventions are beneficial for maintaining and improving physical performance in PD [17]. However, no definitive exercise prescription guidelines for females with PD currently exist [18].

Although the existing literature highlights ‘sex’ and ‘gender’ differences in PD, the terms are often misused. Sex, being either ‘male’ or ‘female’, is defined as a multidimensional construct that encompasses anatomy, physiology, genetics, and hormonal regulation, which play critical roles in health and disease [19]. Gender-research provides important insight into social-cultural outcomes related to being a ‘man’ or ‘woman’ [19]. The focus of this review was to examine sex-related differences for physical function in persons with PD. Inclusion of gender-related differences was beyond the scope of this paper.

This systematic review aims to: (1) identify the specific impact that PD may have on the functional abilities of females; and (2) explore opportunities to improve rehabilitation strategies that target biological (sex) differences.

2. Methods

2.1. Literature search strategy

The following electronic databases were searched, following PRISMA 2009 guidelines: PubMed(1980–), Web of Science, EBSCO, SportDISCUS(1980–), PsycINFO(1806–), CINAHL(1982), Ageline(1978–), Embase(1974–), MEDLINE(1950–). Studies were also identified through manual screening of reference lists for relevant papers and personal citation databases. MeSH search terms and key words included: Parkinson’s disease; exercise therapy; exercise; functional assessment; physical therapy modalities; women: female. Studies were selected for abstract-review based on meeting criteria:

1. PD (idiopathic) diagnosis;
2. Functional ability (e.g. balance, range-of-motion, strength, aerobic endurance, ambulation) assessed;
3. Female-specific results reported.

The principal investigator (KPR) reviewed all-full-text articles that met selection criteria to determine inclusion. A secondary-check was performed by six independent blinded-reviewers who were randomly assigned 25–28 articles included for screening. All blinded-reviewers were in complete agreement (100%) with the selected studies.

2.2. Data extraction and quality analysis

Key data were extracted from identified papers, including participant characteristics, inclusion criteria, intervention description (i.e. duration, frequency, intensity), outcomes, design, and female-
specific results. Quality was assessed using the Checklist for the Assessment of Study Quality [20], which consists of 26-items in categories: (1) unbiased information reporting; (2) external validity, generalizability of results; (3) measurement bias; (4) confounding recruitment bias; (5) sufficient statistical power. Maximum score was 32 points.

3. Results

3.1. Literature search

Total of 3845 citations (1980–June 2010) were found. Titles were screened for inclusion criteria and entered into RefWorks (Bethesda, ML) where duplicates were removed (n = 365). Abstracts were assessed and full-text reviews were completed on 158 articles that met inclusion criteria. The majority of full-text reviewed studies (n = 146) did not specifically report female results. This review identified 12 studies, published from 1997 to 2008 (Fig. 1) that included females with PD and involved a functional ability assessment (Table 2).

3.2. Participants

The 12 studies included 302 participants; 134 (44%) were female (mean age = 65.5 ± 8.3) with PD. Participants were diagnosed with mild to moderate idiopathic PD, as per Hoehn and Yahr, in spite of recent criticism [21,22]. All participants were in steady clinical state (i.e. controlled by medication) and testing intervals were consistent within medication regimes (i.e. one to three hours after anti-PD medication).

3.3. Study design

Eight observational reports [23–30], three case studies [18,31,32] and one randomized controlled trial [33] met the inclusion criteria. Duration ranged from single assessments (n = 4) to a 64-week exercise intervention. Outcome measures of functional ability included; gait (n = 4), lower limb strength (n = 2), spinal flexibility and balance (n = 1), cardiorespiratory (n = 1), estrogen and motoric function (n = 1). Three studies included an intervention: (1) Cycling for aerobic exercise—case study of two males and one female with PD [18]; (2) Tai Chi for balance—case study of female with PD [32]; and (3) Estrogen supplementation on motoric function-randomized-control trial [33] (Table 2).

3.4. Quality analysis

Scores on the quality checklist ranged from 9/32 [31] to 31/32 [33], mean score was 20 ± 5.4 (Table 2). Studies that received low (0–16, n = 2) and moderate (17–25, n = 8) scores did not report; recruitment, blinding, randomization, intention-to-treat analysis, adverse events and follow-up characteristics (Table 2).

Fig. 1. Flow diagram of included and excluded studies according to the PRISMA statement.
### Table 2
Results of a systematic literature review on the functional abilities of women with Parkinson's disease.

<table>
<thead>
<tr>
<th>First author</th>
<th>Year</th>
<th>N (#F) with PD</th>
<th>Mean Yrs (SD)</th>
<th>Hoehn and Yahr</th>
<th>Design</th>
<th>Length weeks</th>
<th>Freq/week</th>
<th>Outcome measure</th>
<th>Women-specific conclusions</th>
<th>Quality scorea</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gait</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kokko</td>
<td>1997</td>
<td>40 (13)</td>
<td>67</td>
<td>1–3</td>
<td>Cohort</td>
<td>NA</td>
<td>NA</td>
<td>Walk speed,</td>
<td>Greater cadence</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>cadence, stride</td>
<td>Shorter stride length</td>
<td></td>
</tr>
<tr>
<td>Pedersen</td>
<td>1997</td>
<td>25 (11)</td>
<td>M=63; F=64</td>
<td>1–3</td>
<td>Cohort</td>
<td>NA</td>
<td>NA</td>
<td>Stride frequency,</td>
<td>Lower stride frequency</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>velocity, torque,</td>
<td>Note; men had lower</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>contraction (output)</td>
<td>eccentric contraction</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>and stronger isometric</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>and eccentric</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>contractions, and</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>higher Webster rating</td>
<td></td>
</tr>
<tr>
<td>Morris</td>
<td>1999</td>
<td>1</td>
<td>71</td>
<td>2.5</td>
<td>Case</td>
<td>1</td>
<td>NA</td>
<td>3D trajectories and ground reaction force (kinematic/kinetic profiles); Clinical stride analyzer (spatio-temporal variables)</td>
<td>Reduced speed</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Freezing</td>
<td></td>
</tr>
<tr>
<td>Lamberti</td>
<td>1997</td>
<td>100 (30)</td>
<td>61 (9.1)</td>
<td>1–3</td>
<td>Cohort</td>
<td>NA</td>
<td>NA</td>
<td>VRT, chair rise time, RFD, VGRF, MF</td>
<td>More frequent freezing of gait</td>
<td>20</td>
</tr>
<tr>
<td><strong>Lower limb force</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pääsuke</td>
<td>2002</td>
<td>14 (14)</td>
<td>72.6 (2.2)</td>
<td>1–3</td>
<td>Cohort</td>
<td>NA</td>
<td>NA</td>
<td></td>
<td>Longer VRT and lower</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>maximal RFD and MF</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>in PD. Chair rise</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>time correlated negatively</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>with MF. VGRF</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>positively correlated</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>with MF and RFD</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>when rising from a</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>chair</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lower BL and MF</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>relative to body mass,</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>higher BL strength</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>deficits, and lower</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>max VGRF in PD.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Decreased functional</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>reach</td>
<td></td>
</tr>
<tr>
<td>Pääsuke</td>
<td>2004</td>
<td>12 (12)</td>
<td>74.3 (6.9)</td>
<td>1–3</td>
<td>Cohort</td>
<td>NA</td>
<td>NA</td>
<td>MF, chair rise time, VGRF, RFD,</td>
<td>Decreased functional</td>
<td>21</td>
</tr>
<tr>
<td><strong>Spinal flexibility</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schenkman</td>
<td>2000</td>
<td>56 (14)</td>
<td>70.7 (7.4)</td>
<td>2–3</td>
<td>Cohort</td>
<td>NA</td>
<td>NA</td>
<td>FAR, FRT, 10 m walk, 360-turn, supine to standing</td>
<td>Higher VO2max</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>FAR, FRT, 10 m walk, 360-turn, supine to standing</td>
<td>*Note VO2max values</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>probably indicate</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>VO2 peak</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Trends indicate</td>
<td>serum levels of estrogen correlated with UPDRS motor subscale</td>
<td></td>
</tr>
<tr>
<td><strong>Cardio-respiratory Endurance</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stanley</td>
<td>1999</td>
<td>20 (7)</td>
<td>M=64; F=65</td>
<td>2–3</td>
<td>Cohort</td>
<td>NA</td>
<td>NA</td>
<td>V02max, time to maximal exercise (min)</td>
<td>Higher VO2max</td>
<td>19</td>
</tr>
<tr>
<td><strong>Estrogen and motoric function</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kompoliti</td>
<td>2000</td>
<td>10 (10)</td>
<td>42.3 (5.8)</td>
<td>1–3</td>
<td>Cohort</td>
<td>5</td>
<td>NA</td>
<td>UPDRS (motor, behaviour, ADL) S&amp;E (ADL)</td>
<td>Trends indicate</td>
<td>26</td>
</tr>
</tbody>
</table>

a Quality scores range from 1 (lowest) to 25 (highest).
3.5. Outcome measures

3.5.1. Functional capabilities

Gait. Kokko et al. examined postural locomotion, balance, stride length, and cadence in 40 subjects (13 females, mean age = 67, range 35–84) with PD (mean duration n = 5.5 years, range 2–19) [23]. Investigators reported ambulatory cadence (143 steps/min) and shorter relative stride length (1.7 m) was greater in females than males (132 steps/min, 1.9 m; p < 0.05).

Pedersen et al. assessed cadence and stride length in 14 males (mean age = 63.4 years, range 50–69) and 11 females (mean age = 64, range 60–69) with PD (duration 1–8 years) age-matched to 37 healthy active seniors (18 females) [28]. Cadence was significantly slower in females with PD at maximum velocity than both controls and males with PD.

Morris et al. examined the stride length, gait speed of a 71-year-old female with PD (duration 20 years) [31]. Results were compared to an age-and height-matched female. The female with PD had slower gait speed (56 vs. 75 m/min) and shortened gait cycle length (0.97 vs. 1.3 m) compared to her peer.

Lamberti and colleagues assessed the occurrence of freezing of gait and fall characteristics (questionnaire) in 100 people with PD (30 females, mean age = 61 ± 9.1, mean duration = 6.5 ± 4.0 years) [25]. In this study, freezing of gait occurred more frequently (p < 0.05) in females (70%, OR = 1.50 [1.28–1.81]) than males (55%, OR = 0.66 [0.61–0.73]) with PD. The results did not differ significantly when comparing on and off medication.

Lower limb strength. Pääsuke et al. investigated the relationship between force preparation and production in 14 females with PD (mean age = 72.6 ± 2.2, mean duration = 10.3 ± 1.2) compared to 12 ‘healthy’ age-matched females (mean age = 72.8 ± 0.8) [26]. Females with PD had a 12% prolonged reaction time in the right leg and 14.8% in the left. Maximum isometric force was 15.3% less in the right and 22.1% in the left compared to controls (p < 0.05) [26]. This may reflect postural asymmetry in PD, or the contribution of cerebral lateralization to lower leg function [34].

In a subsequent study, Pääsuke et al. measured bilateral isometric leg-extension force and chair-rise performance in 12 females with PD (mean age = 74.3 ± 6.9 years, mean duration = 10.7 ± 4.5 years) compared to 16 healthy age-matched females (mean age = 71.7 ± 4.4 years) [27]. Females with PD exhibited 19.4% weaker bilateral maximal force, 29.8% slower rate of force development, and took 24.4% longer to complete chair-rise assessment than controls (p < 0.05).

Pedersen, as described above, assessed ankle dorsi-flexion of the tibialis anterior and triceps surae. They reported males had stronger isometric and eccentric contractions of ankle dorsi-flexors (p < 0.03) than females with PD [28].

Spinal flexibility and balance control. Schenkman measured spinal flexibility (functional axial rotation), and dynamic balance (functional reach), timed supine to standing, 10-m walk, and 360-degree standing turn in people with (n = 56, 14 females, mean age = 70.7 ± 7.4 years) and without (n = 195, 129 females, mean age = 71.4 ± 5.0 years) PD [29]. Spinal flexibility was moderately correlated to functional limitations (R = 0.488; p = 0.0001). Regressions analysis revealed that being female contributed significantly to poor spinal flexibility and balance control in PD.

Cardiorespiratory fitness. Stanley and colleagues compared maximal oxygen consumption (VO2max) and exercise tolerance during stationary cycling in males (n = 13, mean age = 64 ± 7 years, mean duration = 7.4 ± 4 years) and females (n = 7, mean age = 65 ± 8 years, mean duration 10.6 ± 4.4 years) with PD relative to healthy age-matched males (n = 7, mean age = 66 ± 6 years) and females (n = 16, mean age = 66 ± 8 years) [30]. No significant differences for VO2max were observed between males (23.5 mL·kg⁻¹·min⁻¹) and females (20.1 mL·kg⁻¹·min⁻¹) with PD. Also, individuals with PD did not diff-
fer significantly from healthy males (25.5 mL·kg⁻¹·min⁻¹, \( p = 0.50 \)) and females (16.2 mL·kg⁻¹·min⁻¹, \( p = 0.35 \)). Although not significantly different, males (9.5 min) and females (5.2 min) with PD were unable to tolerate the exercise test as long as male (13.1 min, \( p = 0.02 \)) and female (5.4 min, \( p = 0.20 \)) controls [30]. Problems in interpreting study results stem from; low statistical power, varying fitness levels (i.e. female controls had poor cardiopulmonary fitness) and it is unlikely the subjects achieved true VO₂max [30]. The poor cardiopulmonary scores in the controls might suggest another underlying pathology; therefore, may not represent a healthy comparison.

*Estrogen and motoric function.* Estrogen may influence PD symptoms in premenopausal females. Kompoliti investigated ten premenopausal females (mean age = 42.3 ± 5.8 years) prospectively during their ‘off-state’ for five weeks [24]. Menstruating females with PD experienced cyclical changes in their motor skills, as measured by the UPDRS (mean change = 10.9 ± 6.4), although changes were not correlated with serum levels of estrogen (\( p = 0.09 \)).

Although the evidence presented is scarce, existing research demonstrates that functional ability is likely limited in females with PD. Results present restrictions in gait, lower-limb strength and balance in females with PD. This suggests that further investigation into specific physiological patterns and interventions specific to females with PD is warranted.

3.5.2. Intervention studies

*Balance.* Venglar administered a twice-weekly (group/home) Tai Chi intervention for eight-weeks [32]. This single-subject case-study of a 63-year-old female diagnosed with PD (duration = 20 years) had previously reported frequent loss of balance and falls. Immediately post group-intervention (eight-weeks), the participant reported further loss of balance (ABC-20%). However, the participant continued to practise Tai Chi at home 3–5 times per week following the conclusion of group-exercise, and improved her Activities Balance Confidence scale score by 40% (20% netgain) at two-month follow-up [32]. Also, the participant reduced their Timed-Up and Go time (12.3–10.6 s) and number of steps (17–14 steps) post-intervention. Authors reported improvements in Functional Reach scores, although no values were given. Finally, the participant self-reported that Tai Chi improved her ability to regain movement after freezing of gait and increased fall-risk awareness [32].

*Aerobic endurance.* Schenkan and colleagues studied two males (60, 72 years) and one female (52 years) with PD as part of a larger randomized controlled trial of a four-month aerobic endurance exercise program [18]. The female’s UPDRS performance declined during the study; however, continuous-scale physical functional performance balance score (16.7%), VO₂max (8.5%) and 6-min-walk distance (16.3%) all improved, but no statistical analysis was performed [18]. Additionally, functional axial rotation improved on the right (+2.5°) but declined on the left-side (−20°), demonstrating the often-asymmetric symptom expression characteristic of PD. This suggests that exercise may improve physical fitness but not delay disease progression in this female with PD.

*Estrogen supplementation and motoric function.* Tsang et al. investigated low-dose estrogen in relation to motoric function in 40 postmenopausal females with PD (>2 years prior menstruation) [33]. Females were randomized to either low-dose estrogen (Premarin, 0.625 mg) or placebo daily for eight-weeks. Mean self-reported ‘on-time’ increased (7%) and ‘off-time’ decreased (4%) and UPDRS motor subscale improved (3.5 points) compared to placebo (\( p < 0.05 \)) [33].

4. Discussion

How PD impacts females is currently under reported which is of concern, as females often cite greater disability and reduced quality of life compared to males [13]. Since no cure exists, PD management in females should emphasize the maintenance of functional independence and quality of life. This review examined 12 studies that reported on the functional abilities of females with PD. Albeit equivocal, literature suggests that females with PD have different gait patterns compared to age-matched healthy females and males with PD. In addition, these studies reported poor balance confidence and increased freezing of gait in females as compared to males with PD. Females experience lower exercise tolerance compared to males with PD and controls. Evidence suggests that low-dose estrogen in postmenopausal females with PD may improve duration of medication effectiveness (‘on-time’) and UPDRS motor scores. Although the studies offer insight into gait, balance, and motor function characteristics in females with PD, these insights are limited due to methodological concerns.

Studies presented use a variety of methodologies and measure different functional outcomes, making it difficult to compare. To make conclusive statements regarding the specific impact of PD on females is premature, and these conclusions should be interpreted with caution. Future investigations, sufficiently powered with equal sex-distributions would enable more conclusive statements for defining sex-differences in functional limitations, and the contribution of female physiology to PD symptom expression. In addition, these results may reflect significant age differences in PD population, as females are typically older [7].

Results support sex-differences in PD gait [28]. Cadence was inconsistently reported in females compared to males with PD [23,31] and healthy controls [28,31]. Subjects achieved speeds differently; females took more steps with shorter stride lengths compared to males [23]. However, biomechanical sex-differences, physical condition and/or stage of PD may account for the variance. Freezing of gait occurs more frequently in females, especially as PD progresses [25].

Lower body muscle strength and size declines with age, especially in combination with decreasing bone density in females; this is associated with falls, fracture and functional dependence [35,36]. Pääsuke and colleagues [26,27] reported slowed reaction time, reduced force generation, and increased chair-stand time in knee-extensors of females with PD compared to age-matched controls. Chair-stand assessment is clinically important and directly applicable to UPDRS. This suggests that females with PD experience greater loss of lower-body muscle strength compared to controls, increasing fall-risk. Isolated laboratory-based electromyography in knee-extension and elbow-flexion show low frequency activation (5–15 Hz) and deficits in modulating muscle activation in persons with PD, especially females [37,38]. Electromyography may determine the influence of muscular strategies on gait and balance control, and thus provide further clinical information relative to functional mobility in persons with PD.

Sex contributed significantly to dynamic balance [29]. Ankle strength contributes to postural control and may explain poor balance control in females with PD. Longer balance interventions may improve confidence, kinesthetic awareness and balance abilities; although current evidence is speculative [37]. It is unclear whether benefits result from improved balance or confidence [39].

Persons with PD reach exercise tolerance thresholds earlier than age-matched controls; biomechanical inefficiency caused by rigidity and slowed movement initiation may contribute [30]. Unfortunately, sex-differences are unclear due to limited female participants. Endurance exercise training improved ambulatory
economy in males and females with PD; however, females were less efficient than males with PD and controls [30]. This is consistent with reports that persons with PD have 20% higher energy expenditure than age- and sex-matched controls [40].

Fluctuating estrogen levels in premenopausal females with PD were not directly related to function [24]. However, in postmenopausal females, daily low-dose estrogen significantly improved on-time and UPDRS motor ability [33]. Future investigations should examine estrogen therapy on motor ability, dosage, and long-term implications [41].

4.1. Recommendations

Future studies should emphasize the potential for sex-differences and consider improved methodology (i.e. sex-matched recruitment, follow-up). In addition, investigators should carefully consider the use of ‘sex’ and ‘gender’ within their research, as they both have distinct meanings. Here we emphasize sex-differences, since biology influences PD symptoms and ultimately impacts the female’s ability for independent function and substantially reduces her quality of life as compared to males with PD. Rehabilitation guidelines need to define the specific dimensions of exercise (i.e. frequency, intensity, time, type) most effective on females with PD.

5. Conclusion

Clinicians make decisions on appropriate treatment options for individuals with PD. This review presents variables that may influence PD expression in females, yet acknowledges that only a small portion of the literature considers disease implications on females. Also, the heterogeneous nature of PD makes it difficult to generalize these findings to all females with PD, whose symptoms and experiences may differ. Additionally, the importance of cognitive, environmental, metabolic and peripheral factors requires further consideration [14, 35]. The impact of gender roles on disease expression, quality of life and what it means to be a woman living with PD deserves further inquiry so intervention studies can be applied appropriately [42].

Contributors

K.P. Roland: Contributed to conception, organization and execution of research project (performed literature review), designed and executed analysis, drafted manuscript, involved in manuscript review and editing. J.M. Jakobi: Contributed to conception of research project, provided project oversight, involved in manuscript review and editing; C. Powell: Provided expert opinion, involved in manuscript review and editing; G.R. Jones: Contributed to conception and organization of research project, provided project oversight, involved in manuscript review and editing.

Conflict of interests

All authors consent to have seen and approved the final version and have no competing interests to disclose.

Financial disclosures

Efforts were supported by Faculty of Health and Social Development, University of British Columbia -Internal Research Award.

Kaitlyn P. Roland is supported by Canadian Institute of Health Research (CIHR) and Parkinson Society Canada – Psychosocial Doctoral Award.

Provenance and peer review

Not commissioned and externally peer reviewed.

Acknowledgements

Authors would like to thank S. Bigsbys, A. Janssens, J. Stanizewski, C. Smith, and D. Uniat for their diligence in reviewing articles.

References


