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1 **Management of Balance and Gait in Older Individuals with Parkinson Disease**

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17 **Summary**

18 Difficulties with walking and balance are common among people with Parkinson disease

19 (PD). Effective management of these walking and balance problems is critical, as these issues

20 can contribute to decreased mobility, falls, social isolation, reduced quality of life, and increased

21 mortality. This review provides an overview of the gait and balance disorders associated with

22 PD and discusses the methods currently utilized to manage gait and balance problems among

23 people with PD. These methods include pharmacological, surgical, and rehabilitative

24 approaches. Remaining challenges and future directions, including the need for

25 comprehensive, multidisciplinary, patient-centered care provided by qualified movement

26 disorders experts, are also highlighted.

27

What is Parkinson Disease?

Parkinson disease (PD) is a progressive neurodegenerative disorder that affects between 1-2% of individuals over 65 years of age and 3-5% of those 85 or older [1]. Age appears to be the greatest risk factor for PD, but many other contributing factors have also been identified [2-4]. At present, PD affects 1-1.5 million people in the United States and an estimated 40 million people worldwide. The number of individuals with PD will increase in coming decades, as the percentage of the U.S. population over age 65 rises from its current level of 12% to over 20% by 2030 [5].

PD is characterized by four cardinal features: tremor, bradykinesia, rigidity, and postural instability. The symptoms of PD arise only after substantial loss of dopaminergic neurons in the substantia nigra pars compacta. In fact, PD was originally attributed only to neuronal loss within the substantia nigra pars compacta, and a concomitant loss of dopamine. Pharmacologic replacement of dopamine is the most common, and arguably most effective, treatment for PD. However, PD is now thought to involve not only the dopaminergic system, but also other neurotransmitter systems whose role may become more prominent as the disease progresses [6]. These non-dopaminergic systems may be particularly implicated in balance and gait disorders, the management of which is the focus of this paper. Balance and gait impairments are particularly problematic for individuals with PD, as they can lead to falls, injury, and fear of future falls. As a result of injury and/or fear of falling, individuals may limit their physical activity which may result in social isolation as well as subsequent muscle weakness and osteoporosis. These in turn may contribute to increased risk of future falls and fall-related injuries [7]. The purpose of this paper is to provide an overview of the gait and balance disorders associated with PD and discusses the methods currently utilized to manage gait and balance problems among people with PD. The ideal combination and prioritization of these approaches needs to be determined on an case by case basis.

Gait, Balance, and Falls in Parkinson Disease

<u>Gait Impairments</u>

Many individuals with PD have gait difficulties that greatly limit functional mobility. The

majority of studies focusing on Parkinsonian gait examined walking in a straight line. These

studies showed that straight ahead walking in PD is characterized by: 1) a flexed posture, 2)

short, shuffling steps, 3) deficits in stride length regulation, 4) reduced foot clearance during

swing, 5) increased cadence, 6) limited extension at the hip and knee and reduced ankle

plantarflexion, 7) reduced transverse rotation of the trunk and pelvis, 8) inappropriate

coactivation of muscle agonist-antagonist pairs, and 9) reduced muscle activation amplitudes [8-

14]. The cause of these gait impairments is thought to be a disturbance in the motor set function

of the basal ganglia, which is involved in regulation of movement amplitude [15]. It has also

been hypothesized that the basal ganglia contribute to the regulation of postural alignment and

motor control, which may play a role in gait dysfunction in PD [16,17].

People with PD often have even more difficulty walking in challenging situations than they

do walking forward. For example, individuals with PD experience exacerbated gait impairments

when required to perform a concurrent task. Specifically, during dual task walking, gait speed

and step length are reduced and stride to stride variability is increased relative to single task

walking [18-23]. In backward walking, gait speed and stride length are also reduced relative to

forward walking in people with PD compared to people without PD [24,25]. Both dual task

walking and backward walking have been recommended as important tasks to evaluate when

assessing gait in people with PD.

In addition to difficulties with dual task walking and backward walking, many people with PD

have more difficulty turning while walking than they do walking in a straight line. Individuals with

PD, particularly those with a history of freezing or falls, use an increased number of steps to turn

as compared to people without PD [26,27]. People with PD also tend to turn en bloc, i.e.

rotating the head and trunk simultaneously rather than in sequence, and require greater time to

82 turn [28-30]. The work of Crenna et al. [28] is particularly interesting because it reveals that

83 turning deficits are present even in individuals with mild PD who as yet have no alteration or

84 impairment in their straight walking. This suggests that turning difficulty may affect individuals

85 with PD even from a very early stage of the disease when other motor symptoms are not yet

86 apparent.

87   Turning is particularly problematic because it is one of the primary triggers for freezing of

88 gait (FOG). FOG, "an episodic inability (lasting seconds) to generate effective stepping", affects

89 more than 50% of patients who have had PD for over 5 years [31,32]. FOG commonly occurs

90 during turning, but may also occur at gait initiation or when walking through doorways or other

91 narrow spaces. Those who experience FOG are more negatively affected than those without

92 FOG by challenging conditions like dual task walking and backward walking [25]. FOG is a

93 prominent cause of falls, particularly during turning [33-35]. Falls that occur during turning are

94 eight times more likely to result in hip fracture than falls during straight line walking [36].

95

96 <u>Balance Impairments</u>

97   Postural instability is one of the cardinal symptoms of PD. Though it is often associated

98 with mid-to-late disease progression, recent studies have shown subclinical manifestations of

99 postural instability in the early stages of PD as well [37-40]. Many different factors are believed

100 to contribute to postural instability including impaired peripheral sensation and somatosensory

101 integration, decreased strength, axial rigidity, and impaired postural responses [41-46].

102 Disturbed motor programming within the basal ganglia as well as abnormally processed

103 proprioceptive signals are thought to be underlying causes of postural instability in PD [47].

104 Recent studies have also consistently shown that postural instability is not relieved with

105 dopaminergic medication, therefore, non-dopaminergic pathways have been hypothesized to

106 contribute to postural instability [48, 41].

107   Many different modes have been used to quantify instability in PD. In a clinical setting,

108 quick screening of postural instability may include the UPDRS Retropulsion/Pull test [49] or the

109 Push and Release test [50]. Assessments of static postural control have found that individuals

110 with PD have increased sway area and abnormal shifts in the center of pressure [38, 39, 51].

111 Dynamic posture, such as during gait and functional activities, has also been shown to be

112 impaired with slower velocities of movement and decreased ability to move the center of mass

113 appropriately [40, 42, 46, 52, 53].

114   Both anticipatory postural adjustments and reactive postural adjustments are impaired in

115 individuals with PD, with decreased amplitude and coordination of these movements [40, 54,

116 55]. An association exists between fear of falling and postural instability, though whether it is a

117 causative relationship or a correlation is unclear [56]. However, postural instability is also related

118 to falls in individuals with PD [57-59].

119

120 <u>Falls</u>

121   Individuals with PD are five to nine times more likely to sustain recurrent falls than age-

122 matched individuals without PD [60, 61]. Falls and fractures are the primary reason for hospital

123 admissions in individuals with PD [62, 63]. Studies have shown that 25-32% of falls result in

124 injury [58, 64] with at least 3% [65] resulting in serious injury requiring medical attention. These

125 are substantial numbers considering in prospective studies, 45-68% of individuals with PD will

126 fall during a 12 month period with 29-51% experiencing two or more falls [58, 61, 64, 66]. In a

127 given six-month period 29% of individuals with PD without a history of falling will experience

128 their first fall [43]. Furthermore, individuals with PD have a 3.2 fold greater risk of hip fracture

129 than age-matched individuals without PD [67]. Falls and subsequent hip fractures carry

130 substantial personal costs, such as fear of falling, withdrawal from social activities, and a

131 decreased quality of life [7, 68]. Hip fractures also represent a substantial financial burden to

132 society, with the cost of hip fracture care in individuals with PD totaling approximately $192

133 million per year in the United States alone [69, 67]. One study suggests that frequent falls in an

134 individual with PD can be used as a marker to predict life expectancy [70].

135   The majority of falls in this population occur in the home and have intrinsic causes (i.e.

136 disease processes such as postural instability, freezing, loss of concentration, etc.) as opposed

137 to extrinsic causes (i.e. a wet floor, obstacle, etc.) [60, 64, 65]. Falls often occur during transfers,

138 when bending or reaching, while walking especially in dual task situations, and during turning as

139 well as due to freezing and tripping/accidental causes [7, 60, 64, 65]. It is interesting to note that

140 2/3 of individuals who fell said their signs and symptoms were under control when they fell [60].

141   Many studies have compared individuals with PD who fall and those who do not fall.

142 Those who fall tend to have longer disease duration, increased disease severity, a history of

143 previous falls, increased levodopa replacement medication use, and increased freezing and

144 dyskinesia [64, 71, 43, 58, 59]. They perform more poorly in balance and functional mobility

145 measures, have increased fear of falling, have increased sway in standing, and have decreased

146 lower extremity strength [60, 71, 43, 72, 59]. Cognitive factors such as decreased memory,

147 power of attention, and reaction time have also been shown to be associated with falling [64,

148 58]. Though cardiovascular issues such as orthostatic hypotension and postprandial

149 hypotension have been shown to be present in individuals with PD, their contribution to falls has

150 been debated [64, 43, 58, 73].

151

152 **Therapeutic Approaches to Management of Gait and Balance in Parkinson Disease**

153 *Pharmacological Treatment*

154   Levodopa (L-DOPA) is often the drug of choice in the pharmacologic management of

155 motor symptoms in PD as it replaces endogenous dopamine which is reduced in individuals with

156 PD [74]. Bradykinesia and rigidity often respond well to treatment with L-DOPA, while there is

157 increased variability in response with respect to tremor [75]. The introduction of L-DOPA also

158 has proven to be beneficial in improving gait disturbances. Several gait parameters are

159   negatively influenced by withdrawal of L-DOPA therapy [26]. The parameters most consistently

160   impacted when patients are *off* L-DOPA are stride length and speed [76-84]. Additional features

161   noted in individuals *off* L-DOPA include decreased arm swing and reduced trunk rotation,

162   decreased ground reaction forces and reduced range of motion at the knee [85], and reduced

163   plantarflexor power [84]. Many studies have demonstrated that stride length and gait speed are

164   responsive to L-DOPA, with one study showing an increase of 0.25 meters/sec from o*ff* to *on*

165   medication [86, 80], while other parameters such as stance duration and arm swing are dopa-

166   resistant [8, 76-78, 87]. These dopa-resistant aspects of gait support the idea that the pathology

167   of PD extends further than just the nigrostriatal dopaminergic system [75].

168   Freezing of gait (FOG) is one of the most debilitating and least understood gait

169   disturbances in PD [88]. Treatment of freezing is often extremely difficult, and specifically

170   regarding L-DOPA, results are mixed. Those patients who experience FOG during the *off* state

171   often experience improvements in freezing after taking L-DOPA [89]. Schaafsma and

172   colleagues found that among those participants who experience primarily *off* state freezing,

173   FOG episodes occurred more frequently, had a longer duration, and also involved significant

174   akinesia. In the same study, the observation of FOG in the *on* state was quite different as the

175   episodes occurred less frequently, had a shorter duration, and did not involve complete blocks

176   in movement [90]. Individuals with PD experiencing *on* state freezing present a much more

177   challenging problem as their FOG is not responsive to L-DOPA. This problem is considered to

178   be quite rare [88], and it has been suggested that dopaminergic agents be reduced in

179   individuals with *on* period freezing [91]. For patients experiencing FOG that is resistant to L-

180   DOPA, other therapeutic options may be considered [92].

181   Some alternative pharmacologic approaches aimed at treating FOG have been

182   somewhat effective, while others have not. Selegiline, an MAO-B inhibitor, was shown to be

183   effective in reducing the development of FOG in patients with early PD [93]. Shoulson and

184   colleagues found similar results in individuals in the advanced stages of PD [94, 95], and it is

185   suggested that this may be of greater clinical significance as FOG and falls are highly related in

186   the later stages of PD [92]. Rasagiline, another MAO-B inhibitor, has also been shown to have a

187   positive effect on FOG, however, the clinical significance of this improvement is not yet

188   understood [92]. Amantadine has been shown to have conflicting results with respect to FOG.

189   Giladi and colleagues reported that those treated with amantadine were less likely to develop

190   FOG [96], while Macht and colleagues reported an association between treatment with L-DOPA

191   and amantadine and increased FOG frequency [97]. Botulinum toxin was originally found to

192   have a positive effect on FOG [98, 99]; however, Gurevich and colleagues found dissimilar

193   results and also found that botulinum toxin increased fall risk [100]. Methylphenidate has also

194   been examined as a treatment for FOG [101, 102]. In a study examining apomorphine, an

195   alternative option for those with advanced PD with motor complications, researchers found that

196   FOG was not improved following a single dose of this medication [103]. In summary, FOG

197   remains a substantial problem that is not well addressed by current pharmacologic approaches.

198

199   *Deep Brain Stimulation*

200   Surgical intervention, in the form of deep brain stimulation (DBS), is an increasingly

201   common treatment method often employed in advanced stages of PD where pharmacological

202   therapy does not adequately control parkinsonian symptoms and/or complications such as

203   wearing off of medication and levodopa-induced dyskinesias have developed. With the intent of

204   improving the predominant symptoms in PD, including gait disturbances and postural instability,

205   the favored target for stimulation is most often the subthalamic nucleus (STN) [104]; however,

206   there is conflicting evidence regarding gait improvement following STN stimulation in those with

207   PD [105-110]. It is important to note that stimulation of the internal globus pallidus (GPi) has

208   been a target for DBS in the past, but STN stimulation is now preferred by many because the

209   antiparkinson medications can typically be reduced more following STN as compared to GPi

210   surgery, and less stimulation energy is needed [111]. Recently, support for stimulation of the

211 pedunculopontine nucleus (PPN) [112-114] has gained traction among surgeons, but again,

212 evidence supporting this technique without pairing it with STN stimulation is controversial [115].

213 It is imperative that healthcare professionals understand these surgical techniques and how

214 they may affect gait and balance in individuals with PD so that intervention plans may be

215 designed properly.

216 Using quantitative measures, STN stimulation has been shown to improve gait

217 parameters such as stride length and gait velocity [109]. In a meta-analysis conducted by

218 Bakker et al., bilateral STN stimulation was found to improve gait disturbances and postural

219 instability, as assessed by the UPDRS, in the *off* medication state [108]. When examining anti-

220 Parkinson medication and STN DBS and their effects on gait and gait stability, Hausdorff et al.

221 [110] noted that combined effects of medication and DBS on gait speed, stride length, and gait

222 stability were larger than effects of DBS alone. Krack et al. [107] reported that STN stimulation

223 provided an initial improvement in gait and postural instability, but performance declined with

224 time, and by five years, patients' gait disturbances and postural instability were more impaired

225 than prior to surgery. For those patients experiencing freezing of gait (FOG) that is responsive

226 to levodopa (L-DOPA), STN stimulation has been shown to fully replicate the L-DOPA induced

227 improvement seen prior to surgery [107, 116-119]. However, regarding L-DOPA resistant FOG,

228 STN stimulation has proven to be ineffective [120, 121, 116, 118]. As such, new surgical targets

229 are necessary to determine if DBS surgery is effective at improving FOG in individuals with PD.

230 It has been proposed by previous reports that the PPN plays a role in the origination of

231 PD motor symptoms, particularly gait disturbances and postural instability [122, 123]. Moro and

232 colleagues examined UPDRS II, III, and IV scores as well as sub-scores in six subjects at three

233 and 12 months post unilateral PPN stimulation [114]. At three months post-surgery, UPDRS II

234 scores significantly improved, predominantly due to marked decreases in sub-scores for falling

235 and freezing [114]. The UPDRS III scores (including gait, postural stability) demonstrated a

236 trend toward improvement; however the scores did not reach significance [114]. UPDRS II sub-

237   scores for falling at 12 months were similar to those at three months, and UPDRS III scores

238   trended toward significant improvement from three to 12 months post-implantation [114]. In

239   contrast, Stefani et al. found that in the *off* medication state, PPN DBS alone did not improve

240   UPDRS III scores [115]. It was also found that PPN DBS + STN DBS when *on* medication

241   improved UPDRS II scores [115]. In both *on* and *off* medication states, dramatic improvements

242   in gait and balance were found in two patients post-PPN stimulation. It is important to note that

243   these differences were found 42 (patient 1) and 16 (patient 2) days post-surgery and as such

244   micro-lesion effects from the surgery might still have been present. Repeated clinical

245   observations at time points more than 3 months post-surgery are necessary to avoid micro-

246   lesion and placebo-like effects following this type of procedure [124]. In summary, while the

247   PPN, especially when paired with STN DBS, has recently been proposed as a surgical target for

248   improving gait and balance in those with PD, it is not yet recommended as a substitute for STN

249   DBS [115]. Current evidence is limited by questions regarding electrode targeting and in some

250   studies it is not clear that electrodes were successfully placed within the PPN. More data are

251   needed to confirm or refute PPN DBS efficacy on gait and balance deficits in those with PD.

252

253   ***Physical Rehabilitation***

254   <u>Treadmill Training</u>

255   Recently, the effects of treadmill training (TT) on gait parameters, balance, quality of life

256   (QOL), and functional tasks have been examined to determine efficacy of this intervention for

257   people with PD. Mehrholz et al. conducted a systematic review of studies investigating the

258   effects of TT on specific gait parameters in those with PD [125]. Eight small studies were

259   included and improvements were noted in gait speed, stride length, and walking distance when

260   comparing individuals who underwent TT and controls [125]. With regards to training intensity,

261   Fisher et al. reported that high-intensity TT yielded significant improvements in self-selected gait

262   speed, stride length, step length, and gait kinematics [126]. When compared with conventional

263 gait training, structured TT led to significant improvements in over-ground walking speed (1.37

264 m/s pre to 1.56 m/s post-training) and stride length (0.72 m pre to 0.78 m post-training), as well

265 as double stance duration [127]. Miyai et al. studied body weight-supported treadmill training

266 (BWSTT) versus conventional physical therapy in individuals with PD and found the BWSTT

267 group maintained improvements in gait speed and stride length at one and four months post

268 intervention [128]. Multi-directional TT (forward, backward, sideways) and step-perturbation

269 training have also been shown to improve cadence and gait speed in men with PD [129].

270   While gait parameters are commonly measured when investigating the effects of TT,

271 other studies have examined its effects on a variety of other outcome measures. Studies by

272 Cakit et al. and Protas et al. have shown that different protocols for TT can improve balance

273 [130], decrease fear of falling [130], and decrease number of falls [129]. A six week TT program

274 in which participants with PD walked at 70%-80% of maximal heart rate led to improvements in

275 lower extremity functional tasks (20-m walking time, timed U-turn, turning around a chair,

276 ascending/descending stairs, standing from a chair, and standing on one foot) [131]. In addition

277 to improvements in lower extremity capabilities and balance, Hermann et al. found that TT

278 significantly improved QOL [132].

279   The mechanisms by which TT improves gait in individuals with PD are not yet fully

280 understood. In a recent study by Bello and colleagues examining these mechanisms, the

281 authors theorized that gait improvements following TT are related simply to the belt movement

282 on the treadmill, which forces stepping through stretch facilitation of hip flexors and

283 plantarflexors and the termination of the stance phase [133]. Other studies support the idea that

284 TT forces step lengthening and may be an influential factor in gait improvements [9, 134, 135].

285 Protas et al. [129] hypothesized that visual and auditory cues, which have been shown to

286 positively impact gait and balance in those with PD [136], provided by the treadmill could have

287 lead to improvements in gait and balance, respectively. Herman et al. theorized that perhaps the

288 treadmill provides an external rhythm that compensates for the ineffective internal rhythm of the

289   basal ganglia in those with PD. Another idea proposed by Herman et al. acknowledges that the

290   intense, repetitive TT may add to motor learning which may explain the lasting improvements in

291   gait five to six weeks post TT [132].

292   Although limited, there is good evidence supporting the short-term benefits of TT for

293   people with PD. While the mechanisms behind the gait and balance improvements are not yet

294   fully understood, the literature documenting such improvements should not go unnoticed. As

295   such, rehabilitation professionals should consider TT as an adjunct to over-ground gait training

296   for people with PD.

297

298   Use of External Cues and Assistive Devices

299   External cues are thought to benefit individuals with PD by bypassing the degenerated

300   basal ganglia and utilizing other neural pathways. It is hypothesized that external cues act via

301   the parieto-premotor pathways or the cerebellar circuits [22, 137]. Auditory, somatosensory, and

302   visual cues have all been studied.

303   Auditory cueing has been shown to improve speed, cadence, stride length, and gait

304   variability, though some studies have shown it has less effect on stride length and gait initiation

305   than visual cueing [22, 138-141]. Auditory and somatosensory cues are comparable for

306   improving turning velocity and in dual task situations in individuals with PD [142, 143]. Visual

307   cueing can increase push off and improve gait initiation, and it has been shown to be most

308   effective at increasing stride length [22, 138]. Some studies have demonstrated, though, that

309   visual cues may decrease cadence and can interfere with dual task items [22, 140].

310   Some studies have attempted to combine different cueing types to see if they have an

311   additive effect. When visual and auditory are combined for gait, it is less effective than either

312   separately [140].However, when an audiovisual system was used to cue sit-to-stand transfers,

313   speed and torque of the transfer were better than without cueing [144]. An attentional strategy

314   and auditory cueing combined are effective in improving gait [143, 145, 146].

315   In a recent review of cueing for individuals with FOG, Nieuwbower [147] concluded that

316   visual cueing may benefit movement initiation while auditory may be more effective to maintain

317   gait symmetry and timing, though neither was able to consistently prevent FOG. Cueing should

318   be individually altered, as some cueing can induce freezing in some individuals, and on-FOG

319   and off-FOG may respond differently [147]. Freezers tend to benefit more from cueing during

320   turns and at -10% of their preferred pace for normal walking [141, 142].

321   Bryant et al. [148] sent individuals home with an auditory stimulator that had been

322   programmed during an initial evaluation. After one week of individuals practicing at home for 30

323   minutes a day, gait speed and stride length showed improvement, and 90% of participants

324   thought the device was helpful and easy to use [148]. Self-cueing techniques can be utilized as

325   well. Counting out loud, saying standard phrases, and singing are sometimes used [149].

326   Teaching individuals to sing in their heads while performing activities has been shown to

327   improve gait and turning in individuals with mild to moderate PD [150].

328   Dual task walking seems to benefit more from cueing than single task walking in

329   individuals with mild to moderate PD. In theory, the cueing allows an individual to decrease the

330   amount of attention necessary for gait, freeing up more attention for the secondary task [139,

331   143].

332   Recent studies have shown short-term carry over after training, though it is believed that

333   the cue must continue to be present to be effective long-term. Training with auditory cues for

334   eight weeks, three times a week while increasing the tempo allowed a plateau in progress to be

335   met, with a benefit in gait parameters (stride length, velocity, and cadence) being sustained six

336   weeks later [151]. Other studies of shorter cue-training duration have shown shorter carryover in

337   turning, dual task benefits, and fear of falling [142, 143].

338   Long-term delivery of cues may be accomplished via specialized assistive devices [152].

339   Assistive devices such as canes and walkers are frequently prescribed for people with PD and

340   can be modified to include a laser that projects lines on the floor that serve as visual cues to

341   facilitate gait. Other devices may offer additional postural support beyond that offered by

342   traditional devices [153]. Limited studies have been conducted to date to determine which

343   assistive devices are optimal, but some guidance is available in the literature [154, 155].

344   Emerging devices may also hold promise for the treatment of FOG [156].

345

346   <u>Resistance Training</u>

347   Evidence suggests that muscle force production is reduced in individuals with PD, even

348   in early stages of the disease, when compared to age-matched controls [157]. In fact, muscle

349   weakness has been described as a primary symptom of PD [158]. Resistance training has

350   been shown to be an effective intervention for improving strength, muscle mass, and function in

351   healthy older adults [159]; however, evidence supporting the efficacy of this type of intervention

352   for individuals with PD is currently limited. Falvo and colleagues suggest that resistive exercise

353   may reduce the presence of PD sequelae such as impaired motor function, muscle and bone

354   weakness, as well as reduced quality of life (QoL) and fear of falling, and as such stress the

355   need for well-controlled clinical trials examining high-intensity resistance training in those with

356   PD [160].

357   Recently, Dibble et al. studied the effects of a 12 week high-intensity, eccentric

358   resistance training program on a variety of outcome measures for individuals with PD [161]. The

359   investigation compared an active control group and an experimental group, both of which

360   partook in the same resistance traditional resistance training program; in addition, the

361   experimental group completed high-intensity eccentric training, while the control group did not.

362   The experimental group had significant improvements in lower extremity muscle force,

363   bradykinesia (measured by functional walking tasks), and QoL [161]. Similar results were found

364   in a study examining eccentric resistance training and its effects on muscle structure, stair

365   descent, and six minute walk test (6MWT) in individuals with PD [162]. Regarding specific gait

366   parameters, Scandalis et al. found that an eight week strengthening program improved stride

367   length (0.83 m pre to 0.95 m post-training) and walking velocity (1.0 m/sec change pre to post-

368   training) in individuals with PD [163]. Examining the effects of resistance training on balance,

369   investigators have found that those with PD undergoing both balance and resistance training

370   demonstrated significant improvements in balance and muscle strength [164, 165].

371

372   Balance Training

373   Balance training is a priority for individuals with PD to address postural instability. A

374   recent systematic review by Dibble et al.[166] found moderate evidence supporting exercise-

375   induced improvements in balance performance in mild to moderate PD. Keus et al.[167]

376   recommend balance training as one of the top four recommendations for physical therapy, and

377   the majority of exercise programs include some form of balance training [149, 166, 168-171].

378   Many mixed exercise programs (not balance training exclusively) have shown improvement in

379   balance assessments (i.e. TUG, BBS, 5-step test speed) and during functional activities (i.e.

380   gait parameters, turning, possible decrease in falls) after treatment [166, 169, 172]. Each of

381   these treatment protocols has been studied for different durations and frequencies, most without

382   specifying the length of balance training specifically. Many different modes of balance training

383   can be utilized including, but not limited to, perturbations on a treadmill, calisthenic/balance

384   exercises, practicing functional tasks that require increased balance, and balance specific

385   training on a force plate [166, 171-173]. Further details on activities included in the balance

386   exercise portion of treatments are not specifically described in most studies and, therefore,

387   cannot be compared between studies.

388   An individual's confidence in his balance should also be addressed during balance

389   training, as decreased balance confidence and fear of falling can negatively impact quality of life

390   and are associated with falls [167]. Whole body vibration was thought to increase balance in

391   individuals with PD, however, more recent studies show no added benefit using this form of

392   therapy [174, 175]. Some individuals with PD might also have vestibular deficits that contribute

393   to their balance impairment; some studies show vestibular rehabilitation techniques may be

394   beneficial [176, 177].

395

396   <u>Flexibility Exercises</u>

397   Since rigidity is known to be one of the cardinal symptoms of PD, stretching is often

398   recommended to be included in a rehabilitation program for this population [167, 170, 149].

399   Many exercise protocols that have shown improvement in individuals with PD include stretching

400   or flexibility as one component of the program [57, 169, 172, 171]. Increased rigidity in the hip

401   and trunk musculature in individuals with PD has been focused on as it is thought that this

402   increased axial rigidity may contribute to poor posture and abnormal coordination during walking

403   and turning [42, 178, 179]. Individuals with PD may have decreased axial flexibility, which can

404   contribute to decreased functional reach [180, 181].

405   Very few studies have truly examined the outcomes of a stretching or flexibility program

406   in individuals with PD. Since studies have shown that axial rigidity is not affected by levodopa

407   replacement therapy, a stretching program may be an effective alternative [182, 179]. Flexibility

408   training has been shown to improve functional reach with subjective improvements in daily tasks

409   such as driving, scratching their back, and rolling in bed but not in other functional tasks such as

410   stand to supine time or six-minute walk distance [180]. The flexibility training focused on

411   decreasing overall activation, relaxation into stretches with emphasis on axial structures, and

412   performing functional task [180]. A promising study by Bartolo et al.[183] evaluated a

413   rehabilitation protocol for individuals with PD who also had lateral trunk deviations. During this

414   exercise program, which included stretching and relaxation exercises, functional strengthening,

415   and gait and balance training, emphasis was placed on correcting postural trunk deviations and

416   improving trunk control. They found improved posture, flexibility, and trunk mobility with gains

417   lasting up to six months [183].

418   In a recent article presenting a new exercise program framework, King and Horak [170]

419   summarize that rigidity impacts posture by increasing flexor tone, decreasing trunk range of

420   motion during functional tasks and walking, and increasing muscular co-contraction which is

421   unfavorable during automatic postural responses. They suggest that activities be performed that

422   have increased emphasis on trunk and head rotation, postural awareness/erect alignment,

423   flexor muscle lengthening, and increasing limits of stability [170]. As of now, this exercise

424   program has not been evaluated for its effectiveness.

425   Neck rigidity, which is also greatly increased in individuals with PD, has recently been

426   shown to correlate with posture and gait as well as have significant impact on functional mobility

427   and balance [182]. At this time, no studies have addressed the efficacy or effectiveness of

428   stretching or neck flexibility exercises on neck rigidity or functional tasks. In summary, there is

429   very little research that supports stretching in individuals with PD; however, expert opinion

430   continues to prioritize the inclusion of stretching and flexibility exercises in rehabilitation and

431   prevention exercise regimens for individuals with PD [169, 172, 167, 170, 149, 171].

432

433   <u>Alternative Exercise Programs</u>

434   Alternative modes of exercise such as dance and Tai Chi have also been shown to be

435   effective for improving balance and gait function in individuals with PD. Dance may be ideally

436   suited to those with PD, as it is a social activity that is inherently motivating [184]. Dance is also

437   performed to music which can provide an external cue to facilitate movement. In addition,

438   dance involves the teaching and practice of specific movement strategies and incorporates

439   dynamic balance challenges. Dance can also result in improved cardiovascular function, a

440   testament to the fact that, if done with sufficient intensity, dance is an excellent form of aerobic

441   exercise [185, 186]. Several studies have reported significant improvements in balance, six

442   minute walk distance, and gait velocity in groups with PD who participated in Argentine tango or

443   waltz/foxtrot classes [187-191]. For a comprehensive review of the literature regarding dance

444 and PD please see Earhart [192]. For recommendations on implementing dance classes for

445 individuals with PD see Hackney & Earhart [193].

446   Tai Chi is another alternative exercise approach that has been examined in several

447 studies with mixed results (for review see 194). Two studies have specifically reported balance

448 outcomes, and both noted reduced falls or improved balance [195, 196]. Many of the Tai Chi

449 studies are limited by a small sample size and some also lack a control group. It is also unclear

450 whether Tai Chi is superior to traditional exercise, as one study found no differences between a

451 conventional exercise group and a Tai Chi group [197].

452

453 Multidisciplinary Care Approaches

454   Most care for individuals with PD is currently performed on an outpatient basis using

455 monodisciplinary care [198]. Few studies have assessed the effectiveness of the use of

456 collaborative, intense inpatient rehabilitation for individuals with PD. One observational study

457 found that individuals who participated in an inpatient rehabilitation program post-DBS

458 placement had expedited optimization of their DBS settings and medications due to the 24-hour

459 monitoring, reducing the process from a period of months to a period of weeks. The intense

460 therapy post-surgery also allowed functional changes and gains to be immediately utilized,

461 balance and gait training optimized, psychological changes to be monitored, and a home

462 exercise program to be created to hopefully maintain gains [199].

463   Ellis et al.[200] further suggests that the comprehensive, multidisciplinary environment

464 might be effective for individuals with PD who are experiencing a decline in function, falling

465 more frequently, or are having more complex symptoms. After an average of 21 days of rehab,

466 71% of the patients in this cohort, including patients who did and did not require medication

467 alterations, showed a clinically important improvement according to the Functional

468 Independence Measure [200]. The inpatient rehabilitation team has been suggested to include

469 some combination of neurosurgeons, neurologists, physical therapists, occupational therapists,

470   speech-language pathologists, nurses, case managers, nutritionists, sexologists, psychiatrists,

471   and physiatrists, as is necessary for the individual patient [198-200]. As of now, however, no

472   comparison of outcomes to standard care or cost analysis has been made. Effects on quality of

473   life, carryover of training into the home environment, long term outcomes after inpatient

474   rehabilitation, and characteristics of individuals who are most appropriate for inpatient

475   rehabilitation are still unknown at this time.

476   Multidisciplinary care has also been advocated for outpatient settings, though research

477   is again limited [198]. Utilization of both medication and physical therapy approaches combined

478   was superior to medication alone [201]. Multidisciplinary care can result in both short-term [202]

479   and long-term benefits, and can help most individuals to maintain or improve function for up to

480   three years [203].

481

482   **Remaining Challenges & Future Directions**

483   While there are multiple approaches to the treatment of gait and balance disorders in

484   PD, and multidisciplinary approaches offer promise for the best overall management of these

485   conditions, several areas of challenge remain. One major issue is the fact that many aspects of

486   gait and balance are unresponsive to levodopa and likely represent non-dopaminergic features

487   of disease. Freezing of gait is an example of a very disabling symptom that is currently not well

488   addressed by any approach. Another area of challenge is that of motor complications, i.e.

489   dyskinesias and wearing off phenomena, that arise after long-term treatment with levodopa. In

490   addition to the lack of effective treatments and the presence of treatment side effects, there is

491   also challenge related to a lack of medical professionals with the specialized training and

492   knowledge necessary to deliver the most up to date and evidence-based care for people with

493   PD.

494   Future directions for the field of gait and balance management in PD are many and will

495   likely include a shift from monodisciplinary care, where the focus has been on treating the

496   symptoms, to a multidisciplinary approach that is patient-centered and focuses not only on

497   symptoms and impairments but also emphasizes quality of life. Future work is needed to

498   develop new medications, advance the targeting and application of DBS, and implement more

499   uniform and informed approaches to physical rehabilitation using evidence-based guidelines.

500   Several studies are currently underway that will provide new evidence regarding the

501   effectiveness of exercise-based approaches in the management of PD and should serve to

502   inform future care models for individuals with PD.

503

504   **EXECUTIVE SUMMARY**

505●   **Gait, Balance and Falls in Parkinson Disease**

506○   Gait and balance difficulties are a major problem for people with Parkinson disease.

507○   Gait is characterized by shuffling steps, decreased trunk rotation, flexed posture, decreased

508   speed, and in some cases freezing.

509○   Postural instability is one of the four cardinal features of PD and is associated with increased fall

510   rates.

511○

512●   **Therapeutic Approaches to Management of Gait and Balance Problems**

513○   Medical management of PD has, until relatively recently, focused primarily on pharmacological

514   approaches but many aspects of gait and balance impairments are not adequately addressed

515   by medication.

516○   More recently, deep brain stimulation has been added to the arsenal of treatment tools but

517   again does not fully address gait and balance issues.

518○   As such, physical rehabilitation approaches are a key aspect of managing gait and balance in

519   PD and can include specific gait and balance training, resistance training to improve muscle

520   strength, as well as prescription of assistive devices and use of external cueing.

521 o No current treatments effectively deal with all aspects of gait and balance impairments, with

522 freezing of gait being particularly resistant to treatment.

523

524 • **Remaining Challenges and Future Directions**

525 o Multidisciplinary, patient-centered care models are emerging and hold promise for improving

526 quality of care for individuals with PD.

527 o Such approaches will become critical in the management of gait and balance in PD using a

528 combination of medications, surgery, and rehabilitation.

529 o Management of gait and balance in PD is essential as impairments in gait and balance have a

530 major impact on quality of life, and quality of life may become the main outcome measure for

531 evaluating the effectiveness of PD management approaches.

532

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