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1 **Gait Coordination in Parkinson Disease: Effects of Step Length and Cadence**
2 **Manipulations**

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42

43 Abstract

44 **Background:** Gait impairments are well documented in those with PD. Prior studies suggest
45 that gait impairments may be worse and ongoing in those with PD who demonstrate FOG
46 compared to those with PD who do not. **Purpose:** Our aim was to determine the effects of
47 manipulating step length and cadence individually, and together, on gait coordination in those
48 with PD who experience FOG, those with PD who do not experience FOG, healthy older adults,
49 and healthy young adults. **Methods:** Eleven participants with PD and FOG, 16 with PD and no
50 FOG, 18 healthy older, and 19 healthy young adults walked across a GAITRite walkway under
51 four conditions: Natural, Fast (+50% of preferred cadence), Small (-50% of preferred step
52 length), and SmallFast (+50% cadence and -50% step length). Coordination (i.e. phase
53 coordination index) was measured for each participant during each condition and analyzed using
54 mixed model repeated measure ANOVAs. **Results:** FOG was not elicited. Decreasing step
55 length or decreasing step length and increasing cadence together affected coordination. Small
56 steps combined with fast cadence resulted in poorer coordination in both groups with PD
57 compared to healthy young adults and in those with PD and FOG compared to healthy older
58 adults. **Conclusions:** Coordination deficits can be identified in those with PD by having them
59 walk with small steps combined with fast cadence. Short steps produced at high rate elicit worse
60 coordination than short steps or fast steps alone.

61

62 Introduction

63 Gait impairments are well documented in those with Parkinson disease (PD).(1-6)
64 Decreased stride length, decreased velocity, and poor coordination are some impairments that
65 can be become debilitating for an individual with PD. Freezing of gait (FOG),a particularly
66 troubling symptom characterized by a spontaneous increase in cadence and decrease in step
67 length with an accompanying inability to produce effective stepping, (3, 7) is associated with
68 falls and reduced quality of life in this population.(8, 9) It has been suggested that gait
69 impairments in people with PD are worse in those who experience FOG (PD+FOG) than those
70 who do not experience FOG (PD-FOG). For example, those with PD+FOG exhibit increased
71 step-time asymmetry, step length variability, and cadence compared to PD-FOG.(5, 10, 11)

72 Coordination of steps has also been shown to be dysfunctional in those with PD during
73 gait, particularly in PD+FOG. Plotnik et al. demonstrated that those with PD+FOG exhibit
74 poorer coordination during forward walking than those with PD-FOG, even when FOG is not
75 elicited.(5) Danoudis et al. (12) also showed those with PD+FOG have poorer coordination
76 during preferred gait, as well as gait with an imposed decrease in step length. Nanhoe-Mahabier
77 et al. (6) showed those with PD have worse coordination while walking on a treadmill compared
78 to healthy controls, but no differences exist between groups during forward walking overground.
79 These studies demonstrate that gait coordination is affected in those with PD. However, it
80 remains unclear how coordination is affected during gait conditions that are characteristic of
81 FOG (i.e. increased cadence with progressively decreasing step length (3, 13, 14)) and
82 differences in coordination between those with PD+FOG and PD-FOG require further
83 examination. Identifying differences in coordination during conditions characteristic of FOG by

84 manipulating cadence and step length independently of one another and also concurrently may
85 have potential implications for understanding the underlying mechanisms of FOG.

86 In this study, we used PCI, a measure of gait coordination, to study the effects of
87 manipulating step length and cadence independently and in combination on gait coordination in
88 healthy controls (young and old) and those with PD+FOG and PD-FOG. Healthy old individuals
89 were included to determine how those with PD differ from individuals of the same age without
90 PD. Healthy young were included to examine differential effects of aging and PD on
91 coordination. To this end, coordination was measured during: 1) step length manipulation, while
92 holding cadence fixed; 2) cadence manipulation, while holding step length fixed; and 3)
93 combined step length and cadence manipulation. We hypothesized that decreasing step length or
94 increasing cadence would decrease coordination in people with PD compared to healthy controls.
95 We expected these effects to be additive, i.e. coordination would be poorest when step length
96 was reduced and cadence was concomitantly increased. Finally, we hypothesized that the
97 PD+FOG group would demonstrate the poorest coordination and be more affected by gait
98 manipulations compared to PD-FOG and healthy controls. We expected healthy young and
99 healthy older adults to be similarly affected by gait manipulations, and less affected than those
100 with PD.

101 **Methods**

102 **Participants**

103 Individuals with PD, healthy older, and healthy young adults participated. Subjects with
104 PD were divided into PD+FOG and PD-FOG based upon a score of ≥ 2 on item 3 of the Freezing
105 of Gait Questionnaire (FOG-Q)(15), indicating freezing episodes occurring at least once per
106 week. Participants with PD were recruited from the XXXX Movement Disorders Center

107 database. All participants with PD had a diagnosis of idiopathic PD according to established
108 criteria(16) and were asked to come in “OFF” medication (≥ 12 hour overnight withdrawal of
109 anti-parkinson medication). Healthy older adults (>30 years old) were often the spouses of those
110 with PD and were age-matched with the PD group. Healthy young adults (<30 years old) were
111 doctoral students at XXXX. Participants were excluded if they were unable to follow multiple
112 step commands or unable to walk independently without the use of an assistive device. All
113 participants gave informed consent as approved by the XXXX Human Research Protection
114 Office.

115 **Outcome Variables**

116 Phase coordination index (PCI) was the primary outcome measure. PCI quantifies gait
117 coordination by taking into account the accuracy and consistency of the timing of stepping
118 phases and was calculated as defined in previous literature.(17) Higher PCI values indicate
119 poorer coordination.(5, 17) Correlation between PCI and total FOG-Q score was included as a
120 secondary outcome measure. Prior work has only correlated FOG-Q and PCI during natural gait.
121 Therefore, we sought to correlate PCI during gait conditions characteristic of FOG with the
122 FOG-Q.

123 **Data sources/Measurement: Gait**

124 Participants with PD completed the freezing of gait questionnaire (FOG-Q)(15) and were
125 assessed using the Movement Disorder Society Unified Parkinson Disease Rating Scale Motor
126 Subscale III (MDS-UPDRS-3) (18) to quantify disease severity. All participants walked across a
127 4.9 m GAITRite (CIR Systems, Inc., Sparta, NJ) walkway, on level ground in an open room,
128 under four conditions: Natural (preferred cadence and step length), Fast (50% above preferred
129 cadence), Small (50% below preferred step length), and SmallFast (50% above preferred

130 cadence and 50% below preferred step length). The Natural condition was completed first to
131 establish criteria for the three subsequent conditions, which were randomized. Ten trials were
132 performed for each condition. Once a participant completed 10 trials of the Natural gait
133 condition, his/her average natural cadence was calculated from trials 4, 5, and 6, as these trials
134 were near the middle of the 10 trial block and could be analyzed quickly enough to inform
135 settings for the subsequent conditions. For the Fast condition, a metronome was set to +50% of
136 the individual's natural cadence with instructions to "keep as close to your normal step length as
137 possible." For the Small condition, a metronome was set to each participant's natural cadence
138 and the participant was instructed to take small steps (approximately 50% of natural step length)
139 "no bigger than where your heel comes to your big toe" to the metronome. The SmallFast
140 condition was a combination of the Small and Fast conditions in which the metronome was set to
141 +50% of natural cadence and the same instructions for small steps were given as previously
142 described.

143 All participants practiced the Fast, Small, and SmallFast conditions one to two times with
144 the metronome. After practicing, the participant began the recorded trials. The metronome was
145 on at the start of each trial in order to remind the participant of the cadence to keep, but was
146 turned off during data collection as to not provide an external auditory cue during recorded
147 walking. Auditory cues are known to enhance performance in people with PD and the purpose
148 of this study was to observe the effects of cadence and step length manipulation during a natural,
149 uncued state.(19-21)

150 **Data Processing**

151 Individual footfall data such as heel on/off, toe on/off, swing time, and stride time were
152 collected within GAITRite. Footfall data were used to calculate PCI as previously defined using

153 custom written Matlab software (MathWorks, Natick, MA).(17) Cadence and step length were
154 also collected and averaged per condition within GAITRite. Average cadence and step length
155 were analyzed to determine if participants were able to perform each condition as instructed.

156 **Statistical Approach**

157 Mixed model repeated measures ANOVA with an unstructured covariance structure was
158 implemented using SAS v 9.3 (SAS Institute, Inc., Cary, NC, USA). Group (PD+FOG, PD-FOG,
159 healthy old, healthy young) was used as the between subject factor and gait condition (Natural,
160 Fast, Small, SmallFast) as the within subject factor. We corrected for multiple comparisons by
161 dividing alpha 0.05 by the number of comparisons made (Bonferroni correction); a post-hoc p-
162 value of 0.0025 was considered significant for evaluating interactions, while a post-hoc p-value
163 of 0.0033 was considered significant for evaluating between-condition differences. Spearman's
164 correlation was used to determine relationships between FOG-Q scores and PCI. A p-value of
165 <0.05 was considered significant. All measures are reported as mean \pm standard deviation, unless
166 otherwise noted.

167 **Results**

168 Twenty-eight participants with idiopathic PD (16 PD-FOG, 12 PD+FOG), 19 healthy
169 older adults, and 19 healthy young adults participated. One participant with PD was excluded
170 due to the inability to walk independently in all conditions. One healthy older adult was excluded
171 due to the inability to follow directions adequately. Sex, age, and disease severity characteristics
172 are included in Table 1.

173 Mean performance of each group during each condition is shown in Figure 1. All groups
174 were able to decrease step length (Fig. 1A) and increase cadence (Fig. 1B) as instructed. There
175 were no between-group differences in percent change from Natural in step length ($p=0.37$) or in

176 cadence ($p=0.18$) for any condition. There were also no between-group differences in percent
177 change in velocity for any condition ($p=0.62$).

178 **Phase Coordination Index (PCI)**

179 No FOG episodes occurred during this study. Average PCI values across all gait
180 conditions combined were 5.4 ± 1.8 (healthy young), 6.1 ± 2.6 (healthy old), 6.9 ± 3.5 (PD-FOG),
181 and 8.9 ± 4.2 (PD+FOG). Overall, PCI values were significantly different between groups
182 ($p < 0.001$; $DF=3$; $F=9.4$) and conditions ($p < 0.001$; $DF=3$; $F=47.43$). A significant condition x
183 group interaction effect was also observed ($p=0.005$; $DF=9$; $F=2.75$) (Figure 2). Specifically, the
184 SmallFast condition had a more pronounced effect on coordination in the PD group compared to
185 healthy young ($p < 0.0025$). Additionally, those with PD+FOG had poorer coordination during
186 the SmallFast condition compared to healthy old ($p=0.0005$) and poorer coordination during the
187 Natural and Small conditions compared to healthy young ($p < 0.0025$). Those with PD+FOG also
188 had worse coordination during SmallFast compared to their coordination during Natural walking
189 ($p < 0.0033$).

190 **Outcome Data/FOG-Q Correlation**

191 Among those with PD, there was a significant but moderate correlation between FOG-Q
192 score and PCI in the Small condition ($r_s=0.48$; $p=0.01$) and a trend toward significance between
193 FOG-Q and PCI in the SmallFast condition ($r_s=0.36$; $p=0.06$). FOG-Q score was not correlated
194 with PCI in the Natural ($r_s=0.27$; $p=0.17$) or Fast ($r_s=0.17$; $p=0.38$) conditions.

195 **Discussion**

196 The results from this study demonstrate that coordination is somewhat affected in all
197 groups when walking with decreased step length, increased cadence, or both. Post-hoc analyses
198 revealed that when taking short, fast steps, coordination of those with PD is significantly worse

199 than healthy young, and those with PD+FOG exhibit worse coordination during this condition
200 than healthy older adults. Further, coordination during natural gait or gait with short steps is
201 worse in the PD+FOG group compared to healthy young adults. Importantly, these differences
202 are not due to performance differences, as all groups similarly modified their step length and
203 cadence as instructed during each task. Lastly, no FOG episodes occurred during this study.

204 Our results support previous work that demonstrated coordination of steps to be
205 dysfunctional in people with PD. (6, 12, 17) Prior work also linked coordination to FOG(5),
206 though no differences were observed between the PD-FOG and PD+FOG groups in the present
207 study. Additionally, it has been shown that imposing a high cadence or decreased step length on
208 those with PD+FOG can elicit FOG, (10, 13) although no FOG episodes were observed during
209 this study.

210 Plotnik et al. suggest that though FOG is a transient event, there is ongoing gait
211 impairment in those who experience FOG compared to those who do not. (5, 11) Additionally,
212 Danoudis et al. (12) demonstrated those with PD who experience FOG have decreased
213 coordination compared to those who do not experience FOG during preferred gait and gait with
214 decreased step length. Our results agree with this, as the PD+FOG group had on average higher
215 PCI values than the other three groups across all four conditions.

216 Specifically, Danoudis et al. (12) demonstrated that PCI was significantly worse in those
217 with PD+FOG compared to those with PD-FOG during preferred gait and when asked to walk at
218 50% and 75% of normalized step length. At 25% of normalized step length there was no
219 difference in PCI between groups, though there was an increased incidence of FOG in this
220 condition. As such, the authors suggest that coordination may be associated with step length, but
221 may not explain FOG. However, they acknowledge that poor coordination cannot be ruled out

222 as being associated with FOG. We agree that poor coordination may be associated with
223 decreased step length, but may or may not explain FOG. Our data show that conditions with
224 small step lengths resulted in poorer coordination in PD+FOG compared to healthy controls and
225 that coordination in the Small condition was correlated with FOG-Q. Nonetheless, FOG was not
226 elicited by any manipulations.

227 Chee et al.(13) demonstrated that when those with PD+FOG were asked to walk at 25%
228 of normalized step length an increased number of FOG episodes were observed and suggested
229 that decreased step length in combination with the sequence effect (consecutive short steps
230 become even shorter) causes FOG. Likewise, Moreau et al. (10) manipulated cadence and
231 velocity above and below preferred levels in ten individuals with FOG. They concluded that a
232 high cadence or velocity can induce FOG. However, there was a significant decrease in stride
233 length during the imposed fast cadence and an inability to increase step length during fast
234 velocity conditions. Unlike the results from Chee et al.(13) and Moreau et al.(10), those with PD
235 in the current study did not demonstrate reduced stride length during Small or Fast conditions
236 with respect to controls. Our study differs from Chee et al.(13) and Moreau et al.(10) in that
237 participants were instructed to take short steps at their natural cadence and to maintain normal
238 step length during the Fast condition. These instructions may have increased the volitional
239 control of each participant's gait pattern and reduced the chances of eliciting a freezing event.

240 All participants manipulated step length and cadence as instructed in this study. This
241 retained ability to adjust walking patterns as instructed is in keeping with prior work showing
242 that people with PD have the ability to control stepping rate(2) and provision of auditory cues,
243 such as a metronome, can enhance gait performance.(19-21) Though the metronome for this
244 study was turned off during recorded trials, all participants were allowed to practice with it on.

245 Those with PD were able to increase their cadence during the Fast and SmallFast conditions and
246 were able to keep close to their determined natural cadence during the Small condition.
247 However, these complex gait manipulations did not elicit FOG. This suggests that there may be a
248 difference between the volitional reproduction of the gait characteristics associated with FOG
249 and the spontaneously occurring increase in cadence and decreasing step length that occur prior
250 to a freezing event. It remains unclear whether increased cadence compensates for the decreased
251 stride length prior to a freeze(1, 22) or if increased cadence during “pre-freezing” strides is a
252 response that indicates a system out of control, with freezing occurring due to the combination of
253 gait hypokinesia and hastening steps. (3, 14)

254 Several limitations to this study must be acknowledged. Though some findings were
255 statistically significant, we were unable to detect a difference between PD-FOG and PD+FOG.
256 This may be due to a relatively small sample size and the large variation within each condition
257 per group. Further, participants were not matched on sex and the PD-FOG and PD+FOG were
258 not matched on disease severity. This makes it difficult to conclude definitively whether our
259 measures of coordination are attributable to disease severity, FOG status, or both. In addition,
260 we only increased cadence and decreased step length. Though small steps and fast cadence
261 precede FOG and PCI was the worst during the SmallFast condition, we cannot say whether PCI
262 would be different during conditions with slow cadence and/or large steps. PCI was also
263 evaluated while individuals were OFF anti-parkinson medication. The factors contributing to
264 ON medication FOG may be different from OFF medication FOG, therefore PCI values may
265 differ for those who experience FOG while ON medication.

266 Coordination deficits can be identified in those with PD by having them walk with small,
267 fast steps. Future research is needed to determine if PCI is an appropriate measure to investigate

268 whether there is a threshold value of PCI that may distinguish people with PD+FOG from those
269 with PD-FOG. Further, volitional reproduction of gait characteristics associated with FOG does
270 not elicit FOG. Future research may be aimed at identifying the involuntary mechanisms that
271 contribute to the increased cadence and decreasing step length prior to a freezing event.

272

273 **Conflict of Interest Statement:**

274 April J. Williams: Grants TL1RR024995 and UL1RR024992. No other conflicts of interest to
275 disclose.

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279 No other conflicts of interest to disclose.

280

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Table 1. Final Sample Characteristics

Characteristic	Healthy Young N=19	Healthy Old N=18	PD-FOG N=16	PD+FOG N=11
Sex (M/F) *†	9/10	6/12	5/11	10/1
Age (yrs) ‡	25.3±2.9	68.4±7.5	67.6±9.5	70.8 ± 6.9
Average Leg Length (cm)	89.6±7.4	88.3±5.7	85.5±6.1	93.0±6.1
Hoehn&Yahr OFF¥			2.2±.44	2.2 ±.26
MDS-UPDRS-3 OFF*§			26.1±9.4	44.8 ± 11.8
FOG-Q Score*¥			2.8±1.8	11.3±2.2

*all group(s) significantly different; p<0.05

£Young significantly different from all other groups; p<0.05

†Chi square analysis; ‡One way ANOVA;¥ Mann-Whitney U Test;§Independent samples t-test

Abbreviations

M: Male

F: Female

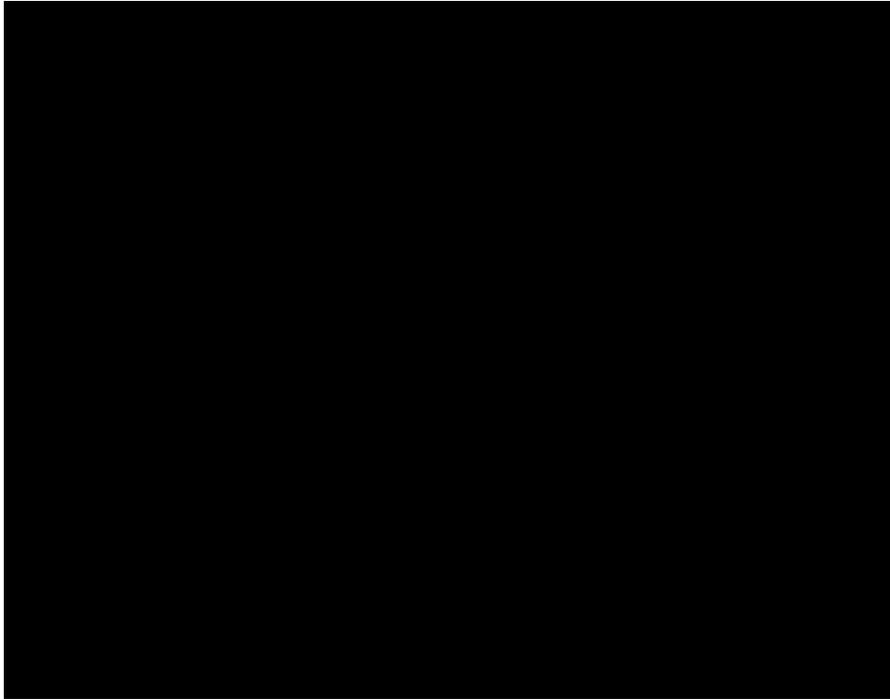
Yrs: years

MDS-UPDRS-3: Movement Disorder Society Unified Parkinson Disease Rating Scale Motor

Subscale 3

FOG-Q: Freezing of Gait Questionnaire

A



B

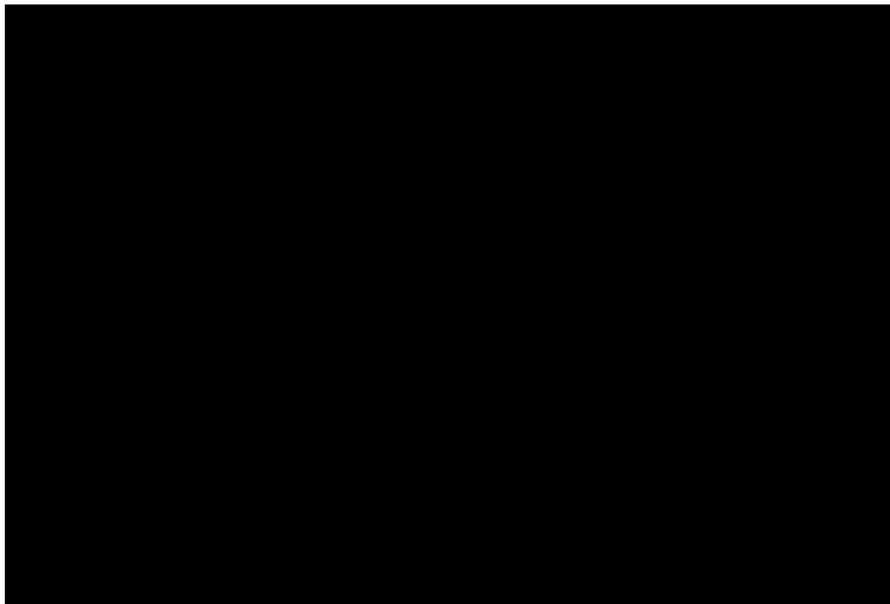


Figure 1. Mean performance (% of Natural) for step length (A) and cadence (B) in each group during Fast, Small, and SmallFast conditions. There were no significant differences between groups within each condition.

Gait Coordination in PD

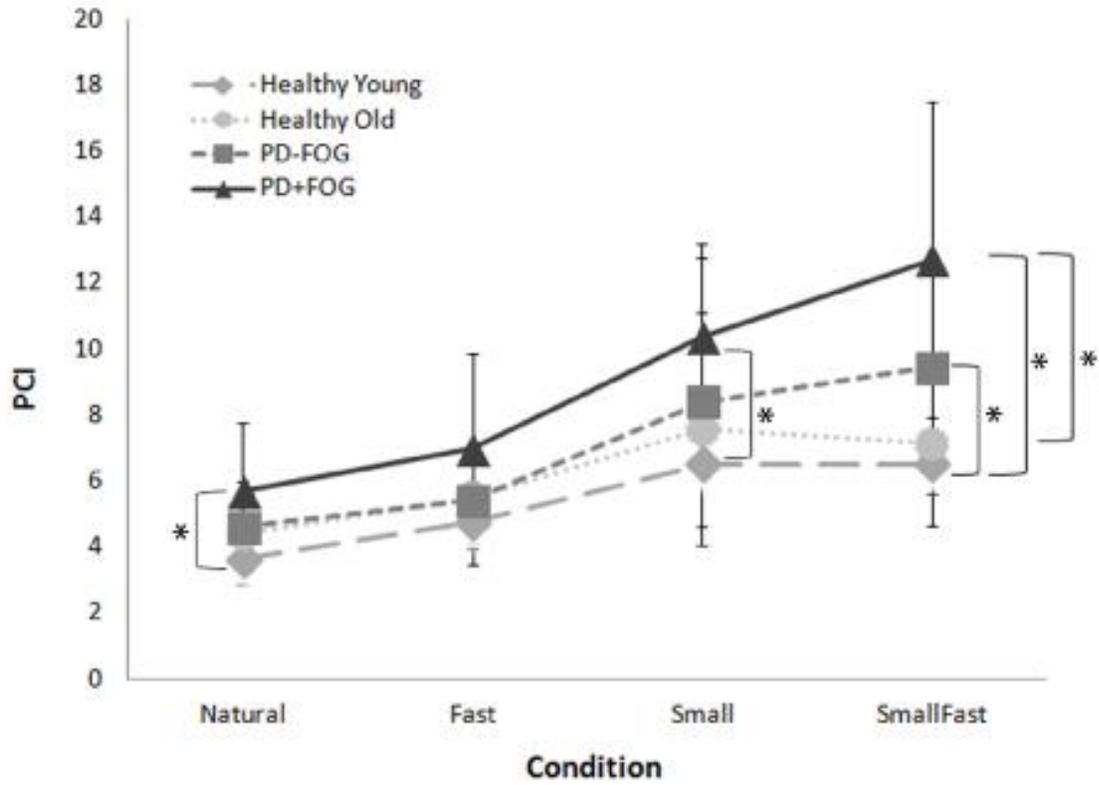


Figure 2. PCI Values of Young, Old, PD-FOG, and PD+FOG in the four different walking conditions. Values are means +/- standard deviations.