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PATIENTS WITH COPD WALK WITH ALTERED STEP TIME AND STEP WIDTH VARIABILITY AS COMPARED TO HEALTHY CONTROLS

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ABSTRACT

Rationale: Compared to controls, chronic obstructive pulmonary disease (COPD) patients have an increased incidence of falls, demonstrate balance deficits, and alterations medio-lateral trunk acceleration while walking. Measures of gait variability have been implicated as indicators of fall risk, fear of falling, and future falls.

Objectives: The aim was to investigate whether alterations in gait variability are found in COPD patients as compared to healthy controls.

Methods: Twenty COPD patients (16 males; 63.6±9.7 years; FEV_1/FVC: 0.52±0.12) and 20 controls (9 males; 62.5±8.2 years) walked for three minutes on a treadmill while gait was recorded. Amount (standard deviation and coefficient of variation) and temporal structure of variability (sample entropy, a measure of regularity) were quantified for step length, time, and width at three walking speeds (self-selected and +/-20% of self-selected speed). Generalized linear mixed models were used to compare dependent variables.

Measurements and Main Results: COPD patients demonstrated increased mean and standard deviation of step time across all speed conditions as compared to controls. They also walked with a narrower step width that increased with increasing speed whereas, the healthy controls walked with a wider step width that decreased as speed increased. Further, COPD patients demonstrated less variability in step width, decreased standard deviation, compared to controls across all speed conditions. No differences in regularity of gait patterns were found between groups.

Conclusions: Patients with COPD walk with increased duration of time between steps and this timing is more variable. They also walk with a narrower step width in which the variability of the step widths from step-to-step was decreased. Changes in these parameters have been related to

increased risk of falling in aging research. This provides a mechanism that could explain the increased prevalence of falls in COPD patients.

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a pulmonary disease that leads to narrowing of the airways, destruction of lung tissue, and dynamic hyperinflation. COPD also affects the structure and function of skeletal muscle(1-3). Patients with COPD demonstrate muscle fatigue(4, 5) and muscle weakness(6) and also manifest gait abnormalities(7-11). These gait abnormalities include biomechanical alterations at the ankle, increased variability of medio-lateral trunk movement, a shorter step length, more time spent in double support, and slower cadence as compared to healthy controls(8, 10-12). Moreover, patients with COPD have increased risk of falls compared to healthy controls(13-17).

A number of gait abnormalities are related to increased fall risk in the general population including alterations in gait variability(18-24). Alterations in the variability of step width have been associated with fall risk, prediction of falls, and fear of falling in older adults(18-21). Step length variability is increased in older adult fallers as compared to older adult non-fallers(22). Increased swing time and stride length variability have predicted a higher risk ratio of future falls in a population of adults aged 70 years and older(23). Increased step time variability has been associated with multiple falls(24).

Gait variability is defined as the natural stride-to-stride fluctuations present during walking. Traditional methods of measuring variability include quantifying the amount of variation (i.e., standard deviation), providing information regarding the magnitude of variability about a central mean. In addition, analysis of the temporal structure of the output provides insight into the control of the system. Temporal variations of a healthy biological system represent the underlying physiologic capability to make flexible adaptations to everyday demands(25, 26). Disease and aging have been associated with a loss of flexible adaptations

making movement patterns either too rigid or too irregular(27, 28). This can be determined by assessing the amount and temporal structure of variability.

Speed of walking is one everyday environmental situation that all persons encounter to complete everyday activities. Gait variability will change while walking at a speed slower or faster than one's self-selected walking speed(29, 30). As speed is commonly used as a rehabilitation tool and is a predictor of survival(31), it is important to understand how gait variability is affected by speed perturbations. Challenging the body to walk at speeds outside of the self-selected walking speed can reveal declines in gait or associations in gait patterns that are otherwise camouflaged at their self-selected walking speed(32).

The aim of the present study was to investigate whether changes in gait variability are present in patients with COPD as compared to healthy controls. It was hypothesized that patients with COPD would demonstrate alterations in the variability of walking patterns as compared to aged-matched, healthy controls while walking at a self-selected speed. It was postulated that patients with COPD would demonstrate reduced variability and a more predictable/regular movement pattern that reflects a more restricted and inflexible, gait. Furthermore, to understand the effect of speed on gait variability, different speed perturbations were utilized. If patients with COPD truly do have less flexible and less adaptable movement patterns, this would be better demonstrated at walking speeds that are slower or faster than their self-selected walking speed.

METHODS

A convenience sample of 20 patients with COPD and 28 healthy controls were recruited to participate in this study. Healthy controls were recruited through the community. Patients with COPD were recruited from the University of Nebraska Medical Center and the Omaha Veterans' Affairs Healthcare Center outpatient clinics. The presence of COPD was determined by previous diagnosis and confirmed with spirometry using the ratio of forced expiratory volume in one second to forced vital capacity (FEV_1/FVC) of less than 0.7(33). Subjects were considered healthy if they had no reported diagnosis of COPD. Smoking history was also collected and current smokers were not excluded. Subjects were excluded if they presented with a history of injury or disease that affected the subject's mobility or any other process limiting the ability to walk. In addition, subjects were excluded if they presented with any co-morbidity that may affect the musculoskeletal, neurological, pulmonary, or cardiovascular systems and their ability to walk. These included but were not limited to: joint abnormalities, joint replacements, acute/chronic lower back pain, multiple sclerosis, Parkinson's disease, peripheral arterial disease, and stroke. Patients with COPD were excluded if they required supplemental oxygen or if they had been hospitalized or experienced an acute exacerbation within the past three months. All subjects were screened in-person by a nurse practitioner to ensure they met the inclusion criteria. The Institutional Review Boards at both institutions approved the study and all subjects provided written informed consent.

In the biomechanics laboratory subjects changed into a form-fitting suit (i.e., wrestling singlet). Retro-reflective markers were placed on the following anatomical locations, bilaterally: lateral and medial metatarsal-phalange joint, base of the second toe, calcaneus, heel, lateral and medial malleolus, mid-shank, tibial tuberosity, lateral and medial knee joint center, top of thigh,

mid-thigh, greater trochanter, anterior and posterior superior iliac spine, and sacrum (34) (Figure 1). Subjects were then asked to walk on a treadmill at their self-selected pace. A self-selected pace was defined for the subjects as a comfortable walking speed, a pace that they would walk from their vehicle to the building. Once a subjects' comfortable walking speed was chosen, they were allowed to rest for a minimum of two minutes. They returned to the treadmill to complete three and a half minutes of walking on the treadmill at their self-selected pace. Three dimensional marker positions from the last three minutes of walking were recorded (Motion Analysis Corp., Santa Rosa, CA; 60 Hz) (Figure 1). The walking trials were repeated again at two additional speeds: +/-20% of their self-selected pace. The order of the last two speeds was randomized for all subjects. After each walking trial, each subject was asked to provide a rating of perceived exertion based on a 6-20 Borg scale(35). Between trials, subjects rested for a minimum of two minutes or as long as needed until they felt rested to prevent fatigue.

Healthy controls were matched one-to-one for speed with the patients with COPD, as speed can influence gait variability. In total 20 patients with COPD and 20 healthy controls were used in the data analysis (Table 1). Unfiltered three dimensional marker data were used to calculate three spatiotemporal time series for each subject and each of the three speeds using custom MATLAB (MathWorks, Inc., Natick, MA) programs. Step length was calculated as the anterior-posterior distance from the heel strike of the right foot to the heel strike of the left foot and vice versa. Step time was calculated by determining the frame number at heel strike of the right foot to the frame number of the left foot heel strike. The total number of frames between the two events was then multiplied by the inverse of the sampling frequency (1/60) to acquire step time. This was repeated for each right and left step. Step width was calculated as the medial-lateral distance from the heel strike of the right foot to the heel strike of the left foot and the same

for continuing contralateral and ipsilateral steps. This included extremely narrow steps, leading to some step widths being a negative number. Generated time series for step length, step time, and step width included consecutive right and left steps from the entire three-minute walking trial. All the time series were then cut to 250 steps. This is based upon the slowest walking subject with the least number of steps. Only three trials did not meet this requirement and were all patients with COPD at the -20% walking speed; they contained 238, 236, and 206 steps and were therefore not included in the sample entropy calculation. The following dependent variables were calculated for each time series: mean, standard deviation, coefficient of variation, and sample entropy (SampEn).

SampEn provides a measure of the regularity within the time series by measuring the loss of information from point to point and has previously been described in detail(36). A perfectly repeatable time series would elicit a SampEn value ~0 and a completely random time series would elicit a SampEn value extending toward infinity. After examining the relative consistency of the group averages for several combinations of parameters(36), r was chosen as 0.25*standard deviation of the time series and m was chosen as 2 for the current study.

Time series were plotted and visually inspected for spikes or outliers greater than three standard deviations. None were found. Mean, standard deviation, coefficient of variation, and SampEn from the step length, step time, and step width time series for both the healthy controls and patients with COPD were calculated (See Supplemental Material). Normality was examined for each dependent variable. A linear mixed model was used to assess differences in mean length, time, and width between groups (COPD vs. controls) and over the three speed conditions (-20%, self-selected, and +20%). This modeling approach allows us to determine differences within and between groups, while accounting for correlation due to repeated measurements and

adjusting for potentially confounding variables. Generalized linear mixed models were used for variables that did not meet the normality assumption. All interactions between speed and group were also investigated. Adjustments for multiple comparisons were made using the simulation technique. Mean difference (MD) between groups or speeds and confidence intervals (CI) were calculated. All statistics were performed using SAS (SAS Institute, Inc., Cary, NC). The significance level was set at $p<0.05$.

RESULTS

Group comparisons

Patients with COPD demonstrated increased mean (MD: -0.082, CI: -0.153-0.012) and standard deviation (MD: -0.30, CI: -0.559-0.035) of step time across all speed conditions, that is, they walked slower with a greater range of speeds than the control subjects ($p=0.02$ and $p=0.03$, respectively) (Figure 3). In addition, patients with COPD demonstrated increased mean step width with increasing speed whereas, the healthy controls decreased mean step width as speed increased ($p=0.04$; Figure 4). Furthermore, patients with COPD demonstrated decreased a standard deviation of step width across all speed conditions (MD:0.004, CI: 0.001-0.007, $p=0.007$). Thus, COPD patients use a wider step width that does not decrease with increase in speed as does the gait of the controls.

Speed comparisons

Mean step length increased with increased speed whereas, step time decreased with increased speed ($p<0.0001$) for both groups. Standard deviation and coefficient of variation of step length and step time decreased as speed increased for both groups ($p<0.001$; Figures 2 & 3). In addition, step time SampEn decreased as speed increased for both groups ($p<0.001$; Figure 3).

DISCUSSION

The current study demonstrates that patients with COPD have an increased mean step time with increased variability (i.e., standard deviation) across all speeds as compared to controls. No differences in regularity of gait patterns were found between groups. Also, in keeping with our hypothesis that if patients with COPD had less flexible and adaptable movement patterns, this would be more apparent at walking speeds that differed from self-selected speed (e.g., too slow or too fast). In this context, patients with COPD demonstrated a narrower step width that increased as speed increased, whereas, the healthy controls had a wider step width that decreased as speed increased. Furthermore, the narrow step width exhibited in patients with COPD was in the context of reduced step width variability, as the standard deviation was decreased across all speeds. Alterations in gait variability have been associated with increased fall risk in the general population(18-21, 24). The increased step time variability and decreased step width variability demonstrated by patients with COPD in the current study may provide a mechanism that could account for, at least part of, the increased fall risk in this population.

A greater mean and standard deviation of step time has been associated with multiple falls over a 12-month prospective study in older individuals(24). However conflicting results have also been published in which no association has been found between step time variability and fall history in older individuals(19). Our current findings demonstrate that patients with COPD walk with an increased step time and intra-subject variability in step timings across all speeds compared to control subjects. Moreover, patients with COPD have increased risk of falls compared to healthy controls(13-17). The degree to which increased step time variability may

account for previous falls, future falls, or fear of falling in patients with COPD has not been investigated.

Step time variability is also associated with other individual characteristics beyond fall history. Women have a stronger association between age and step time variability when gait speed is not controlled, especially as age increases(37). Stride (i.e., two steps) time variability is increased in older adults that are frail(38) or cognitively impaired(39). Further, it is associated with central nervous system impairments(40) and subclinical brain vascular abnormalities(41). Thus, future investigations should explore the association between increased step time variability and falls in patients with COPD while controlling for frailty and cognition.

Just as step time variability has been associated with fall history, step width variability has been associated with fall history and fear of falling(18, 19, 21). Patients with COPD walked with a narrower step width that increased with increasing speed whereas, the healthy controls walked with a wider step width that decreased as speed increased. Further, COPD patients demonstrated less variability in step width, decreased standard deviation, compared to controls across all speed conditions. A reduced variability and a narrower step width leads to a walking pattern that has a smaller base of body support and greater likelihood to result in a cross-over gait. A decrease in the standard deviation of step width may indicate the inability to compensate for instability, thus predisposing an individual to a fall(18, 42). Both increases and decreases in step width variability are associated with fall history in older adults(19, 21). The current findings are not consistent with our previous report that patients with COPD walk with a wider step width as compared to their aged-matched controls(12). This is likely due to the calculation of step width. In our previous study, step width was calculated as the absolute distance between right and left heel position and did not consider any step widths so narrow, causing a negative step

width(12). The current study included steps in which the step width was negative. One control subject ranged 2-12% of negative step widths over the three trials, whereas the patient with COPD ranged 11-34%. The average negative step width was -0.0087 mm for the patient with COPD and -0.007 mm for the control subject. An additional five subjects experienced one to two negative step widths during the trials.

Modulating step width during walking is considerably different than modulating step time or step length. Step width occurs in the medio-lateral (frontal) plane of motion. Medio-lateral movements while walking have been suggested to require increased cognitive regulation of movement in order to adjust for balance disturbances in that plane of motion thus leading to altered variability in this direction of movement(43, 44). This could imply that patients with COPD may have a deficit in controlling the medio-lateral direction. Range and root mean square of displacement of the center of mass while standing in patients with COPD is increased in the medio-lateral direction as compared to aged-matched controls(13). When sensory systems were challenged (e.g., eyes closed, stand on a foam pad or narrow base), patients with COPD continued to demonstrate greater displacement of the center of mass in the medio-lateral direction(13). Furthermore, medio-lateral trunk acceleration while walking in patients with COPD demonstrated a greater variability between strides(8). Based on the evidence of increased falls and fall risk in patients with COPD(13-15, 45-47), patients with COPD could require additional cognitive resources for medio-lateral control.

Future investigations should focus on step width and step time variability in patients with COPD and its potential association with fall risk. Further, pulmonary rehabilitation programs focused on restoration of functional limitations should consider the implementation of exercises targeted at medio-lateral control and/or balance recovery strategies. While implementation of

balance training into pulmonary rehabilitation has been shown to be feasible and effective(48, 49), home exercise protocols designed to progress balance challenging activities may improve the scores on these clinical assessments of balance in patients with COPD as well(50).

As stated earlier, gait variability is defined as the natural stride-to-stride fluctuations present during walking but it can be measured several ways. In order to make comprehensive conclusions regarding the variability of movement, one must examine both the amount and the temporal structure of the variability. In the current study, amount of variation (standard deviation and coefficient of variation) was sensitive to changes between groups and speeds whereas, temporal structure of variation (SampEn) was not sensitive to differences between groups. Spatiotemporal variability measures have strong to moderate construct, predictive, convergent, and predictive validity of falling, whereas most nonlinear measures do not(51). Future work could also include the variability of kinematics of gait in patients with COPD. It is possible that the amount of variability of joint angles is altered in patients with COPD as compared to healthy controls. This has been found in older adults as compared to young adults(52). Kinematics may represent a more global parameter of gait rather than the general spatiotemporal gait parameters in the current study.

This study has limitations. The first limitation is the limited and potentially, heterogeneous sample of patients with COPD recruited to participate in this study(53, 54). The current study included a sample size of 40 (20 per group). As biomechanical motion capture is accurate within 0.5mm, biomechanical studies typically utilize smaller sample sizes(55). Recently, several potential phenotypes (subset) of the COPD syndrome have been identified including a clinical phenotype (age, gender, smoking history), physiological (rapid decline in FEV_1), radiographic or imaging (structural abnormalities), acute exacerbation of COPD,

systemic inflammation, and the presence of co-morbidities (cardiovascular disease, metabolic syndrome, osteoporosis, diabetes, depression) (53, 54). Although all patients were screened by a nurse practitioner before inclusion into the study, it is possible that not all co-morbidities were included in our exclusion criteria. Moreover, it may be that each phenotype presents with a different gait pattern and the sample size of the current study did not allow for this analysis. Second, due to the pathophysiology of the disease, patients with COPD are limited in the length of time in which they can walk on the treadmill. This limits the data length that can be acquired during a trial. Entropy data measures respond differently with longer length of data sets(56). To abate this limitation, sample entropy was utilized as this is robust against different data lengths and tends to respond better to short data lengths(36). Third, the speed perturbations of +/- 20% of their self-selected walking speed may not have been challenging enough. Based on the reported rating of perceived exertion, the fastest speed was not nearly close to their maximal walking speed. Patients with COPD reported an average of 11.7 on the Borg scale whereas the healthy controls reported 10.7, not significantly different. A rating of 11 is considered "fairly light" and 13 is categorized as "somewhat hard". Ratings closer to 16 would suggest working in a range closer to their maximal level. Fourth, it is possible that several of the patients with COPD presented with muscle weakness that was not measured. Lower extremity muscle weakness can alter gait biomechanics as well as gait variability(57). Lastly, there are physiological and biomechanical differences between overground and treadmill walking(58-67). The treadmill could be considered a constraint as it limits fluctuations in walking that are normally present in overground walking. Other measures have shown conflicting results regarding the difference in variability between treadmill and overground walking(68-71). Therefore, it is possible that the variability of the gait data is affected by the use of the treadmill.

In conclusion, patients with COPD demonstrated altered gait variability. Patients with COPD walk with increased duration of time between steps and this timing is more variable compared to controls. They also walk with a decreased step width in which the variability of the step widths from step-to-step is decreased as compared to controls. These differences were manifest at all gait speeds tested. This provides a mechanism that could account for at least part of the increased fall risk present in patients with COPD.

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FIGURE CAPTIONS

Figure 1. Thirty-three markers are placed on the subject for calculation of joint centers during walking (A). During the walking trials, the medial metatarsal-phalange joint, medial malleolus, and medial knee markers are removed. Leaving thirty retro-reflective markers used during walking trials (B). Infrared cameras are placed throughout the laboratory (C). Calibrated cameras triangulate the position of each marker based on the reflection of infrared light back to the camera lens off the retro-reflective marker. The positions of markers are used to calculate step time, length, and width.

Figure 2. The mean (A), standard deviation (B), coefficient of variation (C), and SampEn (D) of step length. As the mean step length increased with increasing speed, standard deviation and coefficient of variation decreased for both groups. Dotted horizontal lines indicated significant ($p<0.05$) differences in speed conditions across both groups.

Figure 3. The mean (A), standard deviation (B), coefficient of variation (C), and SampEn (D) of step time. Patients with COPD had a greater mean and standard deviation of step time as speed increased. An asterisk (*) indicates a significant ($p<0.05$) difference in groups across all speeds. Dotted horizontal lines indicated significant ($p<0.05$) differences in speed conditions across both groups.

Figure 4. The mean (A), standard deviation (B), coefficient of variation (C), and SampEn (D) of step width. Mean step width was narrower for patients with COPD across all speeds as compared to healthy controls. The mean step width increased as speed increased in patients with COPD;

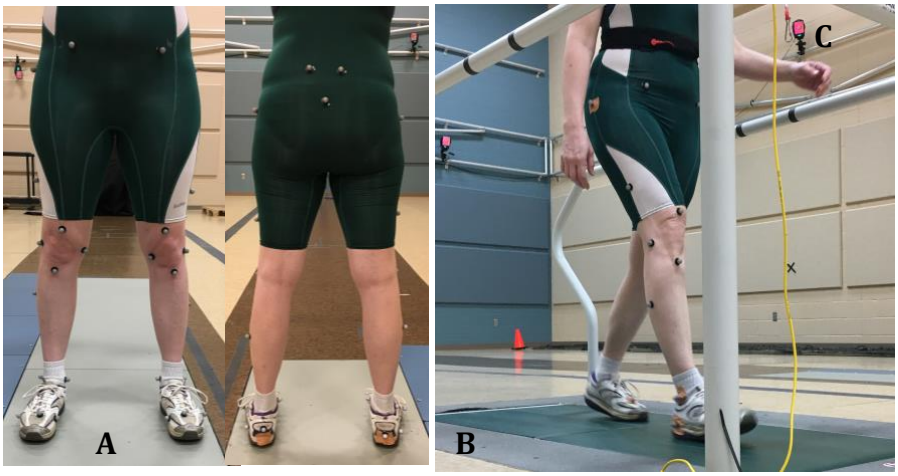
however, mean step width decreased in healthy controls as speed increased. In addition, the step width standard deviation was decreased in patients with COPD as compared to healthy controls across all speeds. An asterisk (*) indicates a significant ($p<0.05$) difference in groups across all speeds. A carrot (^) indicates a interaction ($p<0.05$).

Table 1. Demographics of subjects used for analysis.

	Control Mean (SD) N = 20	COPD Mean (SD) N = 20	p
Gender	Males = 9	Males = 16	
Age (years)	62.5 (8.2)	63.6 (9.7)	0.69
Height (m)	1.68 (0.10)	1.76 (0.11)	0.03*
Weight (kg)	74.7 (15.5)	94.0 (32.7)	0.02*
Self-selected gait speed (m/s)	0.95 (0.22)	0.80 (0.27)	0.06
Rate of perceived exertion -20% pace	7.6 (1.8)	10.1 (2.2)	<0.001*
Rate of perceived exertion SELF pace	9.2 (1.8)	10 (2.7)	0.32
Rate of perceived exertion +20% pace	10.7 (1.8)	11.7 (2.9)	0.25
FEV_1/FVC	0.79 (0.06)	0.52 (0.12)	<0.001*
FEV_1 %predicted	100.3 (16.2)	54.3 (19.2)	<0.001*
Smoking History	2 – ex smoker	7 – ex smoker	
	11 – nonsmoker	9 – current smoker	
	6 – not reported	3 – nonsmoker	
		1 – not reported	

Note: * indicates a significant ($p<0.05$) difference between groups

Figure 1.



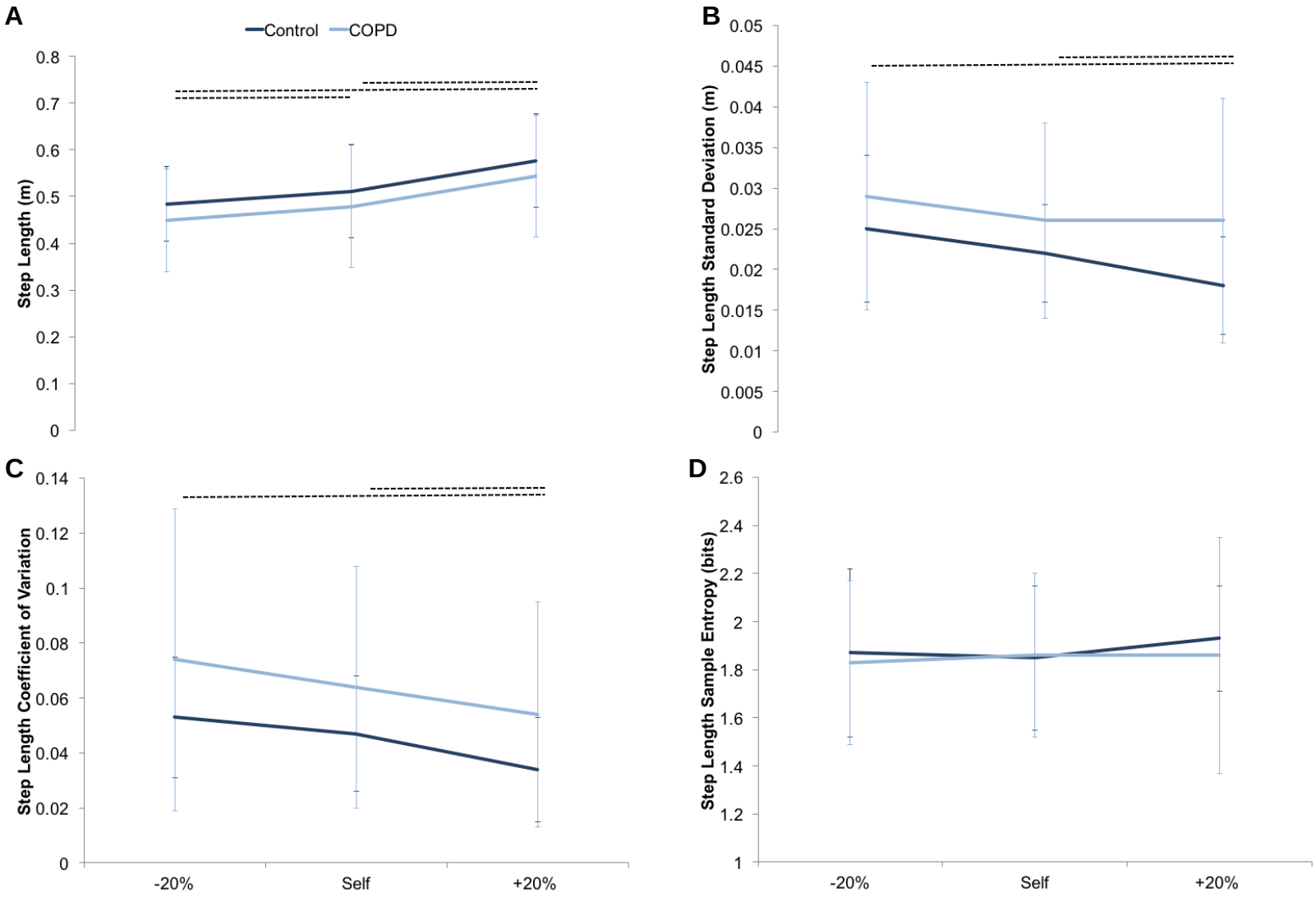

A
Control
COPD
Step Length (m)
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
B
Step Length Standard Deviation (m)
0.05
0.045
0.04
0.035
0.03
0.025
0.02
0.015
0.01
0.005
0
C
Step Length Coefficient of Variation
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
-20%
Self
+20%
D
Step Length Sample Entropy (bits)
2.6
2.4
2.2
2
1.8
1.6
1.4
1.2
1
-20%
Self
+20%

Figure 2.

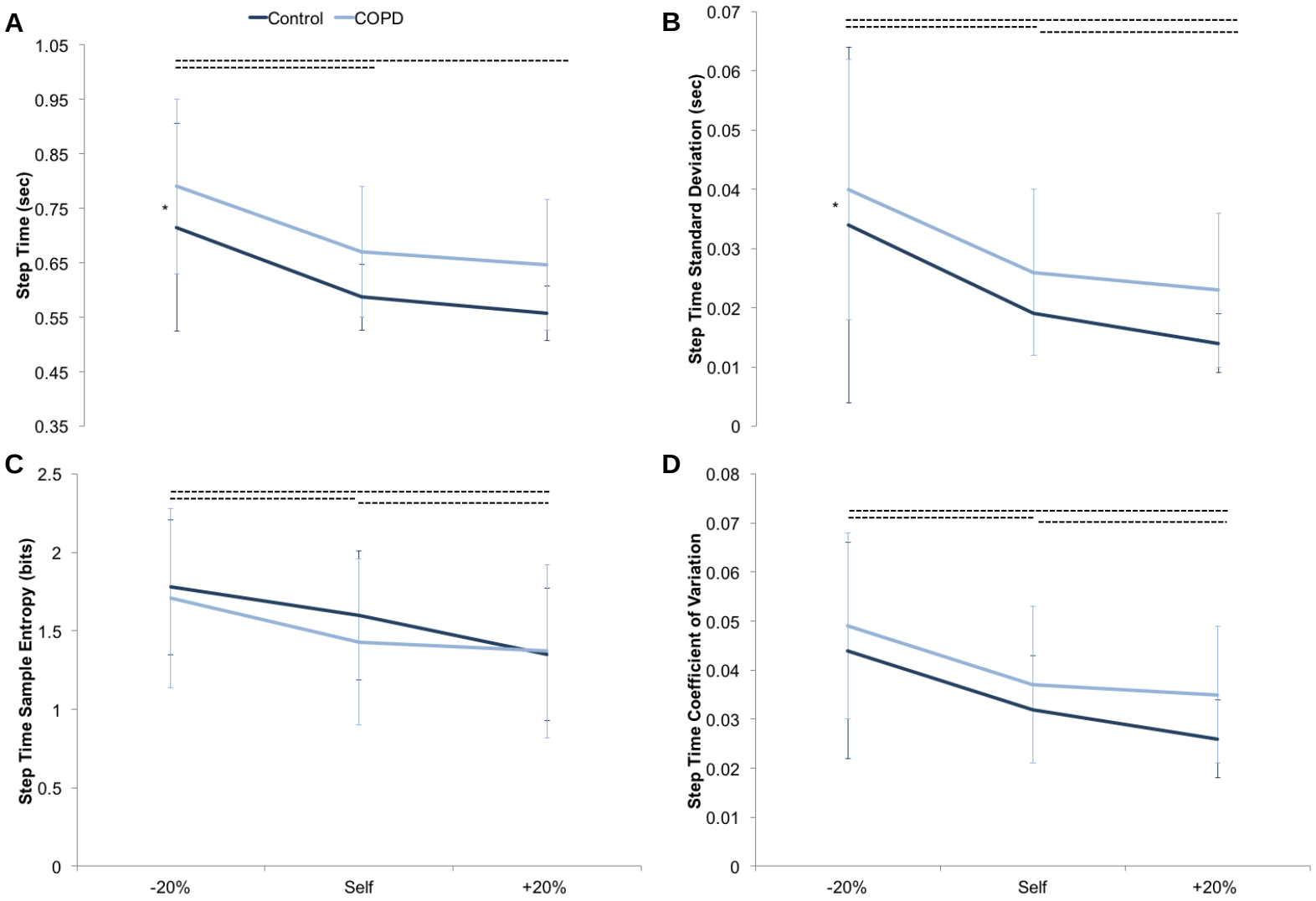

A
Control
COPD
Step Time (sec)
1.05
0.95
0.85
0.75
0.65
0.55
0.45
0.35
*
B
Step Time Standard Deviation (sec)
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
*
C
Step Time Sample Entropy (bits)
2.5
2
1.5
1
0.5
0
-20%
Self
+20%
D
Step Time Coefficient of Variation
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
-20%
Self
+20%

Figure 3.

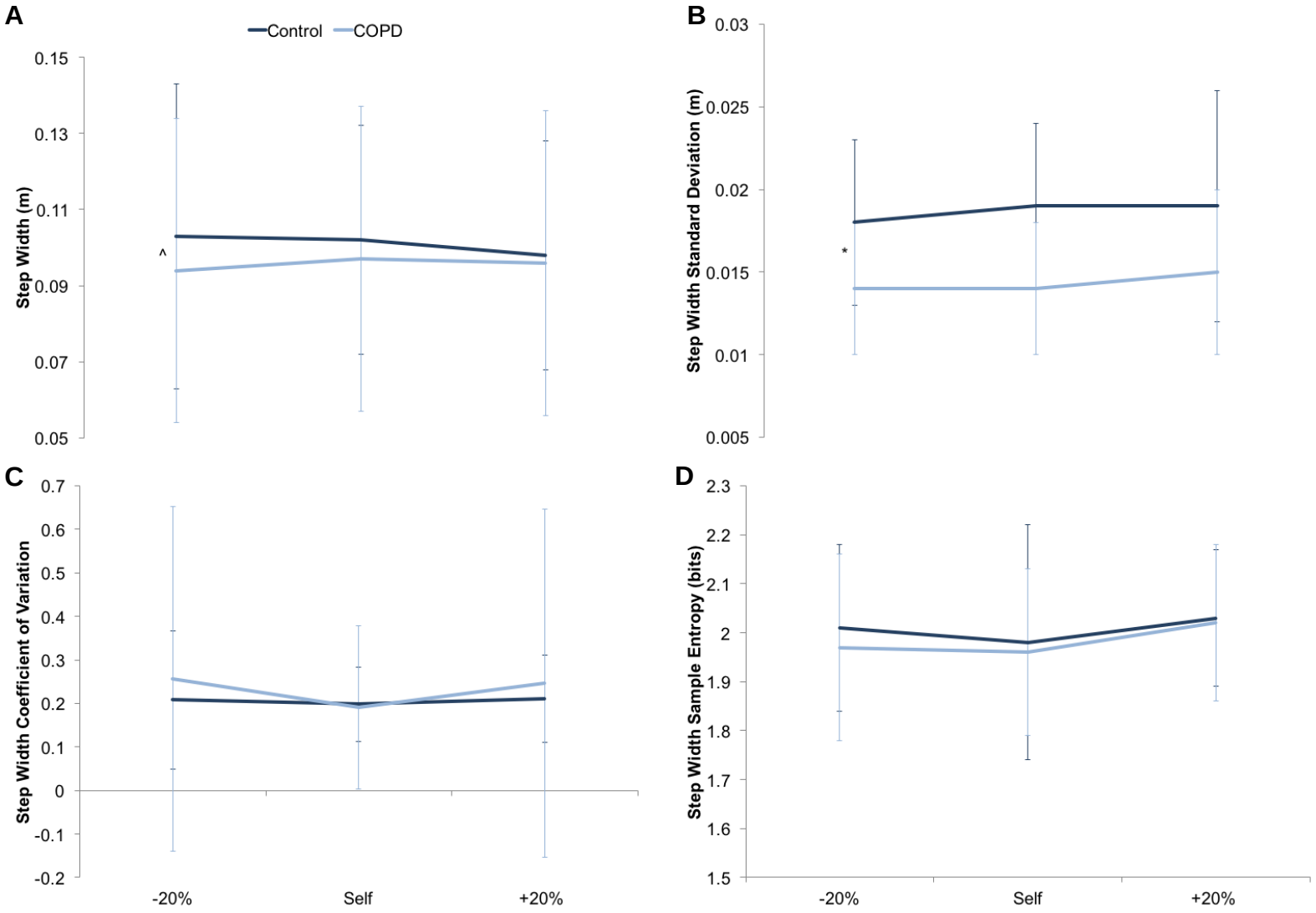

A
Control
COPD
Step Width (m)
0.15
0.13
0.11
0.09
0.07
0.05
^
B
Step Width Standard Deviation (m)
0.03
0.025
0.02
0.015
0.01
0.005
*
C
Step Width Coefficient of Variation
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
-0.1
-0.2
-20%
Self
+20%
D
Step Width Sample Entropy (bits)
2.3
2.2
2.1
2
1.9
1.8
1.7
1.6
1.5
-20%
Self
+20%

Figure 4.

SUPPLEMENTARY DATA

Mean, standard deviation, coefficient of variation, and SampEn from the step length, step time, and step width time series for both the healthy controls and patients with COPD were calculated (Tables 1-4). A linear mixed model was used to assess differences in mean length, time, and width between groups (COPD vs. controls) and over the three speed conditions (-20%, self-selected, and +20%). This modeling approach allows us to determine differences within and between groups, while accounting for correlation due to repeated measurements and adjusting for potentially confounding variables. Generalized linear mixed models were used for variables that did not meet the normality assumption. All interactions between speed and group were also investigated. Adjustments for multiple comparisons were made using the simulation technique.

A main effect is a statistical term used to indicate significance from the linear model. If a main effect is found, post hoc analysis is completed. The group, speed, and interaction terms refer to the main comparisons from the linear models used in the statistics. The main effect of group determines if there is a significant difference in groups across all conditions. The main effect of speed determines if there is a significant difference in speed across both groups. A significant interaction would indicate that the difference in groups is dependent on speed, and vice versa. The *F* value is the value that is calculated in the linear model that is used to determine the *p* value. The larger the *F* value, the smaller the *p* value.

All statistics were performed using SAS (SAS Institute, Inc., Cary, NC). The significance level was set at $p<0.05$.

Table 1. Comparison of mean values between healthy controls and patients with COPD.

Dependent Variable	Group	-20% Mean (SD) N=20	Self-selected Mean (SD) N=20	+20% Mean (SD) N=20	Group F, p	Speed F, p	Interaction F, p
Step Length (m)	Control	0.484 (0.08)	0.511 (0.10)^	0.577 (0.10)^†	0.99, 0.33	80.0, <0.001*	0.03, 0.97
	COPD	0.449 (0.11)	0.479 (0.13)^	0.543 (0.13)^†			
Step Time (sec)	Control	0.715 (0.19)	0.587 (0.06)^	0.557 (0.05)^	5.6, 0.02*	44.5, <0.001*	0.09, 0.92
	COPD	0.790 (0.16)	0.670 (0.12)^	0.646 (0.12)^			
Step Width (m)	Control	0.103 (0.04)	0.102 (0.03)	0.098 (0.03)	0.28, 0.60	1.7, 0.18	3.4, 0.04*
	COPD	0.094 (0.04)	0.097 (0.04)	0.096 (0.04)			

Note: * indicates a significant ($p<0.05$) main effect; ^ indicates pace condition was significant ($p<0.05$) different from -20% pace; † indicates pace condition was significant ($p<0.05$) different from self-selected pace

Table 2. Comparison of standard deviation between healthy controls and patients with COPD.

Dependent Variable	Group	-20% Mean (SD) N=20	Self-selected Mean (SD) N=20	+20% Mean (SD) N=20	Group F, p	Speed F, p	Interaction F, p
Step Length (m)	Control	0.025 (0.009)	0.022 (0.006)	0.018 (0.006)^†	2.2, 0.14	8.5, 0.0005*	1.9, 0.16
	COPD	0.029 (0.014)	0.026 (0.012)	0.026 (0.015)^†			
Step Time (sec)	Control	0.034 (0.030)	0.019 (0.007)^	0.014 (0.005)^†	5.2, 0.03*	80.1, <0.001*	2.2, 0.12
	COPD	0.040 (0.022)	0.026 (0.014)^	0.023 (0.013)^†			
Step Width (m)	Control	0.018 (0.005)	0.019 (0.005)	0.019 (0.007)	8.1, 0.007*	0.98, 0.38	0.45, 0.64
	COPD	0.014 (0.004)	0.014 (0.004)	0.015 (0.005)			

Note: * indicates a significant ($p<0.05$) main effect; ^ indicates pace condition was significant ($p<0.05$) different from -20% pace; † indicates pace condition was significant ($p<0.05$) different from self-selected pace

Table 3. Comparison of coefficient of variation between healthy controls and patients with COPD.

Dependent Variable	Group	-20% Mean (SD) N=20	Self-selected Mean (SD) N=20	+20% Mean (SD) N=20	Group F, p	Speed F, p	Interaction F, p
Step Length	Control	0.053 (0.022)	0.047 (0.021)^	0.034 (0.019)^†	2.4, 0.13	29.7, <0.001*	1.5, 0.23
	COPD	0.074 (0.055)	0.064 (0.044)^	0.054 (0.041)^†			
Step Time	Control	0.044 (0.022)	0.032 (0.011)^	0.026 (0.008)^†	2.5, 0.12	38.5, <0.001*	1.8, 0.18
	COPD	0.049 (0.019)	0.037 (0.016)^	0.035 (0.014)^†			
Step Width	Control	0.208 (0.159)	0.198 (0.085)	0.211 (0.100)	0.5, 0.47	0.8, 0.45	1.6, 0.22
	COPD	0.256 (0.396)	0.191 (0.188)	0.246 (0.400)			

Note: * indicates a significant ($p<0.05$) main effect; ^ indicates pace condition was significant ($p<0.05$) different from -20% pace; † indicates pace condition was significant ($p<0.05$) different from self-selected pace

Table 4. Comparison of sample entropy between healthy controls and patients with COPD.

Dependent Variable	Group	-20% Mean (SD) N=17 (COPD)	Self-selected Mean (SD) N=20	+20% Mean (SD) N=20	Group F, p	Speed F, p	Interaction F, p
Step Length (bits)	Control	1.87 (0.35)	1.85 (0.30)	1.93 (0.22)	0.12, 0.73	0.48, 0.62	0.38, 0.68
	COPD	1.83 (0.34)	1.86 (0.34)	1.86 (0.49)			
Step Time (bits)	Control	1.78 (0.43)	1.60 (0.41)^	1.35 (0.42)^†	0.41, 0.53	16.8, <0.001*	1.1, 0.35
	COPD	1.71 (0.57)	1.43 (0.53)^	1.37 (0.55)^†			
Step Width (bits)	Control	2.02 (0.17)	1.98 (0.24)	2.03 (0.14)	0.33, 0.57	1.4, 0.25	0.15, 0.86
	COPD	1.97 (0.19)	1.96 (0.17)	2.02 (0.16)			

Note: * indicates a significant ($p<0.05$) main effect; ^ indicates pace condition was significant ($p<0.05$) different from -20% pace; † indicates pace condition was significant ($p<0.05$) different from self-selected pace