Vertical displacement of the centre of mass during walking in people with diabetes and diabetic neuropathy does not explain their higher metabolic cost of walking.

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ABSTRACT

People with diabetes display biomechanical gait alterations compared to controls and have a higher metabolic cost of walking (CoW), but it remains unknown whether differences in the vertical displacement of the body centre of mass (CoM) may play a role in this higher CoW. The aim of this study was to investigate vertical CoM displacement (and step length as a potential underpinning factor) as an explanatory factor in the previously observed increased CoW with diabetes. Thirty-one non-diabetic controls (Ctrl); 22 diabetic patients without peripheral neuropathy (DM) and 14 patients with moderate/severe Diabetic Peripheral Neuropathy (DPN), underwent gait analysis using a motion analysis system and force plates while walking at a range of matched speeds between 0.6 and 1.6 m/s. Vertical displacement of the CoM was measured over the gait cycle, and was not different in either diabetes patients with or without diabetic peripheral neuropathy compared to controls across the range of matched walking speeds examined (at 1m/s: Ctrl: 5.59 (SD: 1.6), DM: 5.41 (1.63), DPN: 4.91 (1.66) cm; $p>0.05$). The DPN group displayed significantly shorter steps (at 1m/s: Ctrl: 69, DM: 67, DPN: 64 cm; $p>0.05$) and higher cadence (at 1m/s: Ctrl: 117 (SD1.12), DM: 119 (1.08), DPN: 122 (1.25) steps per minute; $p>0.05$) across all walking speeds compared to controls.

The vertical CoM displacement is therefore unlikely to be a factor in itself that contributes towards the higher CoW observed recently in people with diabetic neuropathy. The higher CoW in patients with diabetes may not be explained by the CoM displacement, but rather may be more related to shorter step lengths, increased cadence and the associated increased internal work and higher muscle forces developed by walking with more flexed joints.

Keywords: biomechanics, diabetes, lower limbs, centre of mass.

INTRODUCTION

Diabetes is a global epidemic with significant morbidity and particularly common with increasing age (International Diabetes Federation, 2013). Diabetes is associated with a range of serious complications that result in reduced quality of life and premature mortality. Diabetic peripheral neuropathy (DPN) is one of the most severe complications of diabetes, occurring in 30–50% of all diabetic patients (Cappozzo, 1981). The main cause is neurovascular alterations to the nerve fibres and blood vessels supplying the nerve endings, resulting in reduced or absent nerve conduction (Diabetes UK: Diabetes in the UK 2011/12: Key Statistics on Diabetes. 2014.). The European association for the study of diabetes defines DPN as "the presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes after the exclusion of other causes" (Boulton, 2005). DPN-related changes in the lower limbs lead to functional gait adaptations including taking shorter steps, having a higher cadence but slower self-selected and maximum walking speed (Brown et al., 2014; Chiles et al., 2014; Ko et al., 2011; Menz et al., 2004; Raspovic, 2013; Sawacha et al., 2009). Consistently smaller ranges of motion at the ankle, knee and hip in the DPN group have been reported from a range of studies and likely underlies the shorter step length reported in diabetes patients (Abate et al., 2012; Gome et al., 2001; Martinelli et al., 2013; Raspovic, 2013; Sacco, 2002). Other major gait adaptations include reduced range of joint movement (Andersen, 2012) and reduced muscle strength and power characteristics (Brown et al., 2014).

We have recently shown how the metabolic cost of walking (CoW) is higher in people with diabetes and particularly in those with DPN compared to controls (Petrovic et al., 2016). During walking, mechanical work is done to continuously raise and lower the body centre of mass (CoM), which requires metabolic energy

expenditure. The CoM in the human body moves like an inverted pendulum during walking, with the pendulum action conserving mechanical energy (Alexander, 1991). More specifically, by keeping the knee relatively straight during the single leg stance phase of gait, giving rise to the arc of the CoM, the leg supports body mass with relatively little muscular force.

Like an inverted pendulum, the CoM rises/decelerates in the first half of the stance phase and then falls/accelerates during the second half of the stance phase (Candrilli et al., 2007; Lamoreux, 1972; Lee and Farley, 1998, Thorstensson and Roberthson, 1987). Consequently, in the first half of the stance phase, kinetic energy is converted into gravitational potential energy (Cavagna et al., 1976; Cavagna and Franzetti, 1986), whereas in the second half of the stance phase, the opposite conversion occurs. Over the gait cycle, the CoM has a sinusoidal pattern in the vertical direction with two peaks occurring. The first vertical peak of the CoM occurs around 30% of the gait cycle during single-limb stance as the CoM is 'vaulted' over the straight stance limb in an inverted pendulum manner, while the second peak occurs around 80% of the gait cycle during the terminal mid-stance phase.

Increasing the CoM displacement in a type of up and down 'bobbing' action leads to an increase in the CoW compared to a normal gait (Neptune et al., 2004; Massaad et al., 2007). Equally, if gait is manipulated to minimise or eliminate any vertical displacement of the CoM by walking in a 'crouched' style with very flexed limbs, there is an increase in the CoW compared to normal gait (Ortega et al., 2007; Massaad et al., 2007; Gordon et al., 2009). Hence, there appears to be an 'optimum' vertical displacement for the CoM in terms of its effect on the metabolic CoW, where deviations from this optimum seem inefficient in terms of energy cost.

Stride length also seems intrinsically linked to the CoM vertical displacement and the associated CoW. It has been shown that stride lengths greater than the optimal, increase the CoM vertical displacement and increase the CoW, while stride lengths lower than the optimal, reduce the vertical displacement of the CoM, but also increase the CoW (Gordon et al., 2009). Since it is known that diabetes patients take shorter steps compared to controls, it might be hypothesised that that this would reduce the vertical displacement of the CoM, thereby increasing the CoW. Because walking speed may be a confounding factor in the relationship between step length and CoM displacement, in the present study we choose to compare the CoM vertical displacement at matched walking speeds between patients with diabetes and controls. Therefore, this study examined the vertical displacement of the CoM while walking at a range of matched speeds between 0.6 and 1.6 m/s. We hypothesised that diabetes patients would have a reduced vertical CoM displacement that might explain our recent findings of a greater CoW, with a reduced step length being a potential factor underpinning the suggested CoM behaviour.

MATERIALS AND METHODS

Participants

After receiving ethical approval from all relevant bodies, 67 participants gave written informed consent to participate in this study. All procedures in this study complied with the declaration of Helsinki. All participants were allocated into one of three groups: patients with diabetes and moderate-severe peripheral neuropathy (DPN, n=14, 14 men), patients with diabetes but no peripheral neuropathy (DM, n=22, 12 men) and healthy controls without diabetes or peripheral neuropathy (Ctrl, n=31, 19 men). The same participant cohort was examined to establish the metabolic CoW

and reported in references (Petrovic et al., 2016). The CoW was significantly higher particularly in the DPN group compared with controls and also in the DM group compared with controls, across a range of matched walking speeds.

All participants were assessed to confirm they satisfied the inclusion criteria for each group. Major exclusion criteria for participation in the study included peripheral vascular disease, musculoskeletal injury or recent surgery affecting gait, any amputation other than 1 or 2 lesser toes and open foot ulcer. A random blood glucose test was performed in the Ctrl group to confirm the absence of diabetes (<7 mmol/l) and the below neuropathy tests conducted to confirm the absence of neuropathy in the Controls. The majority of the DM and the DPN patients reported taking insulin, cholesterol-lowering medication and diabetes medication, while from the whole sample (including controls) only 2 people reported smoking.

Assessment of peripheral neuropathy

A clinical evaluation was undertaken to quantify peripheral neuropathy in diabetic patients and to confirm the absence of neuropathy in healthy controls. Peripheral neuropathy was assessed by using the modified Neuropathy Disability Score (mNDS) and the vibration perception threshold (VPT). The mNDS is a combined score taken from tests measuring the patient's ability to detect temperature, pain, vibration and the Achilles tendon reflex (Boulton, 2005). The VPT was assessed by placing the probe of the biothesiometer (Biomedical Instrument Co, Newbury, OH, USA) on the apex of the hallux and increasing the level of vibration until detected by the participant. Patients were defined as having moderate-to-severe neuropathy and classed as DPN if in either one or both of their feet they displayed either an mNDS score of ≥6 or a VPT of ≥25 V (or both).

Gait analysis

Participants were asked to walk along a 10-metre walkway in the gait laboratory at a series of standardised speeds (0.6, 0.8, 1.0, 1.2, 1.4 and 1.6 m/s). The standardised walking speeds were controlled by measuring the velocity of a marker attached to the sacrum after each trial from the motion analysis data and providing immediate feedback for participants as to whether they needed to walk more quickly or more slowly on the next trial to achieve the required speed. The participant's starting position was altered by the experimenter to ensure a 'clean' (i.e., no overlap outside the force platform) foot-strike on one or two of the force platforms (positioned in the middle of the walkway) per walking trial without alteration to their natural gait. Walking trials were repeated until at least three 'clean' foot contacts with the force platforms were made with each limb, for each walking speed condition. Kinematics were collected at 100 Hz using a 10-camera Vicon motion capture system (Vicon, Oxford, UK) positioned around the 10-meter walkway, tracking a full-body modified Plug-In-Gait marker set consisting of 54 markers. Where possible markers were placed directly onto the skin; to minimise movement artefacts resulting from loose clothing all participants wore tight-fitting shorts and tops. All participants wore specialist diabetic shoes (MedSurg, Darco, Raisting, Germany) with a neutral foot-bed (no rocker bottom outsole), ensuring the diabetic patients walked with safe, appropriate footwear whilst minimising the effect of footwear by standardising across all participants.

Centre of mass displacement

Gait variables (stride length, step length and cadence, vertical displacement of the CoM) were calculated from the kinematic data using Visual 3D software (C-motion

Inc., MD, USA). Motion data collected during gait analysis were processed, and Dempster's segment parameter model (1955) was used to calculate mass distribution for each body segment, thereby allowing accurate calculation of the entire body centre of mass. The vertical displacement of the CoM was calculated as the maximum range of vertical displacement (minimum to maximum peak) of the CoM (Figure 2) during the whole gait cycle, using the mean of the three trials from each person.

Statistics

A one-way analysis of variance (ANOVA) was performed for all variables to assess between group differences. If the ANOVA was significant, a Fisher's least significant difference (LSD) post-hoc test was used to test for differences between the diabetes groups (DM and DPN) and the control group. All values presented are means and standard deviation. Significance was set at $p < 0.05$. The power analysis identified minimum group sizes of $n=7$, for an effect size 0.71 ($\beta=0.1$, $\alpha=1\%$). Analysis of covariance was used to assess the effect of body mass on CoM excursion.

Pearson product-moment correlation coefficients were calculated at each walking speed (and all walking speeds combined) using data from participants in all three experimental groups to determine whether there was a significant correlation between the CoM vertical displacement and the cost of walking (previously published data on CoW, Petrovic et al., 2016).

RESULTS

Participant characteristics

There were significant differences between the groups in age, body mass and BMI, which were significantly greater in the DPN group (Table 1, p<0.01).

Step length and cadence

The DPN group displayed significantly shorter step lengths across all speeds compared to the Ctrl group (Table 2). The DPN group had significantly higher cadence across all speeds compared to the control group.

Centre of mass displacement at different speeds

Across all matched speeds there were no significant differences in the CoM vertical displacement between groups (Fig. 1; Table 3), neither when including a body mass as a covariate.

Pearson's correlations only reached significance at walking speeds of 0.8 and 1.6 m/s, but the r values were consistently low across speeds ranging between -0.287 and 0.262 (Table 4). When combining data for all participants, across all walking speeds Pearson's correlation failed to reach significance, with an r value of -0.08 (Table 4, Figure 3).

DISCUSSION

This study has shown for the first time that the vertical displacement of the CoM during walking is not different between diabetes patients with and without diabetic peripheral neuropathy compared to controls across a range of matched speeds (Fig. 1) and is therefore unlikely to be a factor in itself that contributes towards the

increased CoW observed recently(Petrovic et al., 2016) on the same data set in people with diabetic peripheral neuropathy (at 1.2 m/s: Ctrl: 2.18 (SD: 0.67), DM: 2.20 (0.81), DPN: 2.35 (1.76) $J \cdot kg^{1} \cdot m^{1}$; p>0.05). Furthermore, the relationship between the CoM and CoW was very weak across all walking speeds (Table 4, Figure 3), indicating no clear link between these two variables across participant groups in the present study.

It has previously been shown that stride lengths shorter and longer than the optimum lead to reduced and increased CoM displacements, respectively, but increasing the metabolic CoW in both situations (Gordon et al., 2009). In this previous study, participants increased their metabolic cost when they reduced their vertical CoM movement by taking shorter strides. Participants also expended more metabolic energy when they walked with a greater stride length than their preferred stride length. Previous work (Donelan et al., 2002) has shown that as stride length increases, metabolic energy expenditure and mechanical work performed on the CoM also increase. This is not caused by CoM displacement per se but rather by the additional negative work performed to redirect the CoM velocity during step-to-step transitions and by positive work to restore the energy lost. Although we did find consistently shorter step lengths across matched walking speeds in patients with diabetes and particularly those with diabetic peripheral neuropathy compared to controls, this did not alter the vertical displacement of the CoM compared to controls (Fig. 1).

The lack of effect of stride shortening on the CoM in the present study might be due to the fact that people with diabetes and diabetic peripheral neuropathy have adapted to a different optimal step length, which is consistently shorter compared to controls across the range of walking speeds examined. Alternatively, they could

have adopted a different step length based on the total metabolic CoW rather than the cost associated with CoM displacement. Consistent with the shorter steps taken by both diabetes groups compared to controls, was the higher cadence required to meet the prescribed matched walking speeds by the diabetes patients (Table 2). An increased cadence in the diabetes groups would require greater internal work from the muscles to move the legs during walking (Minetti et al., 1994). Although we have previously found (Petrovic et al, 2016) the joint work developed during a single stance phase to be lower in patients with diabetes and even more so in those with diabetic peripheral neuropathy, this would be repeated more often over a given distance in diabetes patients because of a higher cadence. Therefore, a higher cadence for any given walking speed could explain the higher CoW previously reported in patients with diabetes and those with diabetic peripheral neuropathy through greater cumulative joint work (Petrovic et al., 2016).

In the absence of differences in the CoM vertical displacement, another possible explanation for the higher CoW previously reported in diabetes patients is that they might be producing greater muscle force without performing as much joint work per stance phase. This would be consistent with previous reports from walking with a 'crouched gait' by excessively flexing the joints (Massaad et al., 2007; Ortega et al., 2007). Diabetes patients were observed to walk with shorter steps, which is known to be achieved by greater flexion in the lower limb joints. This likely gives rise to higher muscle forces to sustain the more flexed joint positions as previously observed (Sasaki et al., 2009) and consequently a higher metabolic CoW. Therefore, the effective mechanical advantage (muscle force moment arm/ground reaction force moment arm) may be less favourable in diabetic patients (Petrovic et al., 2017), which would mean that more muscle force would be required to overcome the

moment of the ground reaction force – hence higher CoW. This factor may also explain why diabetes patients have adopted an "optimum" CoM displacement (meaning unaltered compared to controls) per stride length as a strategy to minimise CoW. Gordon et al. (2009) presented in their study a manipulation of step length above and below the optimal and found that the CoM vertical displacement increases and decreases over that observed at the self-selected step length. Both of these situations were associated with a higher metabolic CoW compared to that observed at self-selected step length, suggesting an optimal vertical displacement of the CoM where energy cost is minimised. People who are at higher risk of falls have been shown to take shorter steps (Karamanidis et al., 2008; Schillings et al., 2005) as part of a more cautious strategy to walking, which could be one of a number of potential factors causing them to walk with shorter steps. Another potential reason could relate to reduced ankle range of movement, reduced Achilles tendon elongation and increased Achilles tendon stiffness during walking as we have recently shown (Petrovic et al, 2018).

Other factors contributing to an increased metabolic CoW in patients with diabetes and diabetic peripheral neuropathy could include increased muscle co-activation, which has been shown in older adults without diabetes (Cronin et al., 2010, Mian et al., 2007) and an increased Achilles tendon stiffness (Petrovic et al., 2018). Indeed, we have recently shown how Achilles tendon stiffness is higher in people with diabetes and particularly those with diabetic peripheral neuropathy compared to controls during walking (Petrovic et al., 2018). An increased Achilles tendon stiffness would reduce the elastic energy stored from this long tendon during walking, requiring a relatively greater energy contribution from the plantar flexor muscles, increasing the metabolic CoW.

To the best of our knowledge this is the first study that has investigated the CoM displacement during walking in a diabetic patient population. It could be considered as a limitation of the present study that body mass was significantly different between groups. However, the higher body mass of patients with diabetes (especially those with DPN) is a well-known characteristic of this population described in the literature (Ijzerman et al., 2011; Jor'dan et al., 2014) and is unlikely to have directly affected the CoM vertical displacement. If anything, it might be expected that increased body mass might reduce the extent to which the CoM is displaced, but this was not found in the present study indicating that group differences in body mass did not influence the present results. Although only a mean of 10 years difference, patients in the DPN group were significantly older than controls (66 to 56 years, respectively), which might be considered a confounding factor for some of the variables examined.

We have shown that there are no differences in the vertical displacement of the CoM in patients with diabetes compared with controls when walking speed is matched and no relationship between the CoM vertical displacement and the CoW. The higher CoW in patients with diabetes may not be explained by the vertical CoM displacement, but rather may be more related to shorter step lengths, increased cadence and the associated increased internal work and higher muscles forces developed by walking with more flexed joints.

Conflict of interest statement

The authors confirm that they do not have any financial or personal relationships with other people or organisations that could inappropriately influence this manuscript.

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Table 1. *Participant characteristics and results from neuropathy assessments.*

Variable	Group		
	Ctrl	DM	DPN
Age (yr)	56 (10)	51 (9)**	66 (14)**
Body mass (kg)	76 (10)	80.5 (12)	91.5 (18)**
Height (m)	1.72 (0.12)	1.71 (0.09)	1.73 (0.11)
BMI (kg/m^2)	26 (3)	28 (4)	31 (4)**
NDS (Score/10)	1 (1)	2 (1)	7 (2)**
VPT (Volts)	6.1 (3.4)	8.2 (3.4)	27.4 (9.1)**
Diabetes duration (years)	-	14 (12)	14 (11)
Type 1 diabetes (n)	-	7	4
Type 2 diabetes (n)	-	15	10

Healthy controls (Ctrl, n=31), diabetic patients with no neuropathy (DM, n=22) and diabetic patients with moderate/severe neuropathy (DPN, n=14). Significant differences from the Ctrl group are denoted by ** ($P<0.01$). BMI = body mass index, NDS = neuropathy disability score, VPT = vibration perception threshold. Values are means (standard deviations).

Table 2. *Temporal-spatial gait parameters.*

Variable	Group		
	Ctrl	DM	DPN
0.6 m/s			
Step length (m)	0.59 (0.12)	0.57 (0.12)	0.51 (0.09)**
Cadence (steps/m)	108 (0.61)	108 (0.74)	113 (0.41)**
0.8 m/s			
Step length (m	0.63 (0.14)	0.57 (0.12)	0.53 (0.15)**
Cadence (steps/m)	112 (0.84)	113 (0.67)	116 (0.68)**
1.0 m/s			
Step length (m)	0.69 (0.15)	0.67 (0.05)	0.64 (0.04)*
Cadence (steps/m)	117 (1.12)	119 (1.08)	122 (1.25)**
1.2 m/s			
Step length (m)	0.76 (0.11)	0.75 (0.17)	0.69 (0.07)*
Cadence (steps/m)	124 (1.16)	125 (1.27)	128 (1.08)**
1.4 m/s			
Step length (m)	0.79 (0.12)	0.77 (0.17)	0.71 (0.11)*
Cadence (steps/m)	127 (1.56)	129 (1.47)	131 (1.49)**
1.6 m/s			
Step length (m)	0.81 (0.11)	0.80 (0.04)	0.74 (0.02)*
Cadence (steps/m)	129 (0.98)	132 (0.48)	135 (0.63)**
Maximum walking speed (m/s)	1.92 (0.11)	1.88(0.16)**	1.68 (0.22)**
Step length (m)	0.85 (0.07)	0.79 (0.06)*	0.78 (0.12)**
Cadence (steps/m)	143 (1.18)	140 (1.27)*	129 (0.98)**

Healthy controls (Ctrl, n=31), diabetic patients with no neuropathy (DM, n=22) and diabetic patients with moderate/severe neuropathy (DPN, n=14). Significant differences from the Ctrl group are denoted by *(P<0.05) or **(P<0.01). Values are means (standard deviations). Gait parameters were collected on the laboratory walkway.

Table 3. *Differences in vertical displacement of the CoM in percentages.*

Walking speed	Ctrl (cm)	DM (cm)	DPN (cm)	Diff Ctrl-DM (%)	Diff Ctrl-DPN (%)
0.6 m/s	4.64 (1.51)	4.43 (1.52)	4.50 (1.49)	-4.60	-3.00
0.8 m/s	4.53 (1.55)	4.65 (1.56)	4.71 (1.59)	2.71	3.97
1 m/s	5.59 (1.60)	5.41 (1.63)	4.91 (1.66)	-3.25	-12.14
1.2 m/s	6.19 (1.63)	5.77 (1.68)	4.75 (1.74)	-6.78	-23.32
1.4 m/s	6.68 (1.71)	6.13 (1.70)	6.07 (1.79)	-8.23	-9.23
1.6 m/s	7.09 (1.79)	6.73 (1.76)	7.30 (1.82)	-5.01	3.03
MAX	6.43 (1.87)	6.07 (1.85)	7.73 (1.88)	-5.60	20.22

Centre of mass (CoM) vertical displacement across walking speeds from 0.6 to 1.6 m/s and maximum walking speed for healthy controls (Ctrl, n=31), diabetic patients with no neuropathy (DM, n=22) and diabetic patients with moderate/severe neuropathy (DPN, n=14). Values are means (standard deviations).

Table 4. *Bivariate correlations between vertical centre of mass displacement and cost of walking.*

Walking speed	*R value*	*P value*
0.6 m/s	-.027	.828
0.8 m/s	.262	.032
1.0 m/s	-.218	.077
1.2 m/s	-.223	.069
1.4 m/s	-.214	.082
1.6 m/s	-.287	.019
MAX	-.071	.566
All speeds	-.080	.084

Pearson's correlations encompassing participants in all three groups (DPN, DM and Ctrl, n=67) at each walking speed from 0.6 to 1.6 m/s and maximum walking speed.
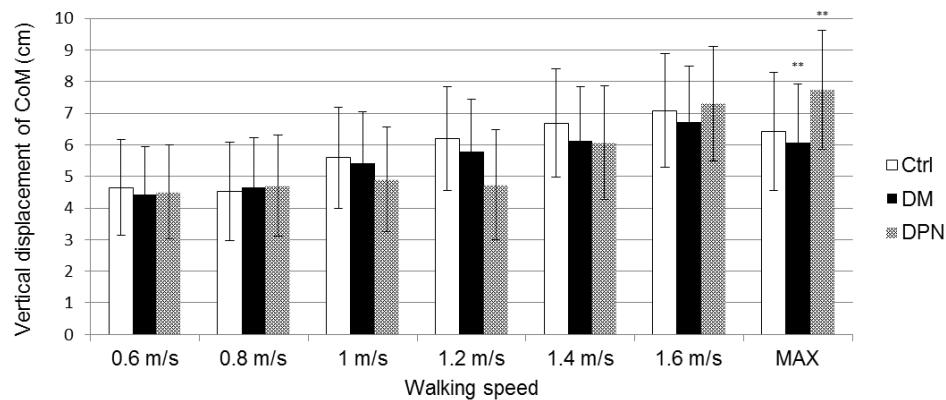
Figure 1. Centre of mass (CoM) vertical (*Z*) displacement across walking speeds from 0.6 to 1.6 m/s and maximum walking speed for healthy controls (Ctrl; n=31), diabetic patients with no neuropathy (DM; n=22) and diabetic patients with moderate/severe neuropathy (DPN; n=14). Values are group means and SD; ** denotes significantly (P<0.01) different from the control group.
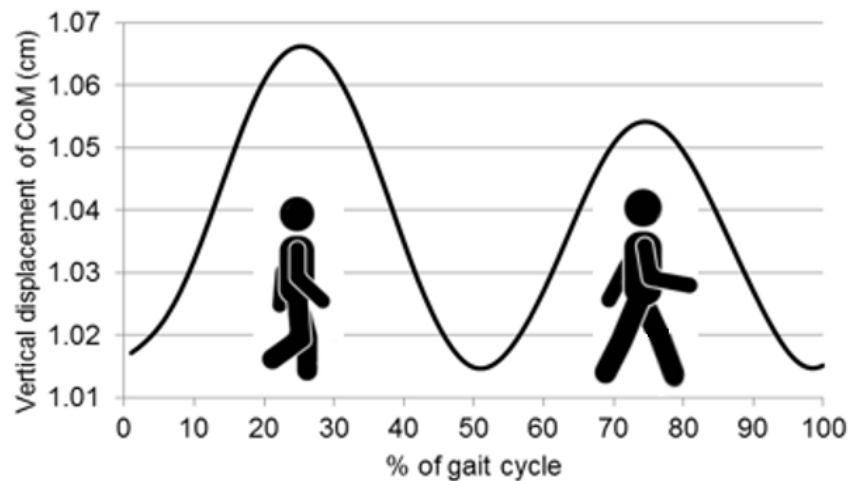

Figure 2. Example trace from one participant showing the vertical displacement of the centre of mass over the gait cycle. The vertical displacement values reported in the present study reflect the minimum to maximum peak value.
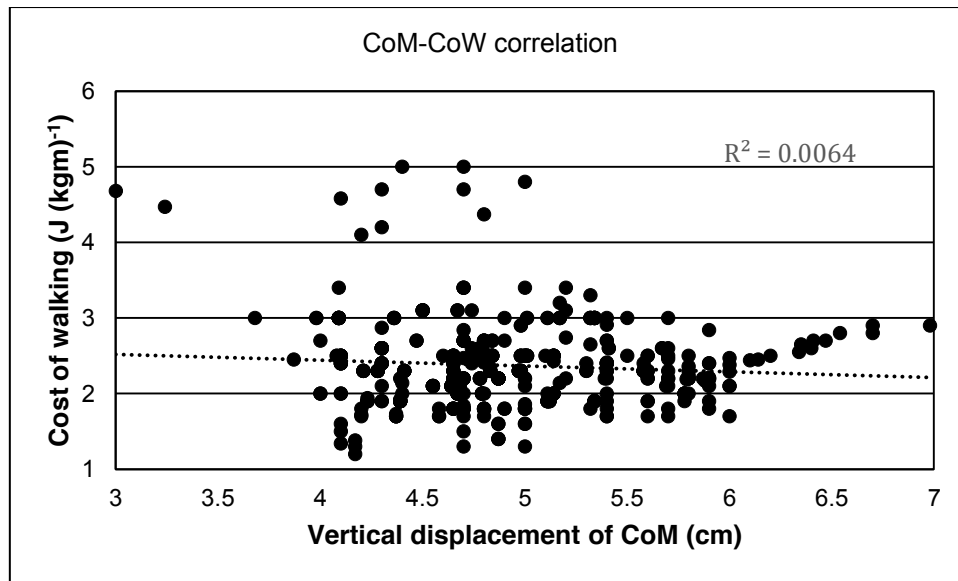
Figure 3. Individual data points for all participants from all three experimental groups (DPN, DM and Ctrl, n=67) and at all measured walking speeds (speed from 0.6 to 1.6 m/s and maximum walking speed). Linear trendline reflects the Pearson's correlation between the two variables (centre of mass and the cost of walking).

Vertical displacement of the centre of mass during walking in people with diabetes and diabetic neuropathy does not explain their higher metabolic cost of walking.

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ABSTRACT

People with diabetes display biomechanical gait alterations compared to controls and have a higher metabolic cost of walking (CoW), but it remains unknown whether differences in the vertical displacement of the body centre of mass (CoM) may play a role in this higher CoW. The aim of this study was to investigate vertical CoM displacement (and step length as a potential underpinning factor) as an explanatory factor in the previously observed increased CoW with diabetes. Thirty-one non-diabetic controls (Ctrl); 22 diabetic patients without peripheral neuropathy (DM) and 14 patients with moderate/severe Diabetic Peripheral Neuropathy (DPN), underwent gait analysis using a motion analysis system and force plates while walking at a range of matched speeds between 0.6 and 1.6 m/s. Vertical displacement of the CoM was measured over the gait cycle, and was not different in either diabetes patients with or without diabetic peripheral neuropathy compared to controls across the range of matched walking speeds examined (at 1m/s: Ctrl: 5.59 (SD: 1.6), DM: 5.41 (1.63), DPN: 4.91 (1.66) cm; $p>0.05$). The DPN group displayed significantly shorter steps (at 1m/s: Ctrl: 69, DM: 67, DPN: 64 cm; $p>0.05$) and higher cadence (at 1m/s: Ctrl: 117 (SD1.12), DM: 119 (1.08), DPN: 122 (1.25) steps per minute; $p>0.05$) across all walking speeds compared to controls.

The vertical CoM displacement is therefore unlikely to be a factor in itself that contributes towards the higher CoW observed recently in people with diabetic neuropathy. The higher CoW in patients with diabetes may not be explained by the CoM displacement, but rather may be more related to shorter step lengths, increased cadence and the associated increased internal work and higher muscle forces developed by walking with more flexed joints.

Keywords: biomechanics, diabetes, lower limbs, centre of mass.

INTRODUCTION

Diabetes is a global epidemic with significant morbidity and particularly common with increasing age (International Diabetes Federation, 2013). Diabetes is associated with a range of serious complications that result in reduced quality of life and premature mortality. Diabetic peripheral neuropathy (DPN) is one of the most severe complications of diabetes, occurring in 30–50% of all diabetic patients (Cappozzo, 1981). The main cause is neurovascular alterations to the nerve fibres and blood vessels supplying the nerve endings, resulting in reduced or absent nerve conduction (Diabetes UK: Diabetes in the UK 2011/12: Key Statistics on Diabetes. 2014.). The European association for the study of diabetes defines DPN as "the presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes after the exclusion of other causes" (Boulton, 2005). DPN-related changes in the lower limbs lead to functional gait adaptations including taking shorter steps, having a higher cadence but slower self-selected and maximum walking speed (Brown et al., 2014; Chiles et al., 2014; Ko et al., 2011; Menz et al., 2004; Raspovic, 2013; Sawacha et al., 2009). Consistently smaller ranges of motion at the ankle, knee and hip in the DPN group have been reported from a range of studies and likely underlies the shorter step length reported in diabetes patients (Abate et al., 2012; Gome et al., 2001; Martinelli et al., 2013; Raspovic, 2013; Sacco, 2002). Other major gait adaptations include reduced range of joint movement (Andersen, 2012) and reduced muscle strength and power characteristics (Brown et al., 2014).

We have recently shown how the metabolic cost of walking (CoW) is higher in people with diabetes and particularly in those with DPN compared to controls (Petrovic et al., 2016). During walking, mechanical work is done to continuously raise and lower the body centre of mass (CoM), which requires metabolic energy

expenditure. The CoM in the human body moves like an inverted pendulum during walking, with the pendulum action conserving mechanical energy (Alexander, 1991). More specifically, by keeping the knee relatively straight during the single leg stance phase of gait, giving rise to the arc of the CoM, the leg supports body mass with relatively little muscular force.

Like an inverted pendulum, the CoM rises/decelerates in the first half of the stance phase and then falls/accelerates during the second half of the stance phase (Candrilli et al., 2007; Lamoreux, 1972; Lee and Farley, 1998, Thorstensson and Roberthson, 1987). Consequently, in the first half of the stance phase, kinetic energy is converted into gravitational potential energy (Cavagna et al., 1976; Cavagna and Franzetti, 1986), whereas in the second half of the stance phase, the opposite conversion occurs. Over the gait cycle, the CoM has a sinusoidal pattern in the vertical direction with two peaks occurring. The first vertical peak of the CoM occurs around 30% of the gait cycle during single-limb stance as the CoM is 'vaulted' over the straight stance limb in an inverted pendulum manner, while the second peak occurs around 80% of the gait cycle during the terminal mid-stance phase.

Increasing the CoM displacement in a type of up and down 'bobbing' action leads to an increase in the CoW compared to a normal gait (Neptune et al., 2004; Massaad et al., 2007). Equally, if gait is manipulated to minimise or eliminate any vertical displacement of the CoM by walking in a 'crouched' style with very flexed limbs, there is an increase in the CoW compared to normal gait (Ortega et al., 2007; Massaad et al., 2007; Gordon et al., 2009). Hence, there appears to be an 'optimum' vertical displacement for the CoM in terms of its effect on the metabolic CoW, where deviations from this optimum seem inefficient in terms of energy cost.

Stride length also seems intrinsically linked to the CoM vertical displacement and the associated CoW. It has been shown that stride lengths greater than the optimal, increase the CoM vertical displacement and increase the CoW, while stride lengths lower than the optimal, reduce the vertical displacement of the CoM, but also increase the CoW (Gordon et al., 2009). Since it is known that diabetes patients take shorter steps compared to controls, it might be hypothesised that that this would reduce the vertical displacement of the CoM, thereby increasing the CoW. Because walking speed may be a confounding factor in the relationship between step length and CoM displacement, in the present study we choose to compare the CoM vertical displacement at matched walking speeds between patients with diabetes and controls. Therefore, this study examined the vertical displacement of the CoM while walking at a range of matched speeds between 0.6 and 1.6 m/s. We hypothesised that diabetes patients would have a reduced vertical CoM displacement that might explain our recent findings of a greater CoW, with a reduced step length being a potential factor underpinning the suggested CoM behaviour.

MATERIALS AND METHODS

Participants

After receiving ethical approval from all relevant bodies, 67 participants gave written informed consent to participate in this study. All procedures in this study complied with the declaration of Helsinki. All participants were allocated into one of three groups: patients with diabetes and moderate-severe peripheral neuropathy (DPN, n=14, 14 men), patients with diabetes but no peripheral neuropathy (DM, n=22, 12 men) and healthy controls without diabetes or peripheral neuropathy (Ctrl, n=31, 19 men). The same participant cohort was examined to establish the metabolic CoW

and reported in references (Petrovic et al., 2016). The CoW was significantly higher particularly in the DPN group compared with controls and also in the DM group compared with controls, across a range of matched walking speeds.

All participants were assessed to confirm they satisfied the inclusion criteria for each group. Major exclusion criteria for participation in the study included peripheral vascular disease, musculoskeletal injury or recent surgery affecting gait, any amputation other than 1 or 2 lesser toes and open foot ulcer. A random blood glucose test was performed in the Ctrl group to confirm the absence of diabetes (<7 mmol/l) and the below neuropathy tests conducted to confirm the absence of neuropathy in the Controls. The majority of the DM and the DPN patients reported taking insulin, cholesterol-lowering medication and diabetes medication, while from the whole sample (including controls) only 2 people reported smoking.

Assessment of peripheral neuropathy

A clinical evaluation was undertaken to quantify peripheral neuropathy in diabetic patients and to confirm the absence of neuropathy in healthy controls. Peripheral neuropathy was assessed by using the modified Neuropathy Disability Score (mNDS) and the vibration perception threshold (VPT). The mNDS is a combined score taken from tests measuring the patient's ability to detect temperature, pain, vibration and the Achilles tendon reflex (Boulton, 2005). The VPT was assessed by placing the probe of the biothesiometer (Biomedical Instrument Co, Newbury, OH, USA) on the apex of the hallux and increasing the level of vibration until detected by the participant. Patients were defined as having moderate-to-severe neuropathy and classed as DPN if in either one or both of their feet they displayed either an mNDS score of ≥6 or a VPT of ≥25 V (or both).

Gait analysis

Participants were asked to walk along a 10-metre walkway in the gait laboratory at a series of standardised speeds (0.6, 0.8, 1.0, 1.2, 1.4 and 1.6 m/s). The standardised walking speeds were controlled by measuring the velocity of a marker attached to the sacrum after each trial from the motion analysis data and providing immediate feedback for participants as to whether they needed to walk more quickly or more slowly on the next trial to achieve the required speed. The participant's starting position was altered by the experimenter to ensure a 'clean' (i.e., no overlap outside the force platform) foot-strike on one or two of the force platforms (positioned in the middle of the walkway) per walking trial without alteration to their natural gait. Walking trials were repeated until at least three 'clean' foot contacts with the force platforms were made with each limb, for each walking speed condition. Kinematics were collected at 100 Hz using a 10-camera Vicon motion capture system (Vicon, Oxford, UK) positioned around the 10-meter walkway, tracking a full-body modified Plug-In-Gait marker set consisting of 54 markers. Where possible markers were placed directly onto the skin; to minimise movement artefacts resulting from loose clothing all participants wore tight-fitting shorts and tops. All participants wore specialist diabetic shoes (MedSurg, Darco, Raisting, Germany) with a neutral foot-bed (no rocker bottom outsole), ensuring the diabetic patients walked with safe, appropriate footwear whilst minimising the effect of footwear by standardising across all participants.

Centre of mass displacement

Gait variables (stride length, step length and cadence, vertical displacement of the CoM) were calculated from the kinematic data using Visual 3D software. The vertical

~~displacement of the CoM was measured from the kinematic data using Visual 3D software~~ (C-motion Inc., MD, USA). Motion data collected during gait analysis were processed, and Dempster's segment parameter model (1955) was used to calculate mass distribution for each body segment, thereby allowing accurate calculation of the entire body centre of mass. The vertical displacement of the CoM was calculated as the maximum range of vertical displacement (minimum to maximum peak) of the CoM (Figure 2) during the whole gait cycle, using the mean of the three trials from each person.

Statistics

A one-way analysis of variance (ANOVA) was performed for all variables to assess between group differences. If the ANOVA was significant, a Fisher's least significant difference (LSD) post-hoc test was used to test for differences between the diabetes groups (DM and DPN) and the control group. All values presented are means and standard deviation. Significance was set at $p < 0.05$. The power analysis identified minimum group sizes of n=7, for an effect size 0.71 (β=0.1, α=1%). Analysis of covariance was used to assess the effect of body mass on CoM excursion.

Pearson product-moment correlation coefficients were calculated at each walking speed (and all walking speeds combined) using data from participants in all three experimental groups to determine whether there was a significant correlation between the CoM vertical displacement and the cost of walking (previously published data on CoW, Petrovic et al., 2016).

RESULTS

Participant characteristics

There were significant differences between the groups in age, body mass and BMI, which were significantly greater in the DPN group (Table 1, p<0.01).

Step length and cadence

The DPN group displayed significantly shorter step lengths across all speeds compared to the Ctrl group (Table 2). The DPN group had significantly higher cadence across all speeds compared to the control group.

Centre of mass displacement at different speeds

Across all matched speeds there were no significant differences in the CoM vertical displacement between groups (Fig. 1; Table 3), neither when including a body mass as a covariate.

Pearson's correlations only reached significance at walking speeds of 0.8 and 1.6 m/s, but the r values were consistently low across speeds ranging between -0.287 and 0.262 (Table 4). When combining data for all participants, across all walking speeds Pearson's correlation failed to reach significance, with an r value of -0.08 (Table 4, Figure 3).

DISCUSSION

This study has shown for the first time that the vertical displacement of the CoM during walking is not different between diabetes patients with and without diabetic peripheral neuropathy compared to controls across a range of matched speeds (Fig. 1) and is therefore unlikely to be a factor in itself that contributes towards the

increased CoW observed recently(Petrovic et al., 2016) on the same data set in people with diabetic peripheral neuropathy (at 1.2 m/s: Ctrl: 2.18 (SD: 0.67), DM: 2.20 (0.81), DPN: 2.35 (1.76) J·kg^{1}·m^{1}; p>0.05). Furthermore, the relationship between the CoM and CoW was very weak across all walking speeds (Table 4, Figure 3), indicating no clear link between these two variables across participant groups in the present study.

It has previously been shown that stride lengths shorter and longer than the optimum lead to reduced and increased CoM displacements, respectively, but increasing the metabolic CoW in both situations (Gordon et al., 2009). In this previous study, participants increased their metabolic cost when they reduced their vertical CoM movement by taking shorter strides. Participants also expended more metabolic energy when they walked with a greater stride length than their preferred stride length. Previous work (Donelan et al., 2002) has shown that as stride length increases, metabolic energy expenditure and mechanical work performed on the CoM also increase. This is not caused by CoM displacement per se but rather by the additional negative work performed to redirect the CoM velocity during step-to-step transitions and by positive work to restore the energy lost. Although we did find consistently shorter step lengths across matched walking speeds in patients with diabetes and particularly those with diabetic peripheral neuropathy compared to controls, this did not alter the vertical displacement of the CoM compared to controls (Fig. 1).

The lack of effect of stride shortening on the CoM in the present study might be due to the fact that people with diabetes and diabetic peripheral neuropathy have adapted to a different optimal step length, which is consistently shorter compared to controls across the range of walking speeds examined. Alternatively, they could

have adopted a different step length based on the total metabolic CoW rather than the cost associated with CoM displacement. Consistent with the shorter steps taken by both diabetes groups compared to controls, was the higher cadence required to meet the prescribed matched walking speeds by the diabetes patients (Table 2). An increased cadence in the diabetes groups would require greater internal work from the muscles to move the legs during walking (Minetti et al., 1994). Although we have previously found (Petrovic et al, 2016) the joint work developed during a single stance phase to be lower in patients with diabetes and even more so in those with diabetic peripheral neuropathy, this would be repeated more often over a given distance in diabetes patients because of a higher cadence. Therefore, a higher cadence for any given walking speed could explain the higher CoW previously reported in patients with diabetes and those with diabetic peripheral neuropathy through greater cumulative joint work (Petrovic et al., 2016).

In the absence of differences in the CoM vertical displacement, another possible explanation for the higher CoW previously reported in diabetes patients is that they might be producing greater muscle force without performing as much joint work per stance phase. This would be consistent with previous reports from walking with a 'crouched gait' by excessively flexing the joints (Massaad et al., 2007; Ortega et al., 2007). Diabetes patients were observed to walk with shorter steps, which is known to be achieved by greater flexion in the lower limb joints. This likely gives rise to higher muscle forces to sustain the more flexed joint positions as previously observed (Sasaki et al., 2009) and consequently a higher metabolic CoW. Therefore, the effective mechanical advantage (muscle force moment arm/ground reaction force moment arm) may be less favourable in diabetic patients (Petrovic et al., 2017), which would mean that more muscle force would be required to overcome the

moment of the ground reaction force – hence higher CoW. This factor may also explain why diabetes patients have adopted an "optimum" CoM displacement (meaning unaltered compared to controls) per stride length as a strategy to minimise CoW. Gordon et al. (2009) presented in their study a manipulation of step length above and below the optimal and found that the CoM vertical displacement increases and decreases over that observed at the self-selected step length. Both of these situations were associated with a higher metabolic CoW compared to that observed at self-selected step length, suggesting an optimal vertical displacement of the CoM where energy cost is minimised. People who are at higher risk of falls have been shown to take shorter steps (Karamanidis et al., 2008; Schillings et al., 2005) as part of a more cautious strategy to walking, which could be one of a number of potential factors causing them to walk with shorter steps. Another potential reason could relate to reduced ankle range of movement, reduced Achilles tendon elongation and increased Achilles tendon stiffness during walking as we have recently shown (Petrovic et al, 2018).

Other factors contributing to an increased metabolic CoW in patients with diabetes and diabetic peripheral neuropathy could include increased muscle co-activation, which has been shown in older adults without diabetes (Cronin et al., 2010, Mian et al., 2007) and an increased Achilles tendon stiffness (Petrovic et al., 2018). Indeed, we have recently shown how Achilles tendon stiffness is higher in people with diabetes and particularly those with diabetic peripheral neuropathy compared to controls during walking (Petrovic et al., 2018). An increased Achilles tendon stiffness would reduce the elastic energy stored from this long tendon during walking, requiring a relatively greater energy contribution from the plantar flexor muscles, increasing the metabolic CoW.

To the best of our knowledge this is the first study that has investigated the CoM displacement during walking in a diabetic patient population. It could be considered as a limitation of the present study that body mass was significantly different between groups. However, the higher body mass of patients with diabetes (especially those with DPN) is a well-known characteristic of this population described in the literature (Ijzerman et al., 2011; Jor'dan et al., 2014) and is unlikely to have directly affected the CoM vertical displacement. If anything, it might be expected that increased body mass might reduce the extent to which the CoM is displaced, but this was not found in the present study indicating that group differences in body mass did not influence the present results. Although only a mean of 10 years difference, patients in the DPN group were significantly older than controls (66 to 56 years, respectively), which might be considered a confounding factor for some of the variables examined.

We have shown that there are no differences in the vertical displacement of the CoM in patients with diabetes compared with controls when walking speed is matched and no relationship between the CoM vertical displacement and the CoW. The higher CoW in patients with diabetes may not be explained by the vertical CoM displacement, but rather may be more related to shorter step lengths, increased cadence and the associated increased internal work and higher muscles forces developed by walking with more flexed joints.

Conflict of interest statement

The authors confirm that they do not have any financial or personal relationships with other people or organisations that could inappropriately influence this manuscript.

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