Title: Do Patients with Diabetic Neuropathy Use a Higher Proportion of their Maximum Strength when Walking?

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Abstract:

Diabetic patients have an altered gait strategy during walking and are known to be at high risk of falling, especially when diabetic peripheral neuropathy is present. This study investigated alterations to lower limb joint torques during walking and related these torques to maximum strength in an attempt to elucidate why diabetic patients are more likely to fall. 20 diabetic patients with moderate/severe peripheral neuropathy (DPN), 33 diabetic patients without peripheral neuropathy (DM), and 27 non-diabetic controls (Ctrl) underwent gait analysis using a motion analysis system and force plates to measure kinetic parameters. Lower limb peak joint torques and joint work done (energy expenditure) were calculated during walking. The ratio of peak joint torques and individual maximum joint strengths (measured on a dynamometer) was then calculated for 59 of the 80 participants to yield the 'operating strength' for those participants. During walking DM and DPN patients showed significantly reduced peak torques at the ankle and knee. Maximum joint strengths at the knee were significantly less in both DM and DPN groups than Ctrls, and for the DPN group at the ankle. Operating strengths were significantly higher at the ankle in the DPN group compared to the Ctrls. These findings show that diabetic patients walk with reduced lower limb joint torques, however due to a decrement in their maximum ability at the ankle and knee, their operating strengths are higher. This allows less reserve strength if responding to a perturbation in balance, potentially increasing their risk of falling.

Introduction:

Diabetes is a major health concern in many developed countries, in the UK affecting almost 5% of the entire population (Diabetes UK, 2010), and the number is growing. One of the major complications of diabetes is diabetic peripheral neuropathy (DPN), which may be present in 30-40% of patients (Boulton et al., 2004). Diabetic peripheral neuropathy affects sensory and motor nerves, predominantly in the feet and lower limbs. Both sensory and motor aspects of DPN have the potential to impact upon gait. Sensory neuropathy impairs perception of foot-ground contact, therefore influencing sensory feedback and balance control. Motor neuropathy impairs the force producing capabilities of muscles via impaired motor nerve function, and therefore impacts on the torques generated around lower limb joints. However, even before the development of DPN, the effects of non-enzymatic glycation can act on the contractile machinery to impair muscle function (Kindig et al., 1998; Phielix and Mensink, 2008). As a result of these diabetes-related complications there is a marked impact upon gait (Allet et al., 2008; Wrobel and Najafi, 2010), contributing to the fact that diabetes has been shown to increase the risk of falls during daily life (Tilling et al., 2006), with DPN being a particular risk factor (Bonnet and Ray, 2011; Richardson and Hurvitz, 1995). Such falls can often result in injuries, and for the general population of the UK between 2001-2003, 16% of accidents occurring at home or during leisure time and resulting in hospital treatment were due to someone falling during walking (DTI and Industry, 2003). Therefore, given diabetes causes a greater risk of falling there is considerable importance in understanding the possible underlying mechanisms, so that intervention strategies can be aimed at preventing future falls.

The majority of previous studies investigating the biomechanics of walking in diabetic patients have focused primarily upon reporting temporal-spatial characteristics or joint angular alterations. The main observations include a shorter stride length, longer stance times, smaller hip joint range of motion, slower walking speed and reduced cadence in diabetic patients compared to controls (Allet et al., 2009; Ko et al., 2011; Menz et al., 2004;

Mueller et al., 1994; Petrofsky et al., 2005). These gait characteristics, especially a slower gait velocity and shorter stride length are common in other populations with instability such as the elderly (Taylor et al., 2013), and they demonstrate alterations to key movement characteristics. Many studies have investigated the above parameters in patients with DPN (Allet et al., 2009; DeMott et al., 2007; Ko et al., 2011), however some studies have included an additional group of diabetic patients without DPN, showing similar but less pronounced differences than the group with neuropathy (Menz et al., 2004; Mueller et al., 1994). This suggests that DPN may not be the sole factor leading to alterations in gait in diabetic patients.

Although previous studies described above have identified gait pattern alterations in diabetic patients, the parameters reported reveal little of what is actually 'driving' such changes. As all movement starts from muscle contraction, investigating joint kinetics allows us to examine how muscles are acting on the major lower limb joints, and uncover the mechanisms behind the previously reported pattern alterations. It has been shown that during walking diabetic patients develop lower peak joint torques at all three lower limb joints (Ko et al., 2011; Mueller et al., 1994; Sawacha et al., 2009), indicating an altered muscular gait strategy. Although joint torque developed during gait provides an indication of the 'strength' requirements of the task, we also need to understand how this relates to the physical capabilities of the individual. Maximum muscular strength, which has previously been identified as a key factor for falls in the elderly (Pijnappels et al., 2008a, 2008b), is reduced in diabetic patients with DPN compared to healthy controls (Andersen et al., 2004; Andreassen et al., 2006). This may also mean that diabetic patients are operating closer to the limits of their physical capabilities during walking, a finding already observed in healthy elderly people during stair ascent (Reeves et al., 2009). Operating closer to maximum ability while walking would leave a smaller 'reserve capacity' to meet the increased joint torque demands required to maintain balance and prevent a fall in response to any perturbation, or unexpected challenge to balance therefore this may provide further insight as to why this

population is more likely to fall. The present study investigated peak joint torques generated at the lower limb joints during walking and how these torque levels relate to the physical capabilities of the individual. The aim of the study was to investigate the influence of diabetes and DPN on lower limb kinetics relative to maximal capabilities during walking, and consider the implications this has for stability.

Methods

Participants: After receiving ethical approval for the study from all relevant bodies, a total of 80 participants were recruited, who gave their written informed consent to participate. Participants were allocated into one of three groups based upon defined criteria: patients with diabetes and moderate-severe peripheral neuropathy (DPN, n=20), patients with diabetes but no neuropathy (DM, n=33) and healthy controls without diabetes or peripheral neuropathy (Ctrl, N=27).

Clinical Assessment: All participants were assessed to confirm they met the inclusion criteria. Major exclusion criteria included: inability to walk independently of assistance, presence of amputation, open foot ulcers, history of cerebral injury, neurological disorder (other than diabetic aetiology), musculoskeletal injury and visual acuity poorer than 6/18. Presence of peripheral neuropathy was assessed using the modified Neuropathy Disability Score (mNDS) and the vibration perception threshold (VPT). The mNDS is a semi-quantitative composite score derived from assessment of temperature perception, pain, vibration, and the Achilles tendon reflex (Boulton, 2005) and the VPT is a quantitative assessment performed using a neurosthesiometer (Bailey Instruments Ltd., Manchester, UK; (Boulton et al., 2004)). Patients were considered to have moderate-severe peripheral neuropathy and allocated to the DPN group if they demonstrated a mNDS ≥6, or a VPT ≥25. Diabetic patients demonstrating a mNDS <6 and a VPT <25 were allocated to the DM group without neuropathy. Blood glucose levels were assessed from the Ctrl group to confirm the absence of diabetes and the above neuropathy tests conducted to confirm the absence of neuropathy in the Ctrl group resulting from any aetiology.

Gait analysis: Kinematics were collected at 100Hz using a full-body modified Helen-Hayes marker set, and a 10-camera Vicon motion capture system (Vicon, Oxford UK) positioned around an 8-meter walkway. Kinetics were simultaneously collected at 1000Hz from 3 Kistler force platforms embedded into the middle of the walkway. Where possible markers were placed directly onto the skin, to eliminate 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, ensuring the diabetes patients with DPN walked with safe, appropriate footwear whilst minimising the effect of footwear and standardising across all participants. Participants were instructed to walk the length of the walkway at their self-selected speed. Participant's starting position was altered by the experimenters to ensure a 'clean' (i.e., no overlap outside the force platform) foot-strike on one or two of the force platforms per walk without alteration to their natural gait. Walking trials were repeated until at least three 'clean' foot contacts with the force platforms were made per limb.

Gait variables and joint kinetics: Joint torques and temporal-spatial parameters (gait velocity, stance time) were then calculated using Visual 3D software (C-motion Inc., MD, USA), using the process of inverse dynamics to calculate joint torques and powers. Peak joint torques during stance were calculated for each participant from left and right legs for each of the 3 trials. Mean peak torques (ankle, knee, and hip) were calculated taking into account data from both legs, across all three trials, and were subsequently normalised to body mass. This approach (mean across both legs and three trials; kinetics normalised to body mass) was used for all variables presented. Power curves during stance were calculated to assess concentric and eccentric work done; positive (concentric) and negative (eccentric) periods of power during the stance period were isolated to separately define concentric and eccentric work done which was defined as the power-time integral (area under the curve) during these periods. Periods of eccentric (muscle lengthening) and concentric (muscle shortening) power were isolated to calculate eccentric and concentric work done respectively, and were then subsequently normalised to body mass.

Maximum joint torque reference value assessment: Individual maximal torque reference values were assessed for the ankle plantar flexors and knee extensors using an isokinetic dynamometer (Cybex Norm, USA). These muscle groups were selected because they are the predominant muscle groups contributing to propulsion and weight-acceptance during

walking. These maximum effort contractions were performed for the purpose of relating the maximum muscle capabilities to that of the joint torque demands during walking for calculation of what we term from here on as 'operating strength' (see below). Measurements were taken with participants in a seated position on the dynamometer for knee extension, and prone for ankle plantar flexion. Maximal torque was recorded at four different joint angular velocities ($60°s^{-1}$, $120°s^{-1}$, $180°s^{-1}$ & $240°s^{-1}$) for both concentric (shortening) and eccentric (lengthening) contractions, in order to cover a range of joint angular velocities that are experienced during normal gait. Individual maximum eccentric and concentric joint torques were also calculated across the speeds in order to compare the variations in maximal abilities between groups.

Operating strength calculations: Operating strength was defined as the ratio of the peak joint torque developed during gait, to the maximum joint torque reference value produced at the same joint, under matched conditions (i.e., muscle action and joint angular velocity; values presented as percentages). Essentially, this measure (operating strength) expresses the peak demands of walking relative to the participant's maximum muscular capabilities. Operating strength was calculated for 59 of the original 80 participants due to non-completion of assessment for the maximum reference values; this occurred either when a participant failed to return for this data collection session, or were physically unable to perform the tests. The group sizes for the operating strengths are therefore Ctrl: n=18, DM: n=27, DPN: n=14. The starting point for the operating strengths calculation was to identify the peak knee and ankle joint torque occurring during the gait cycle. Peak torque values were identified and normalised to the appropriate maximum joint torque reference value, matched for muscle action (eccentric/concentric) and joint angular velocity at the time of the peak; this was done for individual peaks before a mean value was ultimately calculated for each participant from the 3 trials and two legs.

Statistical analysis: Between-group comparisons of the variables were performed using a single mean value for each individual, calculated as the mean of six results for each variable

per participant: obtained from three different repetitions of the trial per each of the two legs. A one-way analysis of variance (ANOVA) was performed for all variables with Tukey post-hoc tests to assess between group differences (Ctrl, DM & DPN). An analysis of covariance (ANCOVA) was subsequently performed for peak torques and work done using stance time as the covariate since gait velocity and stance time were found to be significantly lower in patients with DPN (Table 1). Stance time was used as the covariate rather than gait velocity due to the direct relationship to the work done, allowing work done to be assessed to see more precisely whether the differences are due to the magnitude of power, or duration of stance.

Results

Participant Characteristics: There were no significant differences between any group with regards to age, but height, body mass and BMI were all significantly greater in the DPN group (Table 1, $p<0.05$).

Neuropathy Assessments: As expected, the DPN group displayed significantly higher values for the VPT and the modified NDS compared to both the Ctrl and DM groups (Table 1). The VPT and mNDS for the DM group were not significantly different from the Ctrls, underlining that this diabetic patient group had no neuropathy (Table 1).

Temporal-Spatial Gait Parameters: The DPN group displayed significantly lower gait velocity and increased stance time compared to the Ctrl group (Table 2). There was no significant difference in gait velocity and stance time between the DM and Ctrl groups.

Peak Joint Torques during Walking: Peak ankle plantar flexion torque was significantly lower in both DPN ($p<0.01$) and DM ($p=0.01$) groups compared to Ctrl (Fig. 1 and Table 2), but there was no significant difference between groups in peak dorsiflexion torque (Table 2). Peak knee extension torque was significantly lower in DPN ($p<0.05$) and DM ($p<0.01$) groups relative to Ctrl (Figure 1b; Table 2). Peak hip extension torque was significantly lower in the DM group relative to Ctrl ($p<0.05$; Table 2), but this did not reach significance in the DPN group ($p=0.08$). Hip flexion torque was not significantly different between any of the groups (Table 2).

Work Done during Walking: Concentric work done at the ankle was significantly lower in the DPN group compared to the Ctrl group ($p<0.05$), but did not reach significance in the DM group ($p=0.09$). In the DPN group, eccentric work done at the knee was significantly reduced compared to the Ctrl group ($p<0.01$), but there was no significant difference between these two groups in concentric work done at the knee. In the DM group at the knee, concentric and eccentric work done was significantly ($p<0.05$) reduced compared to Ctrl (Table 2). No

differences were found between any of the groups in the concentric or eccentric work done at the hip.

Gait Velocity (stance time) as a Covariate: Results of the ANCOVA showed that all variables previously demonstrating significant differences continued to do so following this statistical adjustment (Table 3).

Operating Strengths: The operating strength at the ankle was significantly higher in the DPN group only compared to the Ctrl group ($p<0.01$; Bar charts in Figure 1c). There were no significant differences in the operating strength at the knee between any of the three groups (Bar charts in Figure 1b).

Maximum Joint Torques: At the ankle, the eccentric and concentric maximum joint torque reference values were significantly lower in the DPN group compared to the Ctrl (Table 4); but no significant differences were found between the DM group and the Ctrls. At the knee, eccentric and concentric maximum joint torque reference values were significantly lower in the DPN and DM groups compared to the Ctrl (Table 4).

Discussion:

The main findings from this study are that diabetic patients both with neuropathy and without neuropathy display reduced lower limb joint torques during walking joints (hip [Significant for DM group only], knee and ankle; Table 2). Despite lowering the demands of walking by developing lower joint torques, diabetic patients with peripheral neuropathy operated at a higher proportion of their muscular capabilities at the ankle, as evidenced by the higher 'operating strength' (Figure 1b & c; bar charts). This higher operating strength at the ankle was significant only in the DPN group compared to the Ctrl group and was explained by markedly weaker ankle plantar flexors (Table 4). Although significant differences in the ankle operating strength were found only in the DPN group, the DM group displayed a similar non-significant increase compared to the Ctrls ($p=0.07$). Whilst the operating strength was also higher in both diabetes groups at the knee it did not reach significance when compared to Ctrls, likely due to high within-group variance in the diabetes groups (Figure 1b & c, bar charts). Similar to the ankle, our findings at the knee were underpinned by significant weakness of the knee extensors in both diabetes groups (Table 4).

The present finding of reduced peak joint torque at the ankle, knee and hip agrees with the findings of Sawacha et al. (Sawacha et al., 2009) in a similar cohort (67 participants, split into three 'equal' sized groups of controls, and diabetes patients with and without neuropathy) of patients during walking. Mueller et al. (Mueller et al., 1994) also presented findings in agreement with reduced ankle joint torque in diabetes patients, however found no significant differences at the knee or hip. Mueller et al. (Mueller et al., 1994) however had a smaller sample and less stringent neuropathy criteria than the present study or Sawacha's (Sawacha et al., 2009), which may explain the discrepancies. These findings also agree with previous studies in other populations known to be at risk of falls such as the elderly (Crozara et al., 2013), re-enforcing that joint moments are important when maintaining a stable gait.

Our results show that whilst the diabetic patient groups, and in particular the DPN group are developing much lower joint torques, the DPN group's higher operating strength at the ankle

indicates that their muscles are working at a higher level of their capability. This may be a crucial factor in understanding why diabetic patients are more likely to fall during walking. Lower maximal lower limb joint strength has previously been identified as a key factor also present in other populations with high fall risk (Crozara et al., 2013; Thelen et al., 1996), and influences whether an individual is able to recover after a trip and thereby prevent a fall (Pijnappels et al., 2008b). Also increased operating strengths have been reported in the elderly (another population at high risk of falling) during stair ascent (Reeves et al., 2009). Therefore the higher operating strength may be crucial to understanding why a fall becomes more likely to occur, as when a perturbation occurs during gait, joint demands have a sudden increase in order to recover and prevent a fall (Pijnappels et al., 2008a, 2004). Heightened operating strengths during normal gait may therefore present a problem in diabetes patients if the sudden increase in requirements during a perturbation remains proportional to those that we present here. A healthy individual maintains a larger proportion of their strength as reserve ability, but a diabetic patient who is already operating at a higher level of their muscular capability may be unable to generate sufficient extra torque to meet the demands and prevent a fall. This may be exacerbated in daily life compared to the current lab-based study in which the participants were allowed time to rest; during everyday life the duration of walking and other activities will likely far exceed those experienced during our tests, introducing a further issue of fatigue. Fatigue will further lower the strength capabilities of the individual, further limiting strength reserves. Particularly in patients with diabetic peripheral neuropathy who are already working at a higher level of their capabilities this may be a particular issue as fatigue may onset sooner, intensifying a complication that is already increasing their risk of a fall. Clinical recommendations are for patients with DPN to wear footwear at all times due to the high risk of plantar ulceration. Whilst the use footwear (compared to un-shod) may influence some gait parameters (especially those at the foot ground-interface), shod gait is a clinically relevant situation and furthermore here we standardised the type of footwear across all participant groups.

Upon weight acceptance during walking, the knee extensors perform eccentric work as they 'absorb' the impact of the limb contacting the ground. In the present study we found a decrease in eccentric work done at the knee in both DPN and DM groups compared to Ctrls (Table 2). It might be argued that this reduced work done at the knee in both diabetes groups could be explained solely by a decreased gait velocity, which would explain the lower demands, however, using stance phase duration as a covariate (more sensitive than gait velocity for this variable) it did not significantly influence this finding (Table 3). This reduction in work done most likely relates to an inability in diabetes patients to meet the level of demand from the knee extensors during this weight acceptance phase, which is linked to their lower maximum capabilities (Table 4). The ankle plantar flexors provide the concentric 'propulsive' impulse towards the end of the stance phase to propel the body forwards. The present study has shown a reduction in concentric work done at the ankle in the DPN group relative to Ctrls (Table 2). This likely reflects the markedly weaker ankle plantar flexors of the DPN group (Table 4) reducing their ability to produce high levels of concentric work. The extent of muscle weakness is particularly evident in the DPN group for the ankle plantar flexors (Table 4), consistent with the distal-to-proximal progression of peripheral neuropathy (Boulton et al., 2004). Similar reductions in joint strength have been shown previously in studies by Andersen (Andersen et al., 2004, 1996). These previous studies both compared diabetic patients with and without the presence of neuropathy to controls as a single group, but show correlations between the presence of neuropathy and the extent of muscle weakness. This is in line with our finding in Table 4, where the DPN group displays the greatest strength decrements relative to Ctrls. Resistance training has previously been shown as effective for increasing strength in a range of populations, such as elderly adults (Reeves et al., 2004). This form of exercise training could be an effective strategy for increasing maximum muscle strength in diabetic patients and thereby favourably altering the operating strengths.

During walking the operating strengths are at a higher level at the ankle in all three groups when compared to the knee (Figure 1c), which again given the subsequent reduction in reserve ability, highlights the importance of maintaining adequate strength of the ankle plantar flexors in relation to the safety of gait and prevention of falls. In both diabetes groups, the mean operating strength values exceed 100%, whereas in practice we cannot exceed 100% of our muscles operating strength. This apparent discrepancy can be explained by difficulties in perfectly matching muscle contraction conditions between the gait task and the maximum joint torque reference value tests. Although we have accounted for as many variables as possible to match between the two conditions (gait and maximum strength tests), aspects such as the action of bi-articular muscles can impact on muscle length during dynamic activities; also during gait movements are tri-axial rather than the uni-axial nature of strength tests on a dynamometer, which can result in slight length changes to muscle groups acting on the joint as well as rotation of the attachment point altering the fulcrum the major muscle groups are acting on. Unfortunately, as a result a perfect duplication of conditions is beyond current methodologies.

A slower walking speed is a consistent finding of previous studies in diabetic patients (Allet et al., 2009; Menz et al., 2004; Petrofsky et al., 2005). Walking more slowly reduces the joint torque and energy demands (work done) on lower limbs, consistent with a more conservative strategy and our findings in both diabetes groups (Table 2). Since both diabetes groups displayed lower maximum muscular capabilities compared to controls, the reduced gait velocity might be seen as strategy to bring operating strengths down to a lower level. Despite walking more slowly, the diabetic patients with peripheral neuropathy still did not manage to bring their operating strengths at the ankles to a similar level to that of controls, this alongside the decrements in maximum muscular capabilities may contribute to explaining the increased fall risk in this population. Given that gait velocity was significantly lower in the DPN group, stance time was used as a covariate in a subsequent statistical analysis (ANCOVA). The results of the ANCOVA demonstrated that the reductions in peak

torque and work done in the diabetic groups are not solely explained by gait velocity (increased stance time).

In conclusion this study has shown that diabetic patients and particularly those with neuropathy generate reduced peak joint torques and work done at lower limb joints compared to a control group. Despite, lowering the demands of walking a higher ankle operating strength was observed in the diabetes patients with peripheral neuropathy due to the marked muscle weakness. These findings may contribute to our understanding of why people with diabetes are at such high risk of falling.

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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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Tables:

Table 1. Participant characteristics and results from neuropathy assessments, for: healthy controls (Ctrl), diabetic patients with no neuropathy (DM) and diabetic patients with moderate/severe neuropathy (DPN). Significant differences from the Ctrl group are denoted by * (P<0.05) or ** (P<0.01). BMI = Bodymass index, NDS = Neuropathy disability score, VPT = Vibration perception threshold. Values are means (standard deviations).

Variable	Units	Group		
		Ctrl	DM	DPN
Age	(yrs)	51 (19)	58 (12)	57 (9)
Body mass	(kg)	75 (13)	78 (13)	94 (22)**
Height	(m)	1.71 (0.09)	1.67 (0.10)	1.74 (0.10)*
BMI	(kg/m^2)	25 (4)	27 (4)	31 (6)**
NDS	(Score/10)	1 (1)	2 (2)	8 (3)**
VPT	(Volts)	8.2 (5.8)	10.3 (5.4)	30.7 (9.4)**

Table 2. Temporal-spatial and kinetic parameters, for: healthy controls (Ctrl), diabetic patients with no neuropathy (DM) and diabetic patients with moderate/severe neuropathy (DPN). Significant differences from the Ctrl group are denoted by * (P<0.05) or ** (P<0.01).

			Group		
	Variable	Units	Ctrl	DM	DPN
Temporal – spatial parameters	Gait Velocity	(m/s)	1.39 (0.18)	1.28 (0.17)	1.22 (0.22)*
	Stance time	(s)	0.65 (0.05)	0.66 (0.08)	0.71 (0.10)*
Peak Joint Torques	Ankle plantarflexion	(Nm/kg)	1.48 (0.17)	1.32 (0.18)*	1.28 (0.23)**
	Ankle Dorsiflexion		0.22 (0.15)	0.28 (0.08)	0.25 (0.10)
	Knee extension		1.15 (0.26)	0.90 (0.20)**	0.95 (0.38)*
	Hip Flexion		0.94 (0.69)	1.11 (0.24)	1.02 (0.25)
	Hip Extension		0.90 (0.24)	0.69 (0.21)*	0.74 (0.32)
Work Done	Ankle Concentric	(J/kg)	0.27 (0.05)	0.24 (0.05)	0.20 (0.06)*
	Knee Concentric		0.17 (0.06)	0.13 (0.05)*	0.15 (0.09)
	Hip Concentric		0.15 (0.04)	0.14 (0.05)	0.15 (0.05)
	Ankle Eccentric		0.12 (0.04)	0.12 (0.04)	0.14 (0.04)
	Knee Eccentric		0.35 (0.09)	0.29 (0.08)*	0.27 (0.09)**
	Hip Eccentric		0.21 (0.05)	0.21 (0.08)	0.20 (0.08)

Table 3. Comparison of analysis of variance (ANOVA) and covariance (ANCOVA) with stance time as a covariate. Significant differences are denoted by * (P<0.05) or ** (P<0.01). The inter-group differences column indicates which groups are significantly from the healthy control group: diabetic patients with no neuropathy (DM), and/or diabetic patients with moderate/severe neuropathy (PN).

Variable		Significant for ANOVA	Significant for ANCOVA for stance time	Inter-group differences
Peak Joint Torque	Ankle Plantarflexion	YES (p=0.001**)	YES (p=0.003**)	DM / DPN
	Ankle Dorsiflexion	NO (p=0.144)	YES (p=0.022*)	
	Knee Extension	YES (p=0.003**)	YES (p=0.000**)	DM / DPN
	Hip Flexion	NO (p=0.365)	NO (p=0.087)	
	Hip Extension	YES (p=0.007*)	YES (p=0.000**)	DM
Concentric work done	Ankle	YES (p=0.000**)	YES (p=0.000**)	DPN
	Knee	NO (p=0.053)	NO (p=0.059)	
	Hip	NO (p=0.628)	NO (p=0.164)	
Eccentric work done	Ankle	NO (p=0.165)	YES (p=0.001**)	
	Knee	YES (p=0.003**)	YES (p=0.000**)	DM / DPN
	Hip	NO (p=0.735)	NO (p=0.749)	

Table 4. Maximum joint torque reference values, for: healthy controls (Ctrl), diabetic patients with no neuropathy (DM) and diabetic patients with moderate/severe neuropathy (DPN). Significant differences from the Ctrl group are denoted by * (P<0.05) or ** (P<0.01). Values are means (standard deviations).

		Ctrl	DM	DPN	% decrease relative to Ctrls	
Max. Joint Torque	Units	Mean	Mean	Mean	DM	DPN
Eccentric Ankle	(Nm)	1.75 (0.46)	1.55 (0.48)	1.28 (0.55)*	11	27
Concentric Ankle		1.48 (0.43)	1.25 (0.49)	1.05 (0.51)*	16	29
Eccentric Knee		2.96 (0.63)	2.32 (0.58)**	2.07 (0.67)**	22	30
Concentric Knee		1.95 (0.54)	1.33 (0.42)**	1.19 (0.44)**	32	39

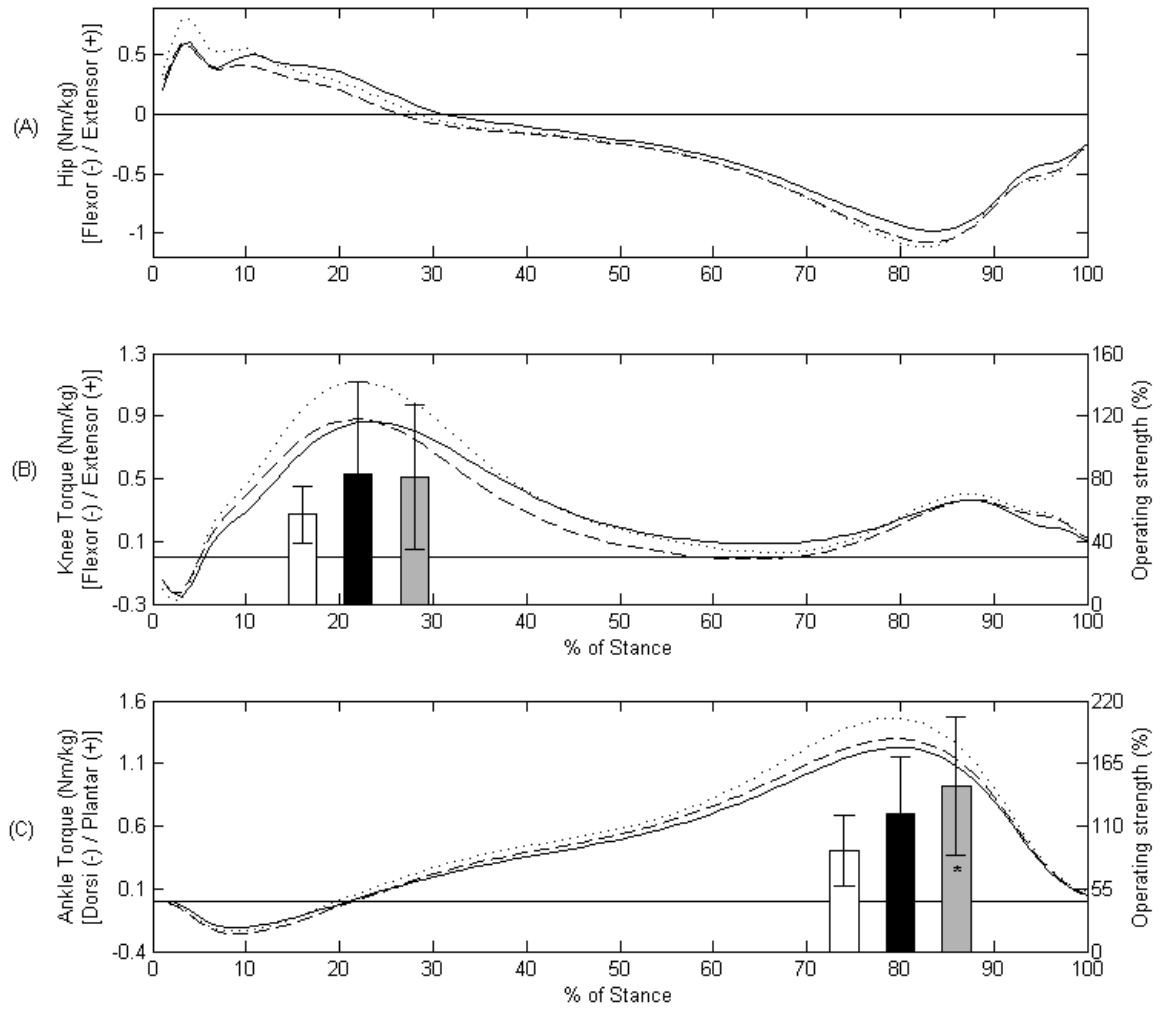

Figure 1. Joint torque profiles during stance & operating strengths for healthy controls (Ctrl), diabetic patients with no neuropathy (DM), and diabetic patients with moderate/severe neuropathy (DPN). Graphs are for (A) hip, (B) knee and (C) ankle joints. Line graphs: joint torque profiles during stance (mean values for Ctrl-dotted line, DM – dashed line, DPN – solid line). Bar chart: Operating strength values (mean ± SD values for Ctrl – white, DM – black, DPN – grey), shown in the approximate area of stance where peak torque occurred and from which operating strength was calculated (see methods). Significant differences ($p<0.05$) from the Ctrl group for the operating strengths are shown by "*" within the bar.