Title: Diabetic peripheral neuropathy compromises balance during daily activities

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Abstract:

Introduction: Diabetic patients with peripheral neuropathy have a well-recognized increased risk of falls that may result in hospitalisation. Whilst balance during standing has been studied in patients with diabetes, little is known about more dynamic activities such as walking, or stair negotiation where falls are most likely to occur. Methods: Gait analysis during level walking and stair negotiation was performed in 22 patients with diabetic neuropathy (DPN). 39 diabetic patients without neuropathy (D) and 28 non-diabetic controls (C) using a motion analysis system and embedded force plates in the stairs and level walkway. Balance was assessed by measuring the separation between the body centre-ofmass and centre-of-pressure during level walking, stair ascent and stair descent. Results: DPN patients demonstrated greater (p<0.05) maximum and range of separations of their centre-of-mass from their centre-of-pressure in the medial-lateral plane during stair descent, stair ascent and level walking compared to controls; as well as increased (p<0.05) mean separation during level walking and stair ascent. The same group also demonstrated greater (p<0.05) maximum anterior separations (towards the staircase) during stair ascent. No differences were observed in D patients. Discussion: Greater separations of the centre-ofmass from the centre-of-pressure present a greater challenge to balance. Therefore, the higher medial-lateral separations found in patients with DPN, will require greater muscular demands to control upright posture. This may contribute to explaining why patients with DPN are more likely to fall, with the higher separations placing them at a higher risk of experiencing a sideways fall than non-diabetic controls.

Keywords: Diabetic Neuropathy, Falls, Proprioception, Balance, stairs, gait.

Abbreviations:

- DPN Diabetic peripheral neuropathy
- VPT Vibration perception threshold

- mNDS modified Neuropathy Disability Score
- ANOVA Analysis of variance
- CoM-CoP Centre-of-mass to centre-of-pressure

Introduction:

Patients with diabetic peripheral neuropathy (DPN) have an altered gait strategy (1–3) and a five-fold increased risk of falling (4–6). Falling is a major health risk in many developed countries, for example, in the general UK population, over a quarter of accidents that required hospital treatment were the result of a fall (7). A fall is preceded by loss of balance, which may be recoverable in some individuals, but requires rapid responses and a high level of strength from the lower limb muscles (8,9). Nevertheless, the more likely an individual is to lose balance, the more likely they will at some point experience a fall. Therefore, quantifying balance control during every day gait activities may be considered one of the closest proxies for the risk of falling.

Measures of 'balance' in patients with diabetes and DPN have been mostly limited to postural sway during quiet standing, showing greater deviations in the centre-of-pressure and increased postural sway (4). Postural movements during both quiet standing and walking have demonstrated greater variability in patients with DPN (3,10,11), which suggests an inherent difficulty in regulating their movements resulting in a need for more frequent adjustments to balance, which in itself could be destabilising.

Previous studies have focussed on the deviation in the centre-of-pressure as a measure for the movement of the body via where the force is applied to the ground. A few studies have quantified postural sway directly by measuring movement of the body centre-of-mass, or accelerations of body regions (10). The use of centre-of-pressure position alone as a measure of 'balance' during quiet standing may provide some useful insights, however, measurements combining body movement together with the centre-of-pressure are more appropriate for exposing underlying balance impairments (12). A person is most stable when their centre-of-mass is directly above their centre-of-pressure, as is the case during quiet standing. Separation of the body centre-of-mass from the centre-of-pressure is proportional to horizontal acceleration (13), and consequentially related to the muscular demands required to remain upright. Therefore, measurement of separation between the centre-of-

mass and centre-of-pressure provides a superior measure as it accounts for both postural movements (via the centre-of-mass) and foot placements (via the centre-of-pressure). Given the implicit relationship between increased separations of the centre-of-mass from the centre-of-pressure and the increase in muscular effort required to maintain upright posture; higher separations between the two represent greater challenges to balance (14,15). Whilst a number of previous studies in other populations have used this measure (15,16), it has only been applied in a diabetic patient population during quiet standing (17) where balance is relatively unchallenged and the risk of falling is low.

During walking activities, when an individual transfers their weight from one limb to another there are brief periods of large separation between the centre-of-mass and the centre-of-pressure. High levels of muscular strength are required to maintain balance during these periods. These large separations between the centre-of-mass and centre-of-pressure experienced during the single stance periods of dynamic gait activities may be a contributing factor toward understanding why the risk of falling during gait activities is much greater than during quiet standing. Few studies, however, have attempted to address the issue of balance during walking in diabetes patients, and none have addressed the much more physically challenging activities of stair ascent and descent, during which the risk of falling is known to be very high (7). We therefore investigated a more 'dynamic' measure of balance during stair ascent, stair descent and level walking: three activities with the highest risk of fall-related injury (7), with the hypothesis that individuals with peripheral neuropathy would display greater separations between their centre-of-mass and centre-of-pressure (i.e. poorer balance), thereby contributing to explaining why they are at high risk of falls.

Methods

Participants: After receiving ethical approval from all relevant bodies, 94 participants were recruited to take part. Participants all gave their informed written consent before being allocated to one of three groups based on defined criteria: patients with diabetes and moderate-severe peripheral neuropathy (DPN; n=22), patients with diabetes but no peripheral neuropathy (D; n=39), and healthy controls without diabetes and without peripheral neuropathy (C; n=28).

Clinical Assessment: All participants underwent a clinical assessment: 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 the assessment of perception of temperature, vibration, pain and Achilles tendon reflex (18). In addition, VPT, a quantitative assessment of vibration perception, was performed using a Neurosthesiometer (Horwell, Nottingham, UK; (19)). 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 a mNDS score of ≥ 6 , or a VPT of ≥ 25 volts (or both). Patients were deemed to have no neuropathy and were grouped as D, if in both feet they displayed scores for the mNDS of \leq 5 and for the VPT of \leq 24. All non-diabetic controls were confirmed to have no peripheral neuropathy (mNDS<6 and VPT<25V). A random blood-glucose reading was also taken from the non-diabetic controls to confirm the absence of diabetes. Major exclusion criteria included: an inability to walk independently of assistance, presence of any lower-limb amputation, significant foot deformity (e.g. Charcot), open foot ulcers, history of cerebral injury and poor visual acuity (less than 6/18 of any aetiology), and a BMI>35kg m⁻². Where possible, duration of diabetes and the most recent HbA1c readings for patients with diabetes were ascertained using hospital records.

Gait analysis: Participants were invited to a gait laboratory with a bespoke 7-step instrumented staircase for assessing stair ascent and descent, and a level 8-meter walkway for assessing 'normal level' walking. Participants were provided with standardised footwear

with a neutral foot-bed (MedSurg, Darco, Raisting, Germany) to ensure no influence on gait from different styles of shoe, whilst also ensuring that the diabetic patients walked with appropriate footwear. Three-dimensional motion data was recorded in the gait lab using a 10-camera motion capture system (Vicon, Oxford, UK) positioned around the test areas. Using a Helen-Hayes-based full-body model, 56 reflective markers were placed at key anatomical positions on the participants to track movement of all body segments. To eliminate movement artefacts in the markers from loose clothing, participants were given close-fitting shorts and tops to wear, and wherever possible markers were placed directly onto the skin. Force data was collected simultaneously to the motion data using 3 embedded force platforms (Kistler, Winterthur, Switzerland) in the level walkway, and 4 embedded force platforms (Kistler, Winterthur, Switzerland) in the middle 4 steps of the staircase. For safety, a full-body harness was worn by all participants during gait analysis on the staircase.

Stair testing (ascent and descent) and level walking were assessed on two separate occasions to allow movement of the camera-based motion analysis system around the staircase or the level walkway. During stair ascent and descent, participants were asked to start at the top/bottom of the staircase close enough to the edge of the step to be ready to take their first step. They were then instructed to ascend/descend the staircase at a speed they felt most comfortable (i.e., their self-selected speed), not using the handrails unless they felt unable to complete the task without them. For walking on a level surface participants were instructed to start behind a mark on the level walkway, and when instructed walk to the other end of the walkway at the speed they felt most comfortable. During level walking the start mark was moved incrementally forwards or backwards to achieve 'clean' (without the foot overlapping the edges) foot contacts with the force plates without the entirety of the centre of the four middle steps so 'clean' foot contacts with the force plates occurred without aid. Stair ascent, descent and level walking tasks were

repeated until achieving at least three trials for each gait task with 'clean' foot contacts with the force plates.

During the session when level walking was assessed, data for quiet standing was also collected to compare against the walking activities, and to provide a reference for comparison with previous studies that have solely investigated quiet standing. Participants were asked to stand comfortably with their feet side-by-side (approximately shoulder width apart) and with one foot placed on each force plate. Motion and force data were then collected for two separate thirty-second long trials: during both participants were asked to stand comfortably still with their arms down by their sides and facing straight ahead. During the first trial they were asked to perform this task with their eyes open, and during the second trial they performed this task with their eyes closed.

Dynamic sway and postural sway: Motion data collected during gait analysis was processed and Dempster's segment parameter model (20) was used to calculate mass distribution for each body segment, thereby allowing calculation of an accurate entire-body centre-of-mass position throughout the trials. Ground reaction force data from the force plates was assessed to calculate the centre-of-pressure (the point from which the resultant ground reaction force originates) during periods when a foot was in contact with the ground. When two feet were simultaneously on two separate force plates, data from the individual force plates were combined using an equation described by Winter (13) to yield a weighted average position for the centre-of-pressure. This enabled the separation between the position of the centre-of-mass and the position of the centre-of-pressure to be calculated throughout the trials in both the medial-lateral and anterior-posterior planes. We have termed these separations between the centre-of-mass and centre-of-pressure: 'dynamic sway' during the gait activities of level walking, stair ascent and stair descent; and 'postural sway' during quiet standing. The *maximum* sway (in the medial-lateral plane, and separately for the anterior-posterior plane) and the range of sway (difference between maximum left and maximum right sway in the medial-lateral plane, and difference between anterior maximum

and posterior maximum in anterior-posterior plane) were measured to quantify extremes in dynamic sway and postural sway. Typical levels of sway throughout the trial were quantified by the *mean* sway in each plane. To quantify the within-participant reproducibility of the main variable (separations between the centre-of-mass and centre-of-pressure), the coefficient of variation for the range of medial-lateral dynamic sway was calculated for all groups across the three gait tasks (results of which are presented within the supplementary table). The reproducibility of this variable will reflect both inherent biological variability (associated with group and task) and methodological (equipment) variability.

Statistical analysis: Variables were calculated for each trial, before an average across the trials of each activity was calculated per participant to give a single result per person for each activity. Between-group differences for all variables were tested using a one-way analysis of variance (ANOVA) and followed up using Tukey post-hoc tests with respect to the control group. The level of agreement between the maximum dynamic sway (chosen as one of the key variables showing significant differences across the gait tasks) and three other variables: VPT, stance width and maximum medial-lateral postural sway during quiet standing with eyes-open, were tested using Pearson's correlations.

Results

Clinical assessment and demographics: There was a higher proportion of male participants in all three groups compared to female participants (Table 1). There were no significant differences between the groups with regards to age or height; but the DPN group were significantly (p<0.05) heavier, and had a higher BMI (Table 1). The D group displayed no significant differences from the control group for either neuropathy test. The DPN group as expected displayed significantly higher scores for both neuropathy tests compared to the control group (p<0.05, Table 1).

Duration since diagnosis of diabetes and HbA1c readings were ascertained for thirty-eight of the sixty-one participants with diabetes (D: 26/39 & DPN: 12/22 participants). There were no significant differences shown between D and DPN group for duration since diabetes diagnosis, or HbA1c readings (Table 1).

Dynamic sway: centre-of-mass – centre-of-pressure separations: During both stair ascent and descent the DPN group demonstrated significantly (p<0.05) greater maximum and range of centre-of-mass to centre-of-pressure separation in the medial-lateral plane when compared against the control group (Table 2a). During level walking the DPN group again showed significantly (p<0.05) greater maximum and range of medial-lateral centre-of-mass to centre-of-pressure separation but also a significant (p<0.05) increase in the mean medial-lateral centre-of-pressure separation but also a significant (p<0.05) increase in the mean medial-lateral centre-of-pressure separation relative to the control group (Table 2a). In the anterior-posterior plane during both stair ascent and descent there was an increased range of separation in the DPN group relative to controls (p<0.05; Table 2a). During stair ascent the DPN group also showed increased maximum anterior separation relative to the control group, and during stair descent the DPN group showed a decreased maximum posterior separation and mean separation relative to the control group (p<0.05; Table 2a). During level walking the DPN group displayed a lower mean separation than the control group (p<0.05; Table 2a). No significant differences were observed between the D

and control groups for any variable, during any gait task in either medial-lateral or anteriorposterior plane.

Gait parameters: Gait velocities were significantly lower in the DPN group compared to the control group during stair ascent, stair descent and level walking (p<0.05, Table 2a); with no significant difference displayed between the D and control groups during stair ascent or descent, but a reduction in gait velocity was observed in the D group relative to the control group during level walking (p<0.05; Table 2a). During stair descent and level walking there were significant increases in step width in the DPN group relative to the control group during stair descent and level walking (p<0.05, Table 2a) but no significant change during stair ascent. Step length was calculated only for level walking, as during stair ascent and descent step length is constrained by the depth of the step. Step length during level walking was significantly lower in both D and DPN groups relative to the control group (p<0.05, Table 2a).

Postural sway during quiet standing: During quiet standing in the eyes open condition the DPN group displayed significantly greater mean and range of anterior-posterior separation relative to the control group, and a greater mean medial-lateral separation (Table 2b). During the eyes closed condition the DPN group demonstrated increased mean and range in separations relative to the control group in both medial-lateral and anterior-posterior planes (Table 2b). The D group demonstrated greater maximum separations in both medial-lateral and anterior-posterior planes relative to the control group in both eyes-open and eyes-closed conditions (Table 2b); but no significant changes in mean or range of separations.

Correlations: Positive correlations were found between the VPT and maximum mediallateral dynamic sway during stair ascent, stair descent and level walking (p<0.05, Figure 2a, b & c). Positive correlations were found between stance width and maximum medial-lateral dynamic sway during all three gait activities of stair ascent, stair descent and level walking (p<0.05; Figure 2 d, e & f). During stair descent maximum medial-lateral postural sway was only weakly correlated with maximum medial-lateral dynamic sway (p<0.05; r=0.27); but no

significant associations were present between these variables for stair ascent and level walking (p>0.05; r=0.23 & r=0.21 respectively).

Discussion:

For the first time we have shown that balance is markedly impaired in patients with DPN during the gait activities of level ground walking, stair ascent and stair descent. This balance impairment in patients with DPN was predominantly in the medial-lateral plane and was greatest during stair descent.

During the gait tasks we found no significant balance impairments in diabetic patients without DPN, clearly emphasising that the link between diabetes and instability is a symptom of peripheral neuropathy. This was further reinforced via a significant positive correlation between one of the key variables - maximum medial-lateral dynamic sway and the extent of peripheral neuropathy (VPT score) (Figure 2a, b & c).

Impairments to balance in patients with DPN were found mainly in the medial-lateral plane, with increased maximum and range of dynamic sway observed in this plane during all three gait activities. During stair ascent there was an indication of impaired anterior-posterior balance by the increased maximum dynamic sway in the anterior direction (Table 2a). However, no increase in posterior dynamic sway (away from the staircase) was observed; suggesting that individuals preferred to lean slightly toward the stairs, potentially falling toward the stairs rather than away if a fall was to occur. During stair descent the DPN group displayed the opposite behaviour, with a decrease in dynamic sway toward the staircase (Table 2a). This may be a response to the decreased haptic feedback and proprioception common to patients with DPN, as a greater reliance is placed on visual stimuli for accurate foot placement, which posterior dynamic sway would occlude. During level walking decreased dynamic sway in the anterior-posterior plane in patients with DPN compared to controls (Table 2a), is likely the result of the shorter step length (Table 2a). Shortening step length is a common strategy in populations known to be at heightened risk of falling, as this maintains a closer control of the centre-of-mass above the centre-of-pressure, thereby reducing muscular demands and decreasing the risk of falling (21,22).

The potential increase in fall risk due to increased dynamic sway and the associated increase in muscular effort to maintain balance is of particular concern when combined with marked muscular deficiencies that are present in patients with DPN (23). Our findings of increased maximum and range of dynamic sway in patients with DPN highlight the extremes of dynamic sway that are occurring during these gait activities. These extremes in dynamic sway show the momentary points when a loss of balance becomes most likely, as the centre-of-mass is at the furthest point from the centre-of-pressure and the muscular demands to maintain balance are highest. Therefore the larger 'extremes' (maximum sway) shown by patients with DPN suggest they are more vulnerable to a fall during these activities. Mean dynamic sway represents a general level of the magnitude of separation throughout the activities, and was significantly higher in the medial-lateral plane in the patients with DPN compared to the controls during level walking alone, indicating a consistently poorer ability to control sway in patients with DPN during this activity.

The magnitude of dynamic sway observed in the present study varies between gait activities. Stair descent is widely recognised as an activity where the risk of falling is highest (7,24,25), and in agreement with these reports, we found the largest magnitudes of dynamic sway in all three participant groups and particularly in patients with DPN. As the difficulty of the gait task decreases, we found the magnitude of the dynamic sway also reduces, as did the extent of difference between the groups; with level walking demonstrating the smallest levels of dynamic sway throughout the groups and yielding the smallest differences between the groups (Table 2).

Our findings have demonstrated an increased stance width in patients with DPN during stair descent and level walking (Table 2a). Normally considered a compensatory mechanism, during dynamic gait activities an increased stance width increases separation between the centre-of-mass and centre-of-pressure (sway) during periods of single limb support when moving away from the supporting limb. Correlations between stance width and maximum medial-lateral dynamic sway showed strong positive correlations during stair descent and

level walking (r=0.78 & r=0.63 respectively; Figure 2e & f) and a weak positive correlation (r=0.33; Figure 2d) during stair ascent. This calls into question the effectiveness of patients with DPN adopting a wider stance as a compensation for instability. Although during double limb support when two feet are in contact with the ground this will create a much better support system, during activities with single limb support periods (i.e., all types of walking activity), we suggest these participants are temporarily increasing their level of instability. The DPN population investigated also demonstrated a significantly higher body mass than the other two groups (Table 1), a common finding amongst populations with neuropathy, who also tend to be less active. Although differences in BMI were observed between the groups, fat mass distribution would be symmetrical and would therefore not impact upon the body centre of mass position in the medial-lateral plane. Increased abdominal fat mass may slightly shift the centre of mass anteriorly, however, fat mass distribution may not differ in a consistent way between groups. During dynamic gait activities the position of the centre of mass and centre of pressure are in constant flux (due to the movement of the limbs) making this unlikely to affect our measurements in the anterior-posterior direction.

This study also demonstrated a greater level of postural sway in patients with DPN during quiet standing both with eyes-open and eyes-closed (Table 2b). Due to the stable nature of quiet standing compared to gait, it is perhaps unsurprising that the magnitudes of postural sway were considerably smaller than those of dynamic sway during the gait activities: none of the groups displayed maximum postural sway values greater than 1.6cm in either plane (Table 2b), opposed to maximum excursions during the gait activities in some cases exceeding 30cm (Table 2a). These small excursions during quiet standing are in agreement with the findings of Corriveau et al in elderly patients with DPN (17), and can be explained by the stable nature of quiet standing. When comparing maximum medial-lateral postural sway during the gait activities we found a significant but poor correlation only during stair descent (p<0.05, r=0.27), and no significant relationship during stair ascent or level walking. This

suggests that whilst the control mechanisms of balance during gait activities and quiet standing are related, postural sway during quiet standing does not provide a very accurate representation of balance when relating to falls, which predominantly occur during gait activities (7,25,26).

Limitations: Duration since diagnosis of diabetes and HbA1c readings were obtained for participants with records at the local hospital; as described in the results, this demographic information was available for just over 50% of the D and DPN groups.

Our sample population included a slight bias towards a higher number of male participants within all three groups; but particularly within the DPN group. Whilst the distribution of the centre-of-mass may differ slightly between males and females; the male: female ratios across the three cohort groups were relatively similar, albeit somewhat higher within the DPN group (% male: C: 54%, D: 51%, DPN: 68%).

Conclusion: We have shown marked impairments in dynamic sway during gait activities in patients with DPN, which become more evident with increasing gait task complexity. Impaired balance in patents with DPN may also be linked to a compensatory mechanism (increased stance width), which is employed due to perceived instability, but may actually increase the risk of falling.

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Mr. Steven Brown is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis

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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.

Contribution Statement

We confirm all authors listed were involved in conception/design/data acquisition/analysis of the study, drafting or revision of the manuscript, and final approval of the version to be published. More specifically author contributions are listed below.

F.L.B, A.J.M.B, and N.D.R were involved in the initial concept of the study. S.J.B., J.C.H and N.D.R. were involved in data acquisition, and initial drafting of the manuscript. All authors were involved in study design, participant recruitment, revision and final approval of the version of the manuscript submitted for publication.

References

- 1. Katoulis EC, Ebdon-Parry M, Lanshammar H, Vileikyte L, Kulkarni J, Boulton AJ. Gait abnormalities in diabetic neuropathy. Diabetes Care [Internet]. 1997 Dec [cited 2014 Apr 7];20(12):1904–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/9405916
- Allet L, Armand S, Golay A, Monnin D, de Bie RA, de Bruin ED. Gait characteristics of diabetic patients: a systematic review. Diabetes Metab Res Rev [Internet]. John Wiley & Sons, Ltd.; 2008;24(3):173–91. Available from: http://dx.doi.org/10.1002/dmrr.809
- Menz HB, Lord SR, St George R, Fitzpatrick RC. Walking stability and sensorimotor function in older people with diabetic peripheral neuropathy. Arch Phys Med Rehabil [Internet]. 2004;85(2):245–52. Available from: http://www.sciencedirect.com/science/article/pii/S0003999303009444
- Bonnet CT, Ray C. Peripheral neuropathy may not be the only fundamental reason explaining increased sway in diabetic individuals. Clin Biomech [Internet].
 2011;26(7):699–706. Available from: http://www.sciencedirect.com/science/article/pii/S0268003311000684
- 5. Richardson JK, Hurvitz EA. Peripheral Neuropathy: A True Risk Factor for Falls. Journals Gerontol Ser A Biol Sci Med Sci [Internet]. 1995;50A(4):M211–5. Available from: http://biomedgerontology.oxfordjournals.org/content/50A/4/M211.abstract
- 6. Tilling LM, Darawil K, Britton M. Falls as a complication of diabetes mellitus in older people. J Diabetes Complications [Internet]. 2006;20(3):158–62. Available from: http://www.sciencedirect.com/science/article/pii/S1056872705000577
- DTI H and L accident surveillance system (HASS), Industry D of T&. 24th (Final) Report of the home and leisure accident surveillance system: 2000, 2001 and 2002 data [Internet]. London, UK; 2003. Available from: http://www.hassandlass.org.uk/query/reports/2000_2002.pdf
- Pijnappels M, Reeves ND, Maganaris CN, van Dieën JH. Tripping without falling; lower limb strength, a limitation for balance recovery and a target for training in the elderly. J Electromyogr Kinesiol [Internet]. 2008 Apr [cited 2014 Mar 23];18(2):188– 96. Available from: http://www.sciencedirect.com/science/article/pii/S1050641107001022
- Pijnappels M, van der Burg PJCE, Reeves ND, van Dieën JH. Identification of elderly fallers by muscle strength measures. Eur J Appl Physiol [Internet]. 2008 Mar [cited 2014 Mar 26];102(5):585–92. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2226001&tool=pmcentrez& rendertype=abstract
- Turcot K, Allet L, Golay A, Hoffmeyer P, Armand S. Investigation of standing balance in diabetic patients with and without peripheral neuropathy using accelerometers. Clin Biomech (Bristol, Avon) [Internet]. 2009 Nov [cited 2014 May 6];24(9):716–21. Available from: http://www.sciencedirect.com/science/article/pii/S0268003309001624
- 11. Morrison S, Colberg SR, Parson HK, Vinik AI. Relation between risk of falling and postural sway complexity in diabetes. Gait & amp; Posture [Internet]. 2012;35(4):662–

8. Available from: http://www.sciencedirect.com/science/article/pii/S0966636211008290

- 12. Benvenuti F, Mecacci R, Gineprari I, Bandinelli S, Benvenuti E, Ferrucci L, et al. Kinematic characteristics of standing disequilibrium: Reliability and validity of a posturographic protocol. Arch Phys Med Rehabil [Internet]. Elsevier; 1999 Mar 3 [cited 2014 Sep 9];80(3):278–87. Available from: http://www.archivespmr.org/article/S0003999399901387/fulltext
- 13. Da W, Winter DA. Human balance and posture control during standing and walking. Gait & amp; Posture [Internet]. 1995;3(4):193–214. Available from: http://www.sciencedirect.com/science/article/pii/0966636296828499
- Zachazewski JE, Riley PO, Krebs DE. Biomechanical analysis of body mass transfer during stair ascent and descent of healthy subjects. J Rehabil Res Dev [Internet].
 1993 Jan [cited 2014 Jun 12];30(4):412–22. Available from: http://www.ncbi.nlm.nih.gov/pubmed/8158557
- 15. Lee H-J, Chou L-S. Balance control during stair negotiation in older adults. J Biomech [Internet]. 2007 Jan [cited 2014 Jul 9];40(11):2530–6. Available from: http://www.sciencedirect.com/science/article/pii/S0021929006004295
- Mian OS, Narici M V, Minetti AE, Baltzopoulos V. Centre of mass motion during stair negotiation in young and older men. Gait Posture [Internet]. 2007 Sep [cited 2014 Oct 9];26(3):463–9. Available from: http://www.sciencedirect.com/science/article/pii/S0966636206005595
- 17. Corriveau H, Prince F, Hebert R, Raiche M, Tessier D, Maheux P, et al. Evaluation of postural stability in elderly with diabetic neuropathy. Diabetes Care. 2000/08/11 ed. 2000;23(8):1187–91.
- 18. Boulton AJM. Management of Diabetic Peripheral Neuropathy. Clin Diabetes. 2005;23(1):9–15.
- 19. Boulton AJ, Malik RA, Arezzo JC, Sosenko JM. Diabetic somatic neuropathies. Diabetes Care [Internet]. 2004/05/27 ed. 2004;27(6):1458–86. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15161806
- 20. Dempster WT. Space Requirements of the Seated Operator: Geometrical, Kinematic, and Mechanical Aspects of the Body with Special Reference to the Limbs /Wilfred Taylor Dempster [Internet]. Wright Air Development Center, Air Research and Development Command, U.S. Air Force; 1955. Available from: http://books.google.co.uk/books?id=Ks1pAAAAMAAJ
- Bhatt T, Wening JD, Pai Y-C. Influence of gait speed on stability: recovery from anterior slips and compensatory stepping. Gait Posture [Internet]. 2005 Feb [cited 2014 May 6];21(2):146–56. Available from: http://www.sciencedirect.com/science/article/pii/S0966636204000232
- Espy DD, Yang F, Bhatt T, Pai Y-C. Independent influence of gait speed and step length on stability and fall risk. Gait Posture [Internet]. 2010 Jul [cited 2014 Feb 24];32(3):378–82. Available from: http://www.sciencedirect.com/science/article/pii/S0966636210001712

- 23. Andreassen CS, Jakobsen J, Andersen H. Muscle weakness: a progressive late complication in diabetic distal symmetric polyneuropathy. Diabetes. 2006/03/01 ed. 2006;55(3):806–12.
- 24. Startzell JK, Owens DA, Mulfinger LM, Cavanagh PR. Stair negotiation in older people: a review. J Am Geriatr Soc [Internet]. 2000 May [cited 2014 Jun 13];48(5):567–80. Available from: http://www.ncbi.nlm.nih.gov/pubmed/10811553
- 25. Svanström L. Falls on stairs: an epidemiological accident study. Scand J Soc Med [Internet]. 1974 Jan [cited 2014 Jun 13];2(3):113–20. Available from: http://www.ncbi.nlm.nih.gov/pubmed/4432054
- Pauls JL. Safety standards, requirements, and litigation in relation to building use and safety, especially safety from falls involving stairs. Saf Sci [Internet]. 1991;14(2):125– 54. Available from: http://www.sciencedirect.com/science/article/pii/0925753591900068

Tables:

Table 1. Clinical measurements and demographics: Values are means (standard deviations). *denotes significant (p<0.05) difference from the control group. **denotes significant (p<0.01) difference from the control group. $^{\circ}$ denotes results are only available for a sample of the entire group, for n=26 in the D group, and n=12 in the DPN group.

Variable		С	D	DPN	
Number		28	39	22	
Male/Female ratio		15/13	20/19	15/7	
Age	(years)	53 (18)	56 (13)	57 (9)	
Body mass	(kg)	75 (13)	78 (12)	93 (22)**	
Height	(m)	1.7 (0.1)	1.7 (0.1)	1.7 (0.1)	
BMI	Kg/m ²	26 (4)	28 (4)	31 (6)**	
NDS	(Score /10)	1 (1)	2 (2)	7 (3)**	
VPT	(Volts)	8 (5)	10 (5)	30 (9)**	
Duration [‡]	(years)		22 (13)	25 (16)	
HbA1c [‡]	(% [mmol/mol])		8.2 [66] (3.7 [17])	9.2 [77] (4.3 [24])	

Table 2. A) Dynamic sway (centre-of-mass to centre-of-pressure separation). B) Postural sway (centre-of-mass to centre-of-pressure separation). Values are means (SD). *denotes significant (p<0.05) difference from the control group. **denotes significant (p<0.01) difference from the control group.

				Means		
	Γ			с	D	DPN
	Activity		Variable			
		Medial/ Lateral	Max (cm)	7.8 (1.9)	7.7 (1.7)	10 (2.6)**
			Range (cm)	13 (2.8)	12.8 (2.4)	16.6 (4.5)**
			Mean (cm)	5.1 (1.1)	4.8 (0.9)	6.1 (1.4)**
		Anterior/ Posterior	Anterior Max (cm)	23.3 (2.8)	22.3 (2.7)	22.6 (3.2)
	امرما		Posterior Max (cm)	31.2 (3.5)	29.4 (4.1)	28.5 (4.4)
	Level		Range (cm)	54.6 (5.2)	51.7 (6)	51.1 (7)
			Mean (cm)	12 (1.1)	11 (1.6)	10.8 (2.2)*
			Gait velocity (m/s)	1.41 (0.2)	1.28 (0.17)*	1.19 (0.17)**
			Stance width (cm)	11.3 (2.1)	10.9 (2.4)	14.3 (3.5)**
			Step length (cm)	72.5 (7.4)	67.4 (6.1)*	65.4 (10.9)**
		Medial/Lateral	Max (cm)	10.4 (2.7)	10.1 (2.3)	13.2 (1.9)**
			Range (cm)	17.5 (4.2)	17.7 (3.8)	23.1 (4.2)**
			Mean (cm)	5.3 (1.4)	4.9 (1.1)	6.1 (1.4)
Δ			Anterior Max (cm)	13 (2.9)	14.6 (3.2)	16.5 (3.6)**
	Stair Ascent	Anterior/Posterior	Posterior Max (cm)	13.5 (2.6)	13.7 (2.2)	13.1 (2.9)
		Antenoly Postenol	Range (cm)	26.5 (2.9)	28.4 (3.1)	29.6 (3.9)**
			Mean (cm)	5.1 (0.5)	5.3 (0.7)	5.3 (0.7)
			Gait velocity (m/s)	0.48 (0.1)	0.44 (0.1)	0.39 (0.1)**
			Stance width (cm)	13.2 (8.1)	11 (2.8)	14.4 (2.2)
		Medial/Lateral	Max (cm)	12.4 (2.7)	12.5 (2.5)	15.6 (3.2)**
			Range (cm)	21.8 (4.4)	22.3 (4.3)	28.2 (5.2)**
			Mean (cm)	6.4 (1.2)	6 (1.2)	7.1 (1.3)
		Anterior/Posterior	Anterior Max (cm)	10.6 (1.9)	10.8 (1.8)	10.7 (2)
	Stair Descent		Posterior Max (cm)	18.6 (3.1)	17.4 (2.2)	16.7 (2.1)*
			Range (cm)	29.2 (2.5)	28.3 (2.3)	27.4 (2.4)*
			Mean (cm)	4.9 (0.6)	4.7 (0.5)	4.4 (0.6)*
			Gait velocity (m/s)	0.53 (0.1)	0.47 (0.1)	0.42 (0.1)**
			Stance width (cm)	15.1 (2.2)	14.9 (2.6)	17.3 (2.7)*
<u> </u>			Max (cm)	1 2 (2 55)	0.74 (0.40)**	1.07/0.40
в -		Medial/ Lateral		1.2 (0.05)	0.74 (0.46)**	1.07 (0.48)
			Maap (cm)	0.54 (0.25)	0.66 (0.54)	0.75 (0.33)
	Quiet standing (Eyes			0.07 (0.04)	0.08 (0.03)	0.1 (0.05)*
	open)		Anterior Max (cm)	1.35 (1.4)	1.15 (1.16)	1.21 (1.22)
				-0.32 (1.09)	0.15 (1.39)	0.45 (1.13)
			Range (cm)	1.03 (0.6)	1.29 (0.62)	1.66 (0.66)**
	ļ	Medial/Lateral		0.14 (0.08)	0.10 (0.05)	U.21 (U.U/)**
			Range (cm)	1.2 (0.02)	0.82 (0.45)*	1.10 (0.51)*
				0.08 (0.24)		0.92 (0.01)*
	Quiet standing (Eyes				0.09 (0.03)	0.13 (0.09)*
	closed)		Posterior Max (cm)	1.55 (1.22)	1.37(1.17)	1.54 (1.26)
			Range (cm)	-0.13 (1.16)	0.20 (1.32)	0.72 (1.18)
			Noon (cm)	1.42 (0.58)	1.63 (0.6)	2.26 (0.98)**
1			iviean (cm)	0.18 (0.08)	0.21 (0.06)	0.29 (0.11)**

Figure legends



Figure 1 – Graphical illustration of the measurement of centre-of-mass to centre-of-pressure separation. The centre-of-mass location is projected downwards and the centre-of-pressure position is projected upwards. Horizontal arrows show the centre-of-mass (CoM) to centre-of-pressure (CoP) separation.



Figure 2 – Correlation results. A-C: Maximum medial-lateral dynamic sway plotted as a function of vibration perception threshold (VPT) score. D-F: Maximum medial-lateral dynamic sway plotted as a function of stance width. Values are individual participant data points, with group indicated by triangles for the DPN group; squares for the D group; and diamonds for the C group.