Resistance exercise training increases lower limb speed of strength generation during stair ascent and descent in people with diabetic peripheral neuropathy

Resistance training increases speed of strength generation

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Conflicts of Interest

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Novelty Statement

Here we examined for the first time, the effects of a resistance exercise based intervention on speed of knee and ankle strength generation in people with diabetic peripheral neuropathy, during stair ascent and descent. We observed that after a 16 week intervention, people with diabetic peripheral neuropathy, and people with diabetes without neuropathy, increased the speed at which strength was developed at the ankle and knee during stair ascent and descent. This is expected to decrease the risk of falling during these movements. Therefore, such exercises could be incorporated into a multi-faceted exercise programme to improve safety in people with diabetes and diabetic peripheral neuropathy.

Aims: People with diabetic peripheral neuropathy (DPN) are slower at generating strength at the ankle and knee, leading to unsteadiness during stair negotiation tasks. This study examines the effects of a 16-week resistance exercise training intervention on the speed of ankle and knee strength generation during stair ascent and descent, in people with neuropathy.

Methods: Forty three participants: 9 patients with DPN; 13 patients with diabetes but no neuropathy (D) and 21 healthy controls (H-CON) ascended and descended a custom-built staircase. The speed at which ankle and knee strength were generated, and muscle activation patterns of the ankle and knee extensor muscles were analyzed before and after a 16-week intervention period.

Results: Ankle and knee strength generation during both stair ascent and descent were significantly higher post-intervention compared to pre-intervention in the participants with diabetes who undertook the resistance exercise intervention ($p<0.05$). Although muscle activations were altered by the intervention, there were no observable patterns that underpinned the observed changes.

Conclusions: The increased speed of ankle and knee strength generation observed after the intervention, are expected to improve stability during the crucial weight acceptance phase of stair ascent and descent, and ultimately contribute towards reducing the risk of falling. Improvements in muscle strength as a result of the

resistance exercise training intervention are expected to be the most influential factor for increasing the speed of strength generation It is advocated that these exercises could be incorporated into a multi-faceted exercise programme to improve safety in people with diabetes and neuropathy.

Introduction

Diabetic peripheral neuropathy is a chronic complication of diabetes, affecting up to 50% of older patients [1, 2]. People with neuropathy are five times more likely to fall than age-matched controls, with over half of sufferers reporting at least one fall per year [3, 4]. Falls whilst walking down stairs account for 60% of all fall-related deaths, making this activity ten times more hazardous than level ground walking [5]. We have previously shown that during stair ascent and stair descent, patients with diabetic peripheral neuropathy are slower to develop strength at the ankle and knee upon initial step contact (measured using the rate of joint torque development), compared to controls [6]. This is important, as previous studies have shown that people who are slower to develop strength at the ankle and knee joints have an increased risk and rate of falling [6-9]. We have also shown that altered knee and ankle extensor muscle activation patterns in people with neuropathy may be related to the slower strength generation observed [6]. Therefore, if the timing and speed of muscle activations can be positively modified in people with neuropathy, the speed of strength generation may consequentially be increased during stair ascent and descent, which could in turn reduce the risk of falling.

In people with diabetes, cardiovascular and resistance exercises have been shown to improve postural sway during standing, and gait characteristics during level ground walking [10, 11]. However, no studies have yet examined the effects of resistance exercise training on factors affecting unsteadiness during the physically challenging and dangerous tasks of stair ascent and descent. Previous studies have shown that targeted resistance exercise training can improve the speed of strength generation in healthy young and older adults, which is expected to decrease the risk of falling [7, 12-14]. It is therefore hypothesised that such training may increase the speed of ankle and knee strength development in people with diabetes (with and without neuropathy), potentially reducing the risk of falling and improving safety during the everyday task of stair walking.

The aim of this study was to investigate the effects of a resistance exercise training intervention on the speed of strength generation at the knee and ankle joints, and muscle activation timings of the knee and ankle extensors in people with diabetes and neuropathy. It was hypothesised that improvements in muscle strength and increases in the speed of muscle activations would facilitate a faster SoSG, which would be indicative of a safer, more stable movement pattern during stair ascent and stair descent.

Methods

Participants

Forty three participants: 9 people with diabetic peripheral neuropathy [DPN], 13 patients with diabetes but no neuropathy [D] and 21 healthy controls [H-CON] gave their written informed consent to participate in this study, which was given ethical approval from the relevant bodies (Table 1). The major exclusion criteria were: open ulcers, requiring the use of a walking aid, a history of any other disorders affecting gait, and a visual acuity of <6/18 (of any aetiology, including retinopathy). The presence and severity of neuropathy was measured using two clinical tests, the modified Neuropathy Disability Score (mNDS) and the Vibration Perception Threshold (VPT) [1, 2]. Patients were deemed to have moderate to severe neuropathy, and grouped as DPN if in either one or both of their feet they displayed either an mNDS score of ≥6, or a VPT of ≥25 Volts (or both).

Study design

Participants ascended and descended a bespoke eight-step staircase with four step-embedded force platforms in the middle four steps of the staircase. A ten-camera motion capture system captured whole body movements (Vicon, Oxford, UK) and ground reaction forces were measured from the step-embedded force platforms (Kistler, Winterthur, Switzerland). Motion and force data were recorded simultaneously at 120Hz and 1,000Hz, respectively. Muscle activity was assessed from representative lower limb muscles, using wireless electromyographic surface electrodes (Delsys, Boston, USA) recording at 1,000Hz. The analogue signals from the electrodes were synchronised with the Vicon motion capture system and force platforms.

Procedure

Gait laboratory preparation

Fifty seven retro-reflective markers were attached to the participant's body according to standard motion analysis preparation methods, creating a 15 segment whole body model. All participants wore specialist diabetic shoes (MedSurg, Darco, Raisting, Germany) to standardise footwear between groups, and to ensure that the diabetic patients walked with appropriate footwear.

Electromyographic electrodes to measure muscle activations were placed on the skin over the muscles representative of the major knee and ankle extensors: the vastus lateralis (knee extensors; KE) and medial gastrocnemius (ankle extensors; AE) of both legs.

Stair negotiation

Participants ascended and descended the staircase until at least five ascents and five descents were recorded, with adequate rest between trials. All participants were supported in a harness for safety in case of a fall, and were asked to not use the handrails unless they felt unable to complete the task safely without, in which case light handrail use was permitted. Data were not analyzed from trials where handrails were used intermittently (and another trial was used for analysis instead).

Resistance exercise training intervention

Diabetes patients were randomly allocated into either the intervention group or a non-exercising control group using a random number generator. To optimize the number of patients undertaking the intervention, we randomized patients to the intervention and control groups at a ratio of 2:1. Sixteen participants were allocated into the intervention group (splitting into D-INT, *n*=10; and DPN-INT, *n*=6 groups for the purpose of data analysis), and six (D: *n*=3; DPN: *n*=3) were allocated into the diabetic control group (combined D-CON group for the purpose of data analysis). To determine the adequacy of the group samples in the present study, the statistical power to detect pre- to post-intervention differences (using knee SoSG during stair descent) was tested for the DPN-INT group (*n*=6). The statistical power was found to be 0.93, indicating the study was well powered to identify true differences with these specific variables.

Patients in the intervention group attended a weekly, one-hour exercise session for 16 weeks. After the 16-week intervention period, patients repeated the stair negotiation task, and pre- and post-intervention measurements were analysed. The post-intervention test took place within one month of the last intervention session. The intervention comprised of two components, high-load dynamic resistance exercises, and isometric exercises. During the intervention sessions, participants were closely supervised by the lead author.

Heavy resistance exercise training

Participants performed a series of exercises previously employed by studies that have induced musculoskeletal adaptations in older people, leading to increased muscle strength and the development of higher joint torques [15-18] The participants were asked to perform three series of up to twelve repetitions on three different machines; 1) a leg extension, 2) a leg press, and 3) an ankle press. One repetition consisted of lifting and lowering the load under control in approximately 2 and 3 seconds, respectively. If the participant could perform three series of twelve repetitions or more in any one session, the load was increased for the subsequent week to maintain the training stimulus. If 36 (3 series of 12) repetitions could not be achieved, the load remained the same and the aim for the following week was to achieve more repetitions than the previous week, ultimately working towards three series of twelve repetitions at a suitable load required to yield improvements in strength.

Isometric exercises

With the primary aim of increasing the speed of muscle response of the ankle and knee flexors, 'quasi-isometric' exercises previously applied to improve SoSG in older adults [19] were performed. Participants performed three series of twelve repetitions on two different machines. On the leg extension machine, participants attempted to rapidly extend the knee from 90˚, activating the knee extensors as quickly as possible, but without knee joint movement due to the immovable load. On the leg press, participants attempted to rapidly plantar flex the ankle from the neutral ankle position, activating the ankle extensors as quickly as possible, but without movement of the ankle joint due to the immovable load. The ankle and knee extensors were activated for half a second (in the respective exercises) followed by a one second rest in between repetitions. One-minute rest was given between series of twelve repetitions.

Data analysis

Speed of strength generation during stair negotiation

The speed of strength generation at the ankle and knee was measured as the rate of joint torque development (RJTD). Joint torques were normalized to body mass to enable valid between-group and pre-post intervention comparisons. The RJTD of the landing leg was calculated from the gradient of the joint torque-time curve for the ankle and knee proceeding initial step contact [6]. In each stair trial, the joint torque values from each of the four step-embedded platforms were used and the mean taken, although in some trials not all four values were available (12% of values unavailable), so as many were used as possible. Due to problems with marker visibility and force platforms, two patients within the D-CON group, and one within the D-INT group were unable to provide accurate strength generation data. (Table 2)

Muscle activation during stair negotiation

The muscle activation (electromyographic) signals were examined from the leg of the foot contacting the upper middle step of the eight-step staircase. Two stages of analysis were performed, the first stage identified when the activation of the muscle began and ended (defined as onset and cessation, respectively) [16, 6], and the second stage identified the peak of the muscle activity profile [6]. The time to peak (TTP) was measured as the time difference between the onset of muscle activity and the peak of the muscle activation. Due to problems with obtaining muscle activation data (caused primarily by subcutaneous fat attenuating the muscle activation signal), data could not be obtained for all participants, and only muscle activations of the patients who provided reliable data both pre- and post-intervention were included in the results (Table 2).

Statistics

Pre- to post-intervention differences for all variables were tested using a repeated measures Student's *t*-test. Pre- and post-intervention values in the diabetes groups (D-INT and DPN-INT) were tested for differences with respect to the H-CON group using a one-way analysis of variance (ANOVA) and Bonferroni post-hoc test. Values are presented as means ± SD; significance was set at $p<0.05$.

Results

Speed of strength generation (Fig. 1a & 1b)

Stair ascent (Fig. 1a)

Ankle and knee speed of strength generation were significantly higher post-intervention compared to pre-intervention in the DPN-INT and D-INT groups ($p<0.01$). The D-CON group displayed no differences pre to post-intervention.

Pre-intervention, speed of strength generation at the knee in both the D-INT and DPN-INT groups was significantly slower than the H-CON group. However, post-intervention, no differences between the diabetes groups and H-CON group were observed. Pre-intervention, the DPN-INT group displayed a similar speed of ankle strength generation to the H-CON group; however, post-intervention, the DPN-INT group displayed a significantly faster strength generation than the H-CON group. Pre-intervention the D-INT group displayed a significantly slower ankle strength generation than the H-CON group. However, post-intervention, no differences between the D-INT and H-CON group were observed.

Stair descent (Fig. 1b)

Speed of ankle and knee strength generation were significantly higher post-intervention compared to pre-intervention, in the DPN-INT and D-INT groups ($p<0.01$) and the D-CON group ($p<0.05$)

Pre-intervention, speed of ankle and knee strength generation in the D-INT group were significantly slower than the H-CON group, but no differences between the groups were observed post-intervention. Pre-intervention, the DPN-INT group displayed a similar speed of strength generation at the ankle and knee to the H-CON group, but displayed a significantly higher speed of strength generation than the H-CON group post-intervention.

Muscle activation timings (Fig. 2a & 2b)

Stair ascent (Fig. 2a)

The D-INT group activated the knee extensors significantly later, and displayed a slower TTP post-intervention compared to pre-intervention. The DPN-INT and D-CON group activated the ankle extensors significantly later post-intervention compared to pre-intervention, but no other changes were observed.

Stair Descent (Fig. 2b)

No changes in the onset of knee or ankle muscle activations were observed in any group. The D-INT and D-CON groups displayed a longer TTP in the knee extensors post-intervention compared to pre-intervention. Pre-intervention, the D-INT TTP of the knee extensors was significantly slower compared to the H-CON group, but no differences existed post-intervention.

Discussion

This study shows for the first time that a resistance exercise training intervention can improve the speed of ankle and knee strength generation during stair ascent and descent in patients with diabetes, and particularly in patients with diabetic peripheral neuropathy. Previous studies have shown that people with a high risk of falling display decreased speed of strength generation [6-9]. Therefore, the increased speed of strength generation of the ankle and knee are expected to improve stability during the initial weight acceptance phase of the stair walking tasks, and ultimately contribute towards reducing the risk of falling on stairs.

During the weight acceptance phase of stair ascent and stair descent, strength is rapidly generated to perform an absorptive action, controlling the flexion of the ankle and knee as gravity acts to 'pull' the body down onto the step. By generating joint strength quicker, the body is stabilised earlier into the stance phase, allowing balance to be more optimally controlled. In a previous study, we identified that the knee and ankle both performed 'absorptive' roles during ascent and descent, with one joint generating strength faster, to primarily dissipate the ground impact and momentum, whilst the other joint contributed to absorption to a lesser extent [6]. Patients with neuropathy whom undertook the intervention, increased the speed of strength generation of the primary 'absorptive' joint by 27% and 35% (the knee during ascent, and the ankle during descent, respectively), whilst the speed of strength generation of the secondary 'absorptive' joint was increase by 60% and 78% (the ankle during ascent, and the knee during descent). This may indicate an altered distribution of ground impact absorption, with the secondary absorptive joint playing a relatively greater role post-intervention in supporting and stabilising the body. Furthermore, despite neuropathy being predominantly a distal disease, similar improvements were observed at the ankle during stair ascent and descent (35% and 60%, respectively) as were observed at the knee during stair descent and ascent (27% and 78%, respectively). This highlights that even distal muscles can still be markedly improved by resistance exercise training in people with diabetic peripheral neuropathy.

Despite the speed at which strength was generated being increased significantly at both joints during stair ascent and descent, the time to peak, previously suggested to be closely related to the speed of strength generation, varied between groups (longer time to peak of the knee extensors in the diabetes intervention groups (with and without neuropathy) groups during stair descent, and a shorter time to peak of the knee extensors during ascent) and showed no changes in line with the increases in the speed of strength generation after the intervention, that were observed previously to differentiate between participant groups (Fig 2a &2b)[6]. An increase in muscle strength as a result of the exercise intervention may therefore be the main causative factor for the faster strength generation observed at the ankle and knee, rather than increased speed of muscular activations. Whilst the time to peak was unaltered by the intervention, if maximum joint moments were increased, and the time to reach this maximum was unaltered (as indicated by the unaltered time to peak), the speed of strength generation would be faster, as was indeed observed. This would indicate that the improvement in strength as a result of the resistance exercise intervention performed must be the most influential factor upon improving the speed of strength generation, rather than improving the speed of muscle response.

Reduced speed of strength generation in other high-risk populations such as the elderly has been attributed to structural alterations to the muscle and neural changes [13, 21]. Resistance exercise training has been identified to be the most effective method of increasing speed of strength generation via improving neural drive and increasing muscle mass, consequently increasing speed of strength generation during dynamic movements and during isolated strength tests [12-14, 22]. In this sample of people with diabetes and diabetic peripheral neuropathy, the muscular adaptations are expected to be more influential than neural adaptations, with the improvements in speed of strength generation observed, expected to be predominantly caused by improvements in muscle strength rather than changes in the speed of muscle activation [21]. This is a particularly pertinent finding as it may partly explain how people with neuropathy can improve speed of strength generation despite presumably irreversible neural damage.

The exercise session was performed by the participants just once a week and took less than one hour. The participants self-reported increased activity levels, and an ability to perform everyday tasks that were previously beyond their capabilities as a result of the increased lower limb strength following the resistance exercise intervention. These self-reported observations should be taken with caution against the main scientific findings, but are in line with previous findings of increased six minute walking distance and daily step counts as a result of exercise [23]. As well as increasing SoSG through strength training, patients with DPN and diabetes should be encouraged to use handrails where possible. Although not shown by this study, it is expected that handrails would improve safety through partial unloading of the lower limbs.

The present findings suggest that one hour of resistance exercise training per week may be an effective method of improving factors contributing to the risk of falling and may therefore translate to reducing fall risk in people with diabetes, with and without neuropathy. Such exercises should therefore be incorporated into multi-faceted exercise interventions to improve safety in people with diabetes, both with and without neuropathy.

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Conflicts of Interest

The authors certify that they have NO affiliations with or involvement in any organisation or entity with any financial interest in the subject matter or materials discussed in this manuscript.

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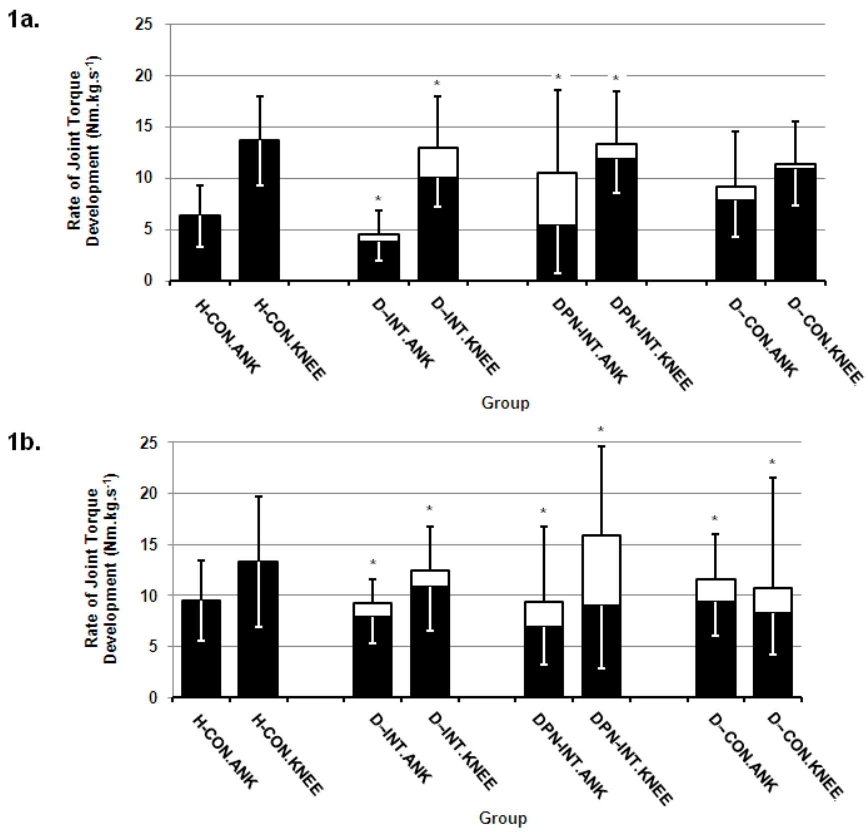

*Figure 1. Ankle (ANK) and knee (KNEE) speed of strength generation (rate of joint torque development; RJTD) during stair ascent (1a) and stair descent (1b). Values are means and SD for healthy controls (H-CON), and pre- and post-intervention results for the diabetes intervention group (D-INT), diabetic peripheral neuropathy intervention group (DPN-INT), and the diabetic control group (D-CON). Pre-intervention values are displayed as the black bars, and improvements in SoSG post-intervention are displayed as the white bar on top (all post-intervention changes were increased compared to pre-intervention). * denotes significantly different SoSG pre- to post-intervention ($p<0.05$).*

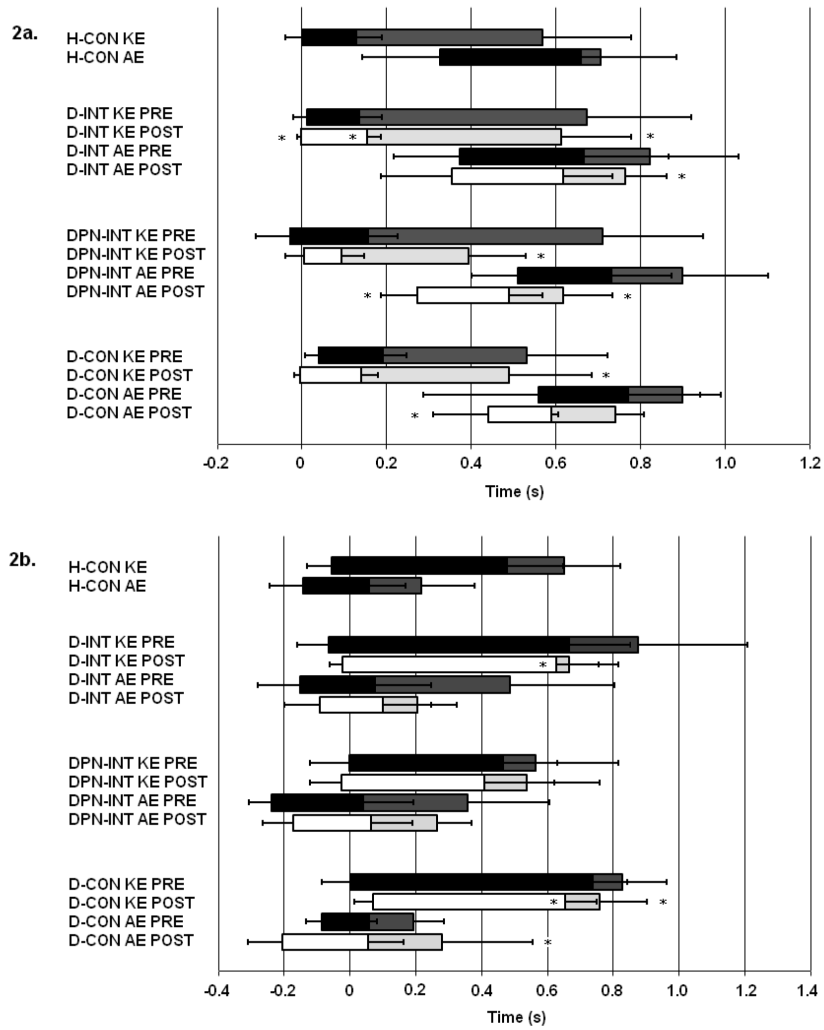

*Figure 2. Periods of activation for the knee extensor (KE) and ankle extensor (AE) muscles with respect to foot-step contact (occurring at time zero) during stair ascent (2a) and stair descent (2b). Values are means and SD for healthy controls (H-CON), and pre- and post-intervention results for the patients with diabetes but without neuropathy who underwent the intervention (D-INT), the patients with diabetic peripheral neuropathy who underwent the intervention (DPN-INT), and the diabetic control group (D-CON). * denotes significantly different (p<0.05) timing between pre- and post-intervention results. Significance is shown for onset (asterisk before bar), time to peak (asterisk after the line within the bar), and duration timings (asterisk after bar).*