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ORIGINAL RESEARCH

# Effects of a Novel Therapeutic Intervention in Patients With Diabetic Peripheral Neuropathy

Adel Alshahrani, DSc,[a] Mark Bussell, DPT,[b] Eric Johnson, DSc,[a] Bryan Tsao, MD,[c] Khalid Bahjri, MD[d]

*From the [a]School of Allied Health Professions, Department of Physical Therapy, Loma Linda University, Loma Linda, CA; [b]East Campus Rehabilitation Services, Department of Physical Therapy, Loma Linda University Medical Center, Loma Linda, CA; [c]Clinical Neurophysiology, Neurology Department, Loma Linda University School of Medicine, Loma Linda, CA; [d]School of Public Health, Department of Public Health, Loma Linda University, Loma Linda, CA.*

**Abstract**

**Objective:** To determine the effect of a novel therapeutic intervention called intraneural facilitation on balance measures and a neuropathy scale in patients with diabetic peripheral neuropathy.

**Design:** Prospective pre- and posttest, single group clinical trial.

**Setting:** Outpatient physical therapy clinic.

**Participants:** Patients with diabetic peripheral neuropathy (N=13).

**Intervention:** Subjects received 10 sessions of intraneural facilitation.

**Main Outcome Measures:** The modified Total Neuropathy Scale, the NeuroCom SMART Balance Master system computerized dynamic posturography (CDP) that includes the Sensory Organization Test (SOT) and the limits of stability (LOS), and the Activities-specific Balance and Confidence (ABC) scale.

**Results:** Subjects in this study showed significant improvement in the modified Total Neuropathy Scale, SOT, and 1 component in the LOS test (movement velocity). There were no significant differences in the ABC scale or in 4 components of the LOS test, which were reaction time, end point excursion, maximum excursion, and directional control.

**Conclusions:** Intraneural facilitation improved objective balance measures and neuropathy symptoms in patients with diabetic peripheral neuropathy. Further study is needed to determine long-term benefits of this intervention.

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Diabetes mellitus (DM) is a common disorder affecting individuals in the United States and in the world.[1] The prevalence of DM has increased noticeably over the last 3 decades with an estimated 380 million people currently diagnosed with the disease.[1] DM is associated with numerous systemic complications that effect the retina, heart, brain, kidneys, and nerves.[2,3]

The most common symptomatic complication of DM is diabetic peripheral neuropathy (DPN), estimated to occur in 50% of patients with DM.[4] Despite therapeutic advances of diabetes care over the last decade, there are few known interventions that appropriately address the progression and treatment of DPN.[5] DPN can occur in many forms, but it most commonly presents as a painless sensorimotor distal symmetric polyneuropathy (DSPN).[2]

Diabetic DSPN causes deterioration of the peripheral nervous system in a length-dependent fashion and can negatively affect the sensory system.[6,7] Impaired proprioceptive input renders these patients more susceptible to loss of balance during static and dynamic conditions.[7-12] This can impair physical function by reducing standing and walking activities because many patient experience fear of falling.[13,14]

The pathogenesis of DPN is multifactorial and mediated by alterations in the polyol pathway, aldose reductase inhibitors, advanced glycation products, disordered biochemistry consequences, essential fatty acids, neurotrophic factors, and oxidative stress. The common pathologic end point is endoneurial microangiopathy and subsequent nerve ischemia and hypoxia.[15,16] As such, patients with DPN are more likely to develop an array of peripheral nerve disorders and balance problems and are at a higher risk of falling.[9-12,15,17-22]

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The current study used an innovative approach termed intraneural facilitation in the treatment of diabetic DSPN. This approach aims to bias blood flow into the neural fascicle, improve endoneurial capillary circulation, and reverse intrafascicular ischemia. This passive technique includes stretching muscles, mobilizing joints, tractioning skin, distending visceral structures, and distorting blood vessels to reroute blood to the ischemic nerves.[23] We sought to determine the effectiveness of intraneural facilitation in DSPN using validated neuropathy scales, objective static measures, dynamic balance measures, subjective balance measures, and quantitative posturography balance measures.[24-27]

# Methods

This institutional review board—approved study was conducted at Loma Linda University, which is a tertiary teaching hospital with an outpatient physical therapy clinic providing care to a diverse group of patients. Study subjects were screened from our clinic between October 2014 and February 2015. Informed consent was obtained, and the assessment and intervention procedures were conducted in our physical therapy area.

Inclusion criteria for this study included the following: men and women with DPN who were from 18 to 85 years of age, DSPN form of DPN confirmed by a medical doctor, and ability to hold static balance for a minimum of 5 minutes.

Potential subjects were excluded if they had comorbidities (eg, open wounds, cardiac disease, other forms of progressive neurologic disease) or peripheral polyneuropathy affecting balance.

## Modified Total Neuropathy Scale

The modified Total Neuropathy Scale is scored from 0 to 24 with each neuropathy rated from 0 to 4 (0 being healthy and 4 being severe neuropathy). The modified Total Neuropathy Scale severity levels are divided into 3 levels: 0 to 8 (mild), 9 to 16 (moderate), and 17 to 24 (severe). The clinical testing for the modified Total Neuropathy Scale includes muscle strength, vibration sense, pin sensation level, and muscle stretch reflexes.[28]

## Static and dynamic balance scales

The NeuroCom SMART Balance Master system[a] computerized dynamic posturography (CDP) was used. This apparatus consists of 2 forceplates that can be pitched up and down and in an anterior-posterior plane. During this test, our subjects wore safety harnesses and were supported by 2 researchers to minimize the risk of falling. The subjects stood upright on the center of the forceplates in a standardized position. In this machine, 2 tests were used. The first was the Sensory Organization Test (SOT), which assesses 3 sensory systems that affect postural control (visual, somatosensory, and vestibular). Six different conditions are tested consecutively with three 20-second trials. In step 1 the patient is required to stand still with eyes open (all sensory information available); in step 2 the patient is required to stand still with their eyes closed; in step 3 the surround moves as the patient moves; in step 4 the forceplate moves as the patient moves; in step 5 the patient closes their eyes and the forceplate moves as the patient moves; and in step 6 the surround and forceplate move as the patient moves. We assessed the composite equilibrium and static balance scores.[29-31] The second was the limits of stability (LOS) test, which quantifies control of the center of gravity. The patient is required to voluntarily sway in 8 directions without losing their balance. The LOS test includes reaction time, movement velocity, end point excursion, maximum excursion, and directional control. We took the composite scores of reaction time, movement velocity, end point excursion, maximum excursion, and directional control from the 8 directions.

***List of abbreviations:***

| | |
|---|---|
| **ABC** | **Activities-specific Balance Confidence** |
| **CDP** | **computerized dynamic posturography** |
| **DM** | **diabetes mellitus** |
| **DPN** | **diabetic peripheral neuropathy** |
| **DSPN** | **distal symmetric polyneuropathy** |
| **LOS** | **limits of stability** |
| **SOT** | **Sensory Organization Test** |

## Activities-specific Balance Confidence scale

The Activities-specific Balance Confidence (ABC) scale[32] is a subjective measure of confidence in performing several activities without losing balance or suffering a sense of wobbliness. It is a 16-item self-report measure in which subjects rate their balance confidence for performing certain activities. Each item ranges from 0 to 100. A score of zero implies falling, and a score of 100 implies patient's confidence of stability. The total score of this scale is derived by adding all items together and then dividing by 16.

## Implementation protocol

The patients were first assessed by a physician and determined to have DPN. The physician then referred the patients to our clinic for physical therapy using intraneural facilitation. At the start of therapy, the patient was given the option to participate in the study or to proceed with treatment without study participation. If the patient chose to participate in the study, baseline data were recorded from an initial CDP test, a modified Total Neuropathy Scale assessment, and ABC balance scores. After the initial assessment, the patient received intraneural facilitation for 10 treatments. On the 12th session, the baseline tests were repeated, and follow-up data were recorded for analysis.

## Data collection

Pretreatment assessment included baseline demographic data, the modified Total Neuropathy Scale, SOT and LOS test scores, and the ABC scale.

Posttreatment data were collected for these same measures after 10 sessions of intraneural facilitation treatment.

## Data management and analysis

### Data management

Two researchers conducted data management using coding manuals for all study measures. All study data were initially reviewed to identify missing values. Methods for missing value adjustment included imputation, list-wise deletion, or case-wise deletion. All modifications were recorded in the data coding manual for future missing data analysis.

**Data analysis**

Data were analyzed using SPSS Statistics 22.[b] Means and SDs were calculated for the outcome measures separately pre- and postintervention. Paired *t* test was used to detect significant change in SOT, reaction time, movement velocity, end point excursion, maximum excursion, and directional control between pre- and postintervention. Wilcoxon signed-rank test was used to compare differences in directional control and modified Total Neuropathy Scale between pre- and postintervention. A $P$ value of $<.05$ was considered significant.

## Results

Of 25 subjects screened for our study, 17 met inclusion criteria and were enrolled. Of these, 13 completed the study (fig 1). Four subjects did not complete the study: 1 developed a foot infection, 1 had insurance problems that prevented ongoing therapy, and 2 elected to exit the study because of time restraints. Subject demographics are listed in table 1.

The modified Total Neuropathy Scale showed significant reduction from pre- and posttreatment measurements ($P=.001$) (table 2). For changes in the SOT, we found a significant increase from pre- and posttreatment measurements ($P=.012$) (table 2). For the LOS test components, the movement velocity showed a significant increase from pre -to posttreatment measurements ($P=.023$) (table 2). The remaining measures of reaction time, directional control, end point excursion, maximum excursion, and the ABC scale showed a trend toward improvement but did not show statistically significant differences before or after intraneural facilitation (see table 2).

## Discussion

The results of our study are consistent with previous reports indicating that patients with DSPN are more susceptible to falls during static and dynamic conditions.[14,19,33] In addition, our results show that intraneural facilitation can improve neuropathy symptoms as measured by the modified Total Neuropathy Scale ($P=.001$), static balance or SOT ($P=.012$), and dynamic balance or movement velocity ($P=.023$) scores. All other LOS test components (reaction time, directional control, end point excursion, and maximum excursion) showed a trend toward posttreatment improvement but were not statistically significant. Medical records indicating the degree of glycemic control were not available to researchers for all subjects.

We chose to use the modified Total Neuropathy Scale in our study because it was easy to use and is a valid tool.[34] CDP has been used extensively in the literature for different conditions as a validated tool to measure static and dynamic balance.[35-37] Whitney et al[38] looked at the relation between falls history and CDP scores. They found that scores <38 increased the likelihood ratio for recognizing repeated fallers in the last 6 months. On subjects with diabetes, Simmons et al[26] measured postural instability in 2 groups: those with or without cutaneous sensory discrepancies and a control nondiabetic group. They found that CDP scores are less for subjects with cutaneous sensory discrepancies; therefore, they are more likely to have postural instability. In another study, Di Nardo et al[39] found that CDP distinguished between subjects with DM with and without peripheral neuropathy.

Although many interventions have tried to mitigate the effect of DPN through exercises, it remains a progressive disease with few effective interventions. There are few systematic physical therapy approaches that are typically used in treating patients with DPN. For instance, Kochman[40] studied the use of monochromatic infrared energy plus strengthening, stretching, and balance exercises on patients with DPN to improve balance. The author reported improved balance and a reduction in the number of falls. Mueller et al[41] investigated weight-bearing exercises versus non—weight-bearing exercises on patients with DPN. The weight-bearing group revealed significant improvement over the non—weight-bearing group.

The effects of therapeutic rehabilitation on balance in patients with DPN have included modalities,[42] combining modalities with exercises,[40] exercises,[41,43] and assistive devices.[44] Ashton-Miller et al[44] divided subjects into 2 groups. One group used a single-point cane, and the other group did not use a cane. In the single point cane group, they found a reduction in failure rate during weight transfer to unipedal stance. Richardson et al[43] divided

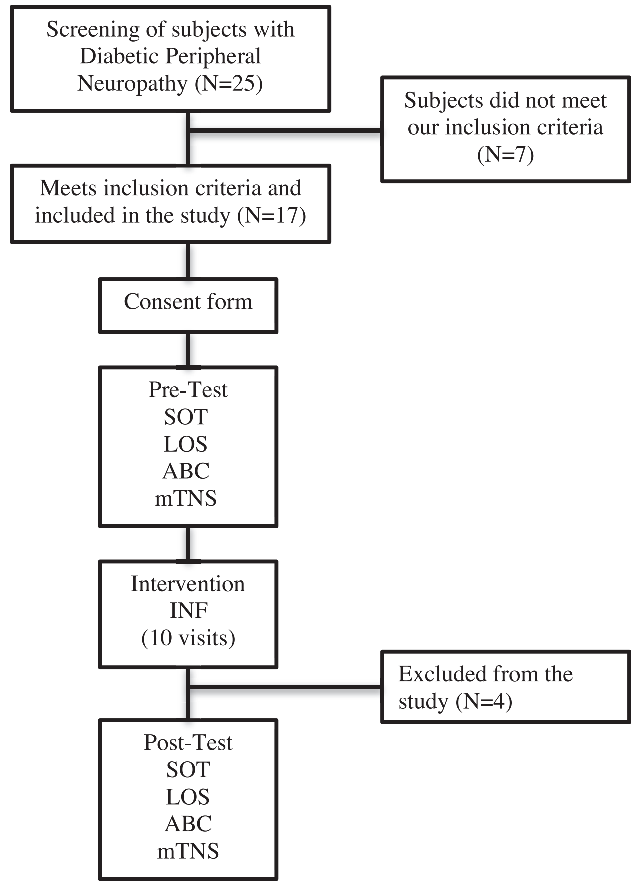


**Fig 1** Subject screening and completion. Abbreviations: ABC, activities of balance confidence; INF, intraneural facilitation; LOS, limit of stability; mTNS, modified total neuropathy scale; SOT, sensory organization test.

**Table 1** Patient demographics (N=13)

| Demographic | Minimum | Maximum | Mean ± SD | Male | Female |
|---|---|---|---|---|---|
| Age (y) | 49 | 73 | 65.15±7.548 | | |
| Sex (n) | | | | 7 | 6 |

**Table 2** Changes in mTNS, SOT, LOS test, and ABC scale (N=13)

| | Preintervention, Mean ± SD | Postintervention, Mean ± SD | Mean Difference | 95% Confidence Interval | *P* |
|---|---|---|---|---|---|
| mTNS | 10.62±4.37 | 7.77±4.19 | −2.85 | −11.28 to 39.60 | .001* |
| SOT | 53.77±21.81 | 66±14.32 | 12.23 | 0.21 to 2.38 | .012† |
| LOS component | | | | | |
| RT | 0.91±0.62 | 0.81±0.36 | −0.10 | −0.46 to 0.25 | .544† |
| DCL | 55.44±32.57 | 63.15±20.45 | 7.71 | −15.38 to 30.80 | .834* |
| EPE | 39.68±23.61 | 48.31±17.15 | 8.62 | −10.03 to 27.28 | .334† |
| MVL | 1.99±1.25 | 3.28±1.26 | 1.29 | 0.21 to 2.38 | .023† |
| MXE | 54.31±31.87 | 68.46±24.14 | 14.15 | −11.28 to 39.59 | .249† |
| ABC | 71.42±25.78 | 78.02±17.01 | 6.60 | NA | .119† |

Abbreviations: DCL, directional control; EPE, end point excursion; mTNS, modified Total Neuropathy Scale; MVL, movement velocity; MXE, maximum excursion; NA, not applicable; RT, reaction time.
* From Wilcoxon signed-rank test.
† From paired *t* test.

subjects into 2 groups. One group received open and closed chain ankle strengthening, wall slides, and single-leg stance, and the other group received neck flexion and scapular stabilization exercises. In the ankle exercises group, they found significant improvements in tandem stance, single-leg stance, and functional reach. Mueller[41] studied weight-bearing exercises versus non−weight-bearing exercises in patients with DPN. The weight-bearing group showed significance improvement over the non−weight-bearing group in the 6-minute walk distance and daily step counts. Exercise may play an important role in patients with DPN. On the other hand, exercise usually needs weight bearing and utilization of painful limbs. Also, recent studies highly recommended minimal physical activity for patients with DPN to prevent adverse events.[45,46] To decrease pain, paresthesia, and lesions associated with DPN through physical therapy, we should limit patients participating with exercise activities to enhance functional outcomes.[45,46] The present study demonstrates decreased neuropathic symptoms and improved balance using intraneural facilitation. By reducing patient neuropathic symptoms, intraneural facilitation may enhance patient participation in therapeutic exercise programs and form a bridge between the inactive painful patient with diabetes and the active nonpainful patient with diabetes who can exercise.

The intraneural facilitation intervention is a novel manual physical therapy approach with anecdotal evidence in reducing peripheral neuropathy symptoms. The main concept of intraneural facilitation is the use of 2 manual holds. The first hold is called facilitation hold (fig 2) and includes putting the contralateral joint in a maximal loose-pack position that is comfortable to the patient. For example, the ankle joint on the contralateral side is placed in full planter flexion and inversion. This position is sustained during the whole session with a stretch strap. It is important to note that there is no muscle activity in the joint where the facilitation is occurring, only a slight stretch. We hypothesize that with the joint in this position, the nerve will move further than the artery because the artery has more elastin. With increased neural excursion in relation to the artery, the nutrient vessels that are clustered at the joint will be stretched. This stretch may enlarge the opening at the junction of the artery and bridging nutrient vessel, therefore consistently creating a vascular bias into the neural epineurial capillaries. Theoretically, this creates increased epifascial vascular pressure.[47] Although anecdotally the effects of intraneural facilitation were observed in the clinic, the authors are unaware of other research evaluating the effects of nonextreme joint positions on nutrient vessel blood flow. Lundborg and Rydevik[48] described a relation between pathologic neural stretching with fascicle deformation and a reduction of blood flow in the nutrient vessels. The authors found it interesting that a relation between neural stretching, albeit extreme, and nutrient vessel blood flow did not exist. However, Lundborg[48] did not study how the nonpathologic gentle holds would affect neurovascular blood flow in nutrient vessels.

With increased endoneurial edema and a strong perineurium, the pressurized blood flow may not push through the

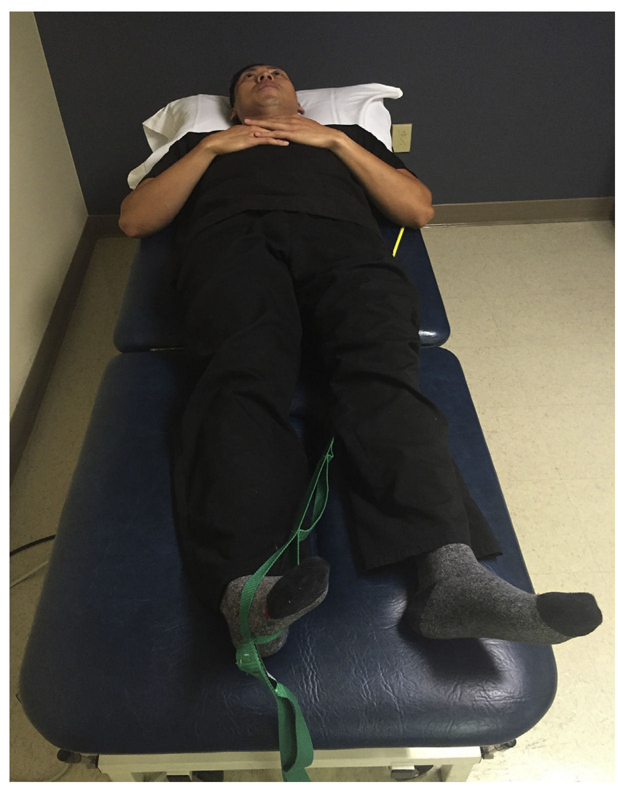

**Fig 2** Facilitation hold includes positioning the contralateral ankle joint in a maximal loose-pack position of plantar flexion and inversion. This position is maintained throughout the entire session.

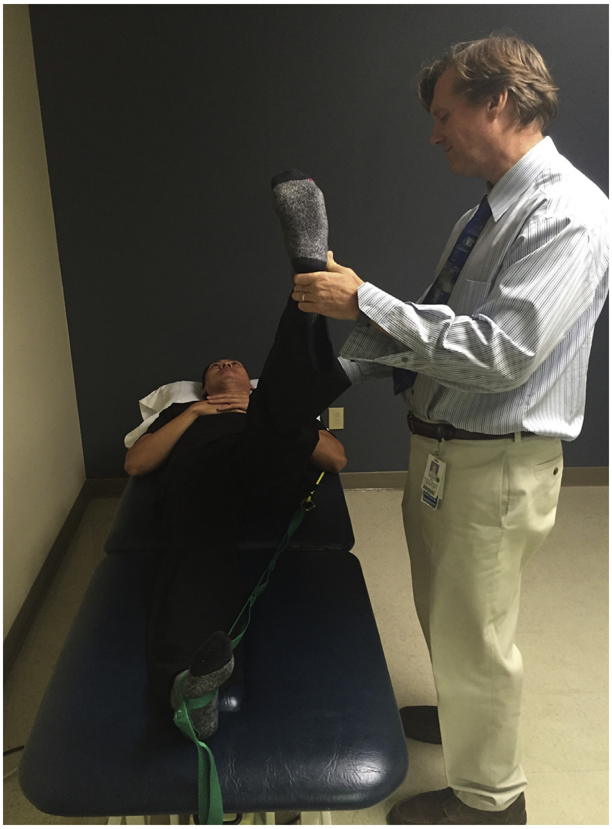

**Fig 3** Secondary hold. In case of impaired sciatic nerve, a hamstring stretch biases blood flow into the sciatic nerve microvasculature.

transperineurial vessels that cross the perineurium into the endoneurial capillaries. A second hold or mild stretch is necessary to bias the increased epineurial blood flow past the perineurium into the endoneurial capillaries. This hold potentially provides an unweighting pressure. The second hold or stretch will also enable the therapist to bias circulation in the neural structures that appear to be most affected. For example a hamstring stretch would bias blood flow into the sciatic nerve microvasculature (fig 3). Previous studies demonstrated short-term exercise effects on endoneurial capillaries, including stimulating endothelial vasodilation, enhancing endoneurial blood flow, improving abnormal nerve perfusion, increasing the release of nitric oxide, and enhancing the concentration of Na/K ATPase.[49-53] We hypothesize that improvements in the modified Total Neuropathy Scale of our subjects were caused by these immediate vascular changes that occurred in the treated extremities; however, more research is need to substantiate this.[23] Medical records indicating the degree of glycemic control were not available to researchers for all subjects.

### Study limitations

Our study limitations include the potential for bias with the modified Total Neuropathy Scale assessment because the clinician who provided the treatment also assessed the modified Total Neuropathy Scale pre- and postintervention. Other limitations were not having a control or sham group and the small sample size that does not allow for generalization of our study findings. Moreover, this study only measured short-term benefits of the intervention.

## Conclusions

This pilot study showed that intraneural facilitation improves static and dynamic balance measures and neuropathy symptoms using validated measures in patients with diabetic DSPN. Whether the improvements in balance measures noted in the intervention subjects translate into decreased fall risk in daily life is uncertain. However, given the minimal risk associated with intraneural facilitation, we believe our results warrant further study of this technique in patients with diabetic and idiopathic DSPN to establish long-term benefits, measure the effect of intraneural facilitation on pain measures, and if possible use a control or sham group.

## Suppliers

a. NeuroCom SMART Balance Master; Natus.
b. SPSS Statistics 22; IBM.


## Keywords

Diabetes mellitus; Diabetic neuropathies; Musculoskeletal manipulations; Rehabilitation


## Corresponding author

Eric Johnson, DSc, 24951 North Circle Dr, Nichol Hall A-712, Loma Linda, CA 92350. *E-mail address:* ejohnson@llu.edu.

## References


1. Whiting DR, Guariguata L, Weil C, Shaw J. IDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030. Diabetes Res Clin Pract 2011;94:311-21.
2. Boulton AJ, Vinik AI, Arezzo JC, et al. Diabetic neuropathies: a statement by the American Diabetes Association. Diabetes Care 2005;28:956-62.
3. Boulton AJ, Malik RA, Arezzo JC, Sosenko JM. Diabetic somatic neuropathies. Diabetes Care 2004;27:1458-86.
4. Vinik AI, Holland MT, Le Beau JM, Liuzzi FJ, Stansberry KB, Colen LB. Diabetic neuropathies. Diabetes Care 1992;15:1926-75.
5. Tesfaye S, Boulton AJ, Dyck PJ, et al. Diabetic neuropathies: update on definitions, diagnostic criteria, estimation of severity, and treatments. Diabetes Care 2010;33:2285-93.
6. Cimbiz A, Cakir O. Evaluation of balance and physical fitness in diabetic neuropathic patients. J Diabetes Complications 2005;19:160-4.
7. Gutierrez EM, Helber MD, Dealva D, Ashton-Miller JA, Richardson JK. Mild diabetic neuropathy affects ankle motor function. Clin Biomech (Bristol, Avon) 2001;16:522-8.
8. Ghanavati T, Shaterzadeh Yazdi MJ, Goharpey S, Arastoo AA. Functional balance in elderly with diabetic neuropathy. Diabetes Res Clin Pract 2012;96:24-8.
9. Oppenheim U, Kohen-Raz R, Alex D, Kohen-Raz A, Azarya M. Postural characteristics of diabetic neuropathy. Diabetes Care 1999;22:328-32.
10. Nardone A, Grasso M, Schieppati M. Balance control in peripheral neuropathy: are patients equally unstable under static and dynamic conditions? Gait Posture 2006;23:364-73.

11. Yamamoto R, Kinoshita T, Momoki T, et al. Postural sway and diabetic peripheral neuropathy. Diabetes Res Clin Pract 2001;52:213-21.
12. Lafond D, Corriveau H, Prince F. Postural control mechanisms during quiet standing in patients with diabetic sensory neuropathy. Diabetes Care 2004;27:173-8.
13. Ites KI, Anderson EJ, Cahill ML, Kearney JA, Post EC, Gilchrist LS. Balance interventions for diabetic peripheral neuropathy: a systematic review. J Geriatr Phys Ther 2011;34:109-16.
14. Boucher P, Teasdale N, Courtemanche R, Bard C, Fleury M. Postural stability in diabetic polyneuropathy. Diabetes Care 1995; 18:638-45.
15. Llewelyn JG, Tomlinson DR, Thomas PK. Diabetic neuropathies. In: Dyck PJ, Thomas PK, editors. Peripheral Neuropathy. 4th ed. Philadelphia: Elsevier; 2005. p 1951-92.
16. Cade WT. Diabetes-related microvascular and macrovascular diseases in the physical therapy setting. Phys Ther 2008;88:1322-35.
17. Maurer MS, Burcham J, Cheng H. Diabetes mellitus is associated with an increased risk of falls in elderly residents of a long-term care facility. J Gerontol Ser A Biol Sci Med Sci 2005;60:1157-62.
18. Ahmmed AU, Mackenzie IJ. Posture changes in diabetes mellitus. J Laryngol Otol 2003;117:358-64.
19. Uccioli L, Giacomini PG, Monticone G, et al. Body sway in diabetic neuropathy. Diabetes Care 1995;18:339-44.
20. Katoulis EC, Ebdon-Parry M, Hollis S, et al. Postural instability in diabetic neuropathic patients at risk of foot ulceration. Diabet Med 1997;14:296-300.
21. Emam AA, Gad AM, Ahmed MM, Assal HS, Mousa SG. Quantitative assessment of posture stability using computerised dynamic posturography in type 2 diabetic patients with neuropathy and its relation to glycaemic control. Singapore Med J 2009;50:614-8.
22. Speers RA, Kuo AD, Horak FB. Contributions of altered sensation and feedback responses to changes in coordination of postural control due to aging. Gait Posture 2002;16:20-30.
23. Bussell MR; inventor. Intraneural facilitation. Google patent US 20120150077A1; 2012.
24. Wallmann HW. Comparison of elderly nonfallers and fallers on performance measures of functional reach, sensory organization, and limits of stability. J Gerontol Ser A Biol Sci Med Sci 2001;56: M580-3.
25. Clark S, Rose DJ, Fujimoto K. Generalizability of the limits of stability test in the evaluation of dynamic balance among older adults. Arch Phys Med Rehabil 1997;78:1078-84.
26. Simmons RW, Richardson C, Pozos R. Postural stability of diabetic patients with and without cutaneous sensory deficit in the foot. Diabetes Res Clin Pract 1997;36:153-60.
27. Jáuregui-Renaud K, Kovacsovics B, Vrethem M, Odjvist LM, Ledin T. Dynamic and randomized perturbed posturography in the follow-up of patients with polyneuropathy. Arch Med Res 1998;29: 39-44.
28. Vasquez S, Guidon M, McHugh E, Lennon O, Grogan L, Breathnach OS. Chemotherapy induced peripheral neuropathy: the modified total neuropathy score in clinical practice. Ir J Med Sci 2014;183:53-8.
29. Peterka RJ, Black FO. Age-related changes in human posture control: sensory organization tests. J Vestib Res 1990-1991;1:73-85.
30. Alexander NB, Shepard N, Gu MJ, Schultz A. Postural control in young and elderly adults when stance is perturbed: kinematics. J Gerontol 1992;47:M79-87.
31. Zane RS, Rauhut MM, Jenkins HA. Vestibular function testing: an evaluation of current techniques. Otolaryngol Head Neck Surg 1991; 104:137-8.
32. Powell LE, Myers AM. The activities-specific balance confidence (ABC) scale. J Gerontol Ser A Biol Sci Med Sci 1995;50:M28-34.
33. Ledin T, Odkvist LM, Vrethem M, Möller C. Dynamic posturography in assessment of polyneuropathic disease. J Vestib Res 1990-1991;1:123-8.
34. Wampler MA, Miaskowski C, Byl N, Rugo H, Topp K. The modified total neuropathy score: a clinically feasible and valid measure of taxane-induced peripheral neuropathy in women with breast cancer. J Support Oncol 2006;4:W9-16.
35. Ford-Smith CD, Wyman JF, Elswick RK Jr, Fernandez T, Newton RA. Test-retest reliability of the sensory organization test in noninstitutionalized older adults. Arch Phys Med Rehabil 1995;76:77-81.
36. Cohen H, Heaton LG, Congdon SL, Jenkins HA. Changes in sensory organization test scores with age. Age Ageing 1996;25:39-44.
37. Juras G, Słomka K, Fredyk A, Sobota G, Bacik B. Evaluation of the limits of stability (LOS) balance test. J Hum Kinet 2008;19:39-52.
38. Whitney SL, Marchetti GF, Schade AI. The relationship between falls history and computerized dynamic posturography in persons with balance and vestibular disorders. Arch Phys Med Rehabil 2006;87:402-7.
39. Di Nardo W, Ghirlanda G, Cercone S, et al. The use of dynamic posturography to detect neurosensorial disorder in IDDM without clinical neuropathy. J Diabetes Complications 1999;13:79-85.
40. Kochman AB. Monochromatic infrared photo energy and physical therapy for peripheral neuropathy: influence on sensation, balance, and falls. J Geriatr Phys Ther 2004;27:18-21.
41. Mueller MJ, Tuttle LJ, Lemaster JW, et al. Weight-bearing versus nonweight-bearing exercise for persons with diabetes and peripheral neuropathy: a randomized controlled trial. Arch Phys Med Rehabil 2013;94:829-38.
42. Leonard DR, Farooqi MH, Myers S. Restoration of sensation, reduced pain, and improved balance in subjects with diabetic peripheral neuropathy. A double-blind, randomized, placebo-controlled study with monochromatic near-infrared treatment. Diabetes Care 2004;27:168-72.
43. Richardson JK, Sandman D, Vela S. A focused exercise regimen improves clinical measures of balance in patients with peripheral neuropathy. Arch Phys Med Rehabil 2001;82:205-9.
44. Ashton-Miller JA, Yeh MW, Richardson JK, Galloway T. A cane reduces loss of balance in patients with peripheral neuropathy: results from a challenging unipedal balance test. Arch Phys Med Rehabil 1996;77:446-52.
45. LeMaster JW, Mueller MJ, Reiber GE, Mehr DR, Madsen RW, Conn VS. Effect of weight-bearing activity on foot ulcer incidence in people with diabetic peripheral neuropathy: feet first randomized controlled trial. Phys Ther 2008;88:1385-98.
46. Otterman NM, van Schie CH, van der Schaaf M, van Bon AC, Busch-Westbroek TE, Nollet F. An exercise programme for patients with diabetic complications: a study on feasibility and preliminary effectiveness. Diabet Med 2011;28:212-7.
47. Topp KS, Boyd BS. Structure and biomechanics of peripheral nerves: nerve responses to physical stresses and implications for physical therapist practice. Phys Ther 2006;86:92-109.
48. Lundborg G, Rydevik B. Effects of stretching the tibial nerve of the rabbit. A preliminary study of the intraneural circulation and the barrier function of the perineurium. J Bone Joint Surg Br 1973;55: 390-401.
49. Gustafsson T, Puntschart A, Kaijser L, Jansson E, Sundberg CJ. Exercise-induced expression of angiogenesis-related transcription and growth factors in human skeletal muscle. Am J Physiol 1999; 276:H679-85.
50. Fuchsjäger-Mayrl G, Pleiner J, Wiesinger GF, et al. Exercise training improves vascular endothelial function in patients with type 1 diabetes. Diabetes Care 2002;25:1795-801.
51. Fukai T, Siegfried MR, Ushio-Fukai M, Cheng Y, Kojda G, Harrison DG. Regulation of the vascular extracellular superoxide dismutase by nitric oxide and exercise training. J Clin Invest 2000; 105:1631-9.
52. Maiorana A, O'Driscoll G, Taylor R, Green D. Exercise and the nitric oxide vasodilator system. Sports Med 2003;33:1013-35.
53. Balducci S, Iacobellis G, Parisi L, et al. Exercise training can modify the natural history of diabetic peripheral neuropathy. J Diabetes Complications 2006;20:216-23.