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Original Article

Sensorimotor and gait training improves proprioception, nerve function, and muscular activation in patients with diabetic peripheral neuropathy: a randomized control trial

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Abstract

Objectives: To examine the effect of sensorimotor and gait training on proprioception, nerve function, and muscle activation in diabetic peripheral neuropathy (DPN) patients. **Methods**: Thirty-eight (25 male and 13 female) participants with DPN were selected and randomly allocated to intervention and control group. Participants in the intervention group were provided sensorimotor and gait training for eight weeks (3 days/week) along with diabetes and foot care education; participants in the control group received diabetes and foot care education only. Outcome measures involved proprioception, nerve conduction studies of peroneal and tibial nerve, and activation of lower limb muscles and multifidus while standing with eyes open and eyes closed, and treadmill walking. **Results**: Mixed ANOVA revealed significant time effect and time×group interaction of proprioception in all four directions ($p<0.05$). The conduction velocity of peroneal nerve revealed significant time effect ($p=0.007$) and time×group interaction ($p=0.022$). Interaction effect was found to be significant for medial gastrocnemius and multifidus while standing with eyes open as well as with eyes closed ($p\leq0.004$). Only multifidus showed significant group ($p=0.002$) and interaction effect ($p=0.003$) during walking. **Conclusions**: Sensorimotor and gait training is an effective tool for improvement of proprioception and nerve function. It benefits muscle activation around ankle and multifidus during postural control and walking in DPN patients. **Clinical Trials Registry** - India, National Institute of Medical Statistics (Indian Council of Medical Research): Registration Number - CTRI/2017/08/009328.

Keywords: Balance Training, Electromyography, Gait Training, Nerve Function, Postural Control

Introduction

Diabetic peripheral neuropathy (DPN) is the most common complication associated with diabetes mellitus, affecting sensory and motor peripheral nerves. Loss of sensory nerve function results a decrease in sensory inputs sensitivity from the extremities[1-3], while loss of motor axons with insufficient re-innervation related to muscle strength deficit and atrophy of lower limb muscles[4]. Somatosensory information from foot, and proprioception are key determinants for motor control during balance and gait. Somatosensory loss in older patients with peripheral neuropathy is associated with greater proprioception thresholds[5,6]. Also, researchers have observed decrease in the compound motor nerve amplitude[5,7], lower conduction velocity[7-9], and increase in the latency[10] in DPN patients, in comparison to healthy controls. Loss of proprioception and motor nerve impairment deteriorate muscle performance during static and dynamic function[11,12].

Both balance and gait are a complex interplay of neural and muscular actions coordinated with skeletal functions. An age-related increase in the muscle activity during static and dynamic postural tasks and gait has been reported owing to decrease in the somatosensory inputs from feet and legs[13-15]. Study showed increase in muscle activity during postural task in DPN patients[16]. The greater muscle activation of agonist as well as antagonist muscles acts as a balance maintaining strategy during static stance or in response to perturbations

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during dynamic task[14,15,17]. This compensatory mechanism of increased joint stiffness enhances stability around the joint.

However, there are inconsistent results in DPN patients regarding muscle activation pattern while walking. Some researchers report a reduction in the electromyographic peak activation of tibialis anterior, gastrocnemius, and vastus lateralis[18-21], while others have observed no difference in muscle activation in DPN patients in comparison to controls[21-23]. Additionally, some researchers have also found an increase in the activity of tibialis anterior[18,21]. Also, prolonged duration of activity of lower limb muscles indicate co-contraction of these muscles for the stabilization of ankle joint and improvement of foot stability during foot flat to mid-stance[19,20,23]. Although Akashi et al. found no difference in the coactivation of tibialis anterior and lateral gastrocnemius in DPN patients as compared with control[20].

Sensorimotor training is considered to be a global approach for balance training. It emphasizes the sensorimotor system function as one unit, and works on enhancing sensory inputs and proper recruitment patterns of various muscles in maintaining joint stability, regulating the movement through central nervous system (CNS)[24]. Any imbalance in the muscles responsible for postural control leads to movement impairments and ultimately changes the motor programming in CNS. To correct these impairments, sensorimotor exercises first facilitate sensory inputs (proprioceptive and somatosensory structures), then corrects muscle imbalance and finally facilitates correct motor programming[24]. Along with improvement in balance and spatiotemporal parameters of gait, balance exercises as a part of sensorimotor training have also been shown to improve trunk proprioception in DPN patients[25]. However, there is a lack of studies about the effect of these exercises on the nerve function and muscular activity of lower limb muscles.

Evidence shows that aerobic[26-28] and tai chi exercises[29] modulate the nerve function in DPN patients. Balducci et al. found that simple exercises as brisk walking modify the natural history of the DPN[30]. But there is paucity of knowledge showing the effect of sensorimotor and gait training on neuromuscular functions. Our study was undertaken to examine the effects of sensorimotor and gait training on proprioception, peroneal and tibial nerve function, and electromyographic activity of the lower limb and trunk muscles during postural tasks and treadmill walking.

Materials and methods

Clinical trial was registered in the Clinical Trials Registry - India, National Institute of Medical Statistics (Indian Council of Medical Research) and approved by the Institutional Ethics Committee, Jamia Millia Islamia (JMI), New Delhi. Subjects were recruited during March 2016 to December 2017. The procedures were explained to the subjects, and written informed consent was obtained from each patient before the procedures began. A preliminary investigation was completed in order to verify the participation criteria which included anthropometric, demographic measures and clinical data.

Participants

The eligibility criteria were: male and female subjects aged between 45 and 75 years; diagnosed diabetes mellitus type 1 or 2 for at least 7 years; BMI was between 18.5 and 29.9 kg/m^2; subjects had scored more than 2/13 points in the Michigan neuropathy screening instrument (MNSI) questionnaire (Appendix 1), indicating the presence of at least two DPN symptoms[31]; scored greater than 1/10 point scale of MNSI physical examination (Appendix 1), including impaired vibration perception[32]; without any episode of plantar ulceration; no partial or total amputation; and ability to walk independently in the laboratory. Patients were excluded from the study if they had any other neurological impairment; any major vascular complication; severe retinopathy; severe nephropathy; severe musculoskeletal impairment to lower limb; cardiovascular complication; and been receiving any supervised physical intervention[32].

The participants were recruited from (a) Diabetic Centre, Ansari Medical Centre, JMI, (b) Out Patient Department Clinic, Centre for Physiotherapy and Rehabilitation Sciences (CPRS), JMI, and (c) advertisement through pamphlet distribution and JMI website.

All subjects went through an assessment to confirm eligibility. Subsequently, the patients went through the baseline measurement. All identifiable information on the consent form and demographic/injury history questionnaire was kept confidential by assigning a number to each subject. Patients allotted to the intervention group were treated in the outpatient department of the CPRS, JMI.

Design

The study was a two-arm, parallel group randomized controlled trial with single blinding (blinding of outcome assessor). Subjects were randomly allocated to either of the two groups using computer generated random numbers. Subjects allocated to the intervention group received sensorimotor and gait training along with diabetes and foot care education whereas subjects in the control group received diabetes and foot care education only. Both groups were assessed at baseline and after eight weeks of the trial. Enrolment and assignment of participants were done by an investigator who was neither part of assessment of outcome measures nor of implementation of exercise or education. Study design is presented in Figure 1.

Interventions

Sensorimotor and gait training

The exercise was conducted thrice a week (alternate days with gap not exceeding more than 48 hours) for eight weeks (total 24 sessions). Each session comprised 10 minutes of warm-up, followed by 50-60 minutes of exercise, followed by 5-10 minutes of cool down. Warm-up exercise included cycle

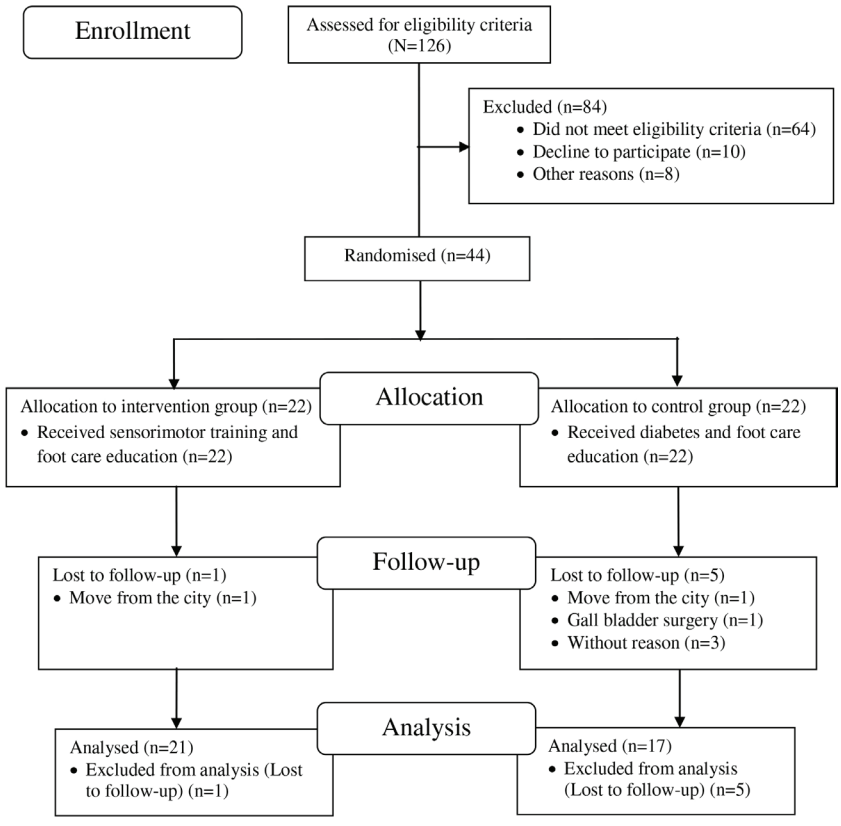

Figure 1. Flow chart of the patients participated in the study.

ergometer or treadmill at intensity of 40-50% maximal heart rate[33]. Heart rate was monitored using heart rate monitor (Polar Electro, RS 400, Kempele, Finland). Sensorimotor and gait training comprised wall slides, bridging exercises, prone plank, sit to stand, wobble board exercises, one leg stance, heel and toe raise, tandem stance gradually progressed to different grades using unstable surface (Thera Band® Stability Trainer) and gait training (different patterns of walking) (Appendix 2 and 3). Following the training session, subjects performed cool-down exercises, which included deep breathing, abdominal breathing and mild stretching. Their participation in the exercise was modified, postponed, or stopped based on the current guidelines of American Diabetes Association. The exercise level was increased after every two weeks, but if the subject was not able to perform at the next level, their exercise level was maintained at the current level.

Materials

An oval-shaped foam (TheraBand® Stability Trainer of soft green, blue and grey colour), round shaped foam (TheraBand® Stability Trainer of soft blue and silver colour), bosu ball (TheraBand®), wobble board (bi-directional and multidirectional TheraBand®) and gym ball (red, green, and blue colour TheraBand®) made up of polyurethane foam were used.

Diabetes and foot care education

Sessions on diabetes and foot care education was conducted once every two weeks for 30 minutes. It comprised material to understand diabetes, diabetes management and foot care guidelines. The education was provided by professional physiotherapist specialized in diabetes care.

Outcome measures

Proprioception

Proprioception was examined using Pedalo®-Sensamove Balance Test Pro with Miniboard. Miniboard comprised of the circular board with hemispherical shaped sensors placed below the board. It is based on the method of adjustment where the difference between adjustable stimulus and reference stimulus is recorded[34]. Prior to the actual testing, patients were familiarized with the testing procedure. They were asked to stand on the miniboard with the cushion placed below the board. Then, the subjects were asked to tilt maximally in four different directions (front, back, right and left). The reference stimulus lies within the maximal tilting angle. Each subject was asked to move his/her centre of pressure on a coloured spot with the help of marker displayed on a screen and to remember the spot. Then the subject was asked to reach the spot without access to the marker. The

Table 1. Demographic characteristics.

Variables	Intervention group	Control group	Independent t-test (p-value)	Mann-whitney U test (p-value)
N (M/F)	21 (15/6)	17 (10/7)	-	-
Age (year)	60.33±8.48	57.24±8.85	0.279	-
Height (cm)	164.31±8.59	161.08±9.12	0.271	-
Weight (kg)	66.52±13.22	67.98±12.05	0.727	-
BMI (kg/m^2)	24.51±3.22	26.2±3.71	0.142	-
Diabetic duration (year)	13.69±6.15	14.11±6.04	0.831	-
HbA1C (%)	8.03±1.21	9.15±1.53	0.017*	-
RBG (mmol/L)	178.38±60.37	203.24±50.23	0.183	-
Medication (Oral/Insulin/Both)	13/3/5	10/0/7	-	-
No. of comorbidities [a]	0 [0;1]	1 [0;1]	-	0.835
Smoker or tobacco intake (Y/N)	4/17	7/10	-	-
No. of falls [a]	0 [0;1]	1 [0;1]	-	0.494
MNSI (Q) [a]	4 [3;5.5]	4 [3;6]	-	0.643
MNSI (Ph) [a]	2.5 [2.25;3.75]	2.5 [1.5;3.5]	-	0.32

*M: Male; F: Female; BMI: Body mass Index; HbA1C: Glycosylated hemoglobin; RBG: Random blood glucose; MNSI: Michigan neuropathy screening instrument; [a]: median [inter quartial range]; *: significant difference.*

height of the screen was kept at the eye level. The difference in the angle was measured between the reference stimulus and the actual position. Measurements in all four directions were taken (Pedalo®-Sensamove Balance Test Version 2.2 User Guide). The reliability of the device has been previously reported in older subjects with ICC value 0.91[35].

Neurophysiological assessment

Nerve conduction studies were carried out for deep peroneal and tibial nerve as recommended by Misra and Kalita[36] and Nasseri et al.[37]. Motor nerve conduction studies were carried out using RMS Salus 2C electromyography/NCV machine. For deep peroneal nerve, an active surface electrode was placed over the extensor digitorum brevis (EDB) muscle and the reference electrode was placed over the tendon of EDB. Distal stimulation was given at 7-8 cm from the active electrode between the extensor digitorum longus and extensor hallucis longus, and proximal stimulation was given just below the head of fibula. For tibial nerve, the active surface electrode was placed over abductor hallucis and the reference electrode was placed distally near metatarsal head. Distal stimulation was given at 9 cm from active electrode behind and proximal to medial malleolus, and proximal stimulation was given slightly laterally to the midline of popliteal fossa, along the flexor crease of the knee. Nerve conduction studies are considered to be the most accurate, reliable and sensitive measure for peripheral nerve functions[37].

Electromyographical assessment

Surface electromyography (EMG) was used to record muscle activity. Surface EMG electrodes were placed on the tibialis anterior, medial gastrocnemius, vastus latralis and multifidus of right limb. The disposable bipolar Ag/AgCl surface electrodes were placed according to the SENIAM recommendations[38]. The diameter of electrodes was 10 mm and the inter-electrode distance was 25 mm. The electrodes were attached to the skin after shaving and cleansing the area with alcohol swab.

Maximal voluntary contractions (MVC) were initially carried out for each muscle as follows: (a) Tibialis anterior: The subject was asked to lie supine with the left leg in full extension and foot restrained in mid-range dorsiflexion. The subject attempted to dorsiflex the ankle joint against manual resistance by the investigator, which was applied at mid-dorsum of the foot. (b) Medial gastrocnemius: In the same position, with foot restrained in mid-range plantar flexion, the ankle of left leg attempted plantar flexion. Resistance was provided at the plantar aspect of mid-foot region. (c) Vastus lateralis: The subject sat upright with knees flexed at 90°, with the ankle of the left leg restrained from extending, and attempted to extend the knee against resistance provided at just above the ankle joint anteriorly. (d) Multifidus: The subjects laid prone on a couch and extended their back against the resistance provided at scapula by the investigator. The lower legs were strapped. In total, three trials of MVC were performed for 5 seconds of isometric phase. The subjects were asked to ensure maximum effort throughout 5 seconds; if not, the MVC were repeated. Electromyographic data was collected for 4700-4800 ms after the holding position started. The mean of 3 trials was calculated for the analysis. Root mean square (RMS) value was used for normalization of the EMG activity during the experimental procedures.

The electromyographical data were collected through

Table 2. Baseline comparison of all variables.

Variables	Intervention group (n=21)	Control group (n=17)	Independent t-test (p-value)	Mann-whitney U test (p-value)
Proprioception (angle difference)				
Front	6.50±3.42	9.07±3.51	0.029*	-
Back	10.41±5.41	9.42±6.96	0.625	-
Left	10.07±5.81	9.55±4.71	0.769	-
Right	8.75±5.17	7.87±6.18	0.633	-
Nerve conduction studies				
Peroneal nerve				
Latency (msec)	4.19±1.20	4.12±1.32	0.87	-
Amplitude (mV)	4.44±2.21	4.45±1.85	0.988	-
Duration (msec)	10.32±2.02	10.61±2.80	0.713	-
NCV (m/sec)	38.37±6.62	36.37±7.90	0.401	-
Tibial nerve				
Latency (msec)	4.80±1.13	4.59±0.79	0.515	-
Amplitude (mV)	6.74±3.83	6.12±3.89	0.629	-
Duration (msec)	8.04±1.34	7.92±2.02	0.829	-
NCV (m/sec)	37.94±7.35	38.39±11.69	0.885	-
Standing with eyes open (%MVIC)				
TA	9.63±6.34	10.03±5.54	0.841	-
MG	47.57±26.53	43.96±23.38	0.663	-
VL	15.04±8.44	13.86±9.12	0.681	-
MF	26.39±13.34	23.58±11.50	0.497	-
Standing with eyes closed (%MVIC)				
TA	24.38±14.07	25.98±10.29	0.697	-
MG	73.85±35.55	77.30±39.63	0.779	-
VL	25.73±13.57	21.69±14.39	0.381	-
MF	37.20±19.65	35.57±16.70	0.788	-
Treadmill walking (%MVIC)				
TA	35.13±15.02	31.09±7.84	-	0.736
MG	90.98±38.78	99.84±40.20	-	0.386
VL	59.70±34.56	60.26±40.16	-	0.918
MF	46.85±23.17	54.02±25.11	-	0.284
Co-contraction index (TA-MG)				
Stand (eyes open)	12.67±8.94	13.62±8.70	-	0.567
Stand (eyes closed)	35.34±24.39	34.18±13.73	0.863	-
Gait	52.39±29.32	42.23±12.48	-	0.509

*NCV: Nerve conduction velocity; MVIC: Muscle voluntary isometric contraction; TA: Tibialis anterior; MG: Medial gastrocnemius; VL: Vastus lateralis; MF: Multifidus; *: significant difference.*

a custom software and hardware design [PL3508 Power Lab 8/35 Data Acquisition System with Lab Chart Pro (AD Instruments, Australia)] at a sampling frequency of 1000 Hz and band-pass filtered between 5 and 500Hz. The signals were analogue/digitally stored on a personal computer.

Subjects then performed the following tasks: (a) bilateral stance on unstable balance board with eyes open; (b) bilateral stance on unstable balance board with eyes closed; and (c) treadmill walking at self-paced speed with hand supported. Balance assessment was performed for 12 seconds while treadmill walk was performed for 3 minutes. The timer was started once the subject had established their balance or reached their self-paced speed during walking. If the subject lost their balance during the task (moved their feet from the specific points), the trial was terminated and restarted when they were able to balance themselves for full 12 seconds. Muscle activity were expressed in percentage MVIC and used for the analysis.

Co-contraction index during postural task and walking was calculated by equation[39]; Co-contraction index = (lower EMG / higher EMG) × (lower EMG + higher EMG), where lower EMG is

Table 3. Measures of proprioception and nerve function before and after 8 weeks of intervention.

Variables	Intervention group (n=21)	Control group (n=17)	Time (T) effect η_p^2 (p-value)	Group (G) effect η_p^2 (p-value)	T×G interaction η_p^2 (p-value)
Proprioception (angle difference)					
Front					
Baseline	6.50±3.42	9.07±3.51	0.308 (<0.001)*	0.132 (0.027)*	0.132 (0.027)*
8th week	4.46±2.27	7.32±4.31			
Back					
Baseline	10.41±5.41	9.42±6.96	0.152 (0.016)*	0.003 (0.737)	0.122 (0.032)*
8th week	7.06±3.84	9.21±6.49			
Left					
Baseline	10.07±5.81	9.55±4.71	0.163 (0.012)*	0.044 (0.205)	0.165 (0.011)*
8th week	5.31±3.29	9.57±6.69			
Right					
Baseline	8.75±5.17	7.87±6.18	0.187 (0.007)*	0.01 (0.557)	0.099 (0.055)
8th week	4.60±2.81	7.10±5.24			
Nerve conduction studies					
Peroneal nerve					
Latency (msec)					
Baseline	4.19±1.2	4.12±1.32	0.071 (0.105)	0.009 (0.579)	0.094 (0.061)
8th week	3.70±0.75	4.15±1.2			
Amplitude (mV)					
Baseline	4.44±2.21	4.45±1.85	0.097 (0.058)	0.012 (0.507)	0.094 (0.061)
8th week	4.44±2.05	4.34±1.67			
Duration (msec)					
Baseline	10.32±2.02	10.61±2.8	<0.001 (0.968)	0.016 (0.453)	0.041 (0.222)
8th week	10.06±2.03	10.86±2.4			
NCV (m/sec)					
Baseline	38.37±6.62	36.37±7.9	0.187 (0.007)*	0.049 (0.183)	0.137 (0.022)*
8th week	40.84±5.88	36.60±8.47			
Tibial nerve					
Latency (msec)					
Baseline	4.80±1.13	4.59±0.79	0.002 (0.803)	0.009 (0.574)	0.125 (0.03)*
8th week	4.39±0.92	4.91±0.94			
Amplitude (mV)					
Baseline	6.74±3.83	6.12±3.89	0.029 (0.311)	0.003 (0.758)	0.032 (0.279)
8th week	6.72±3.56	6.56±4.3			
Duration (msec)					
Baseline	8.04±1.34	7.92±2.02	0.023 (0.367)	0.001 (0.872)	0.025 (0.346)
8th week	8.03±1.71	8.33±2.03			
NCV (m/sec)					
Baseline	37.94±7.35	38.39±11.69	0.315 (<0.001)*	<0.001 (0.941)	0.013 (0.503)
8th week	42.67±8.57	41.78±10.8			

*NCV: Nerve conduction velocity; *: significant difference.*

the level of activity in the less active muscle and higher EMG is the level of activity in the more active muscle represented in the normalized RMS value. This method provided an estimate of the relative activation of the pair of muscles as well as the magnitude of co-contraction.

Sample size calculation

The number of subjects was determined by G. Power 3.15. In a previous study, peroneal nerve conduction velocity (NCV) in DPN patients was 36.6±4.1 m/s compared with 42.8±4.1 m/s in healthy controls[8]. Allowing that DPN patients might

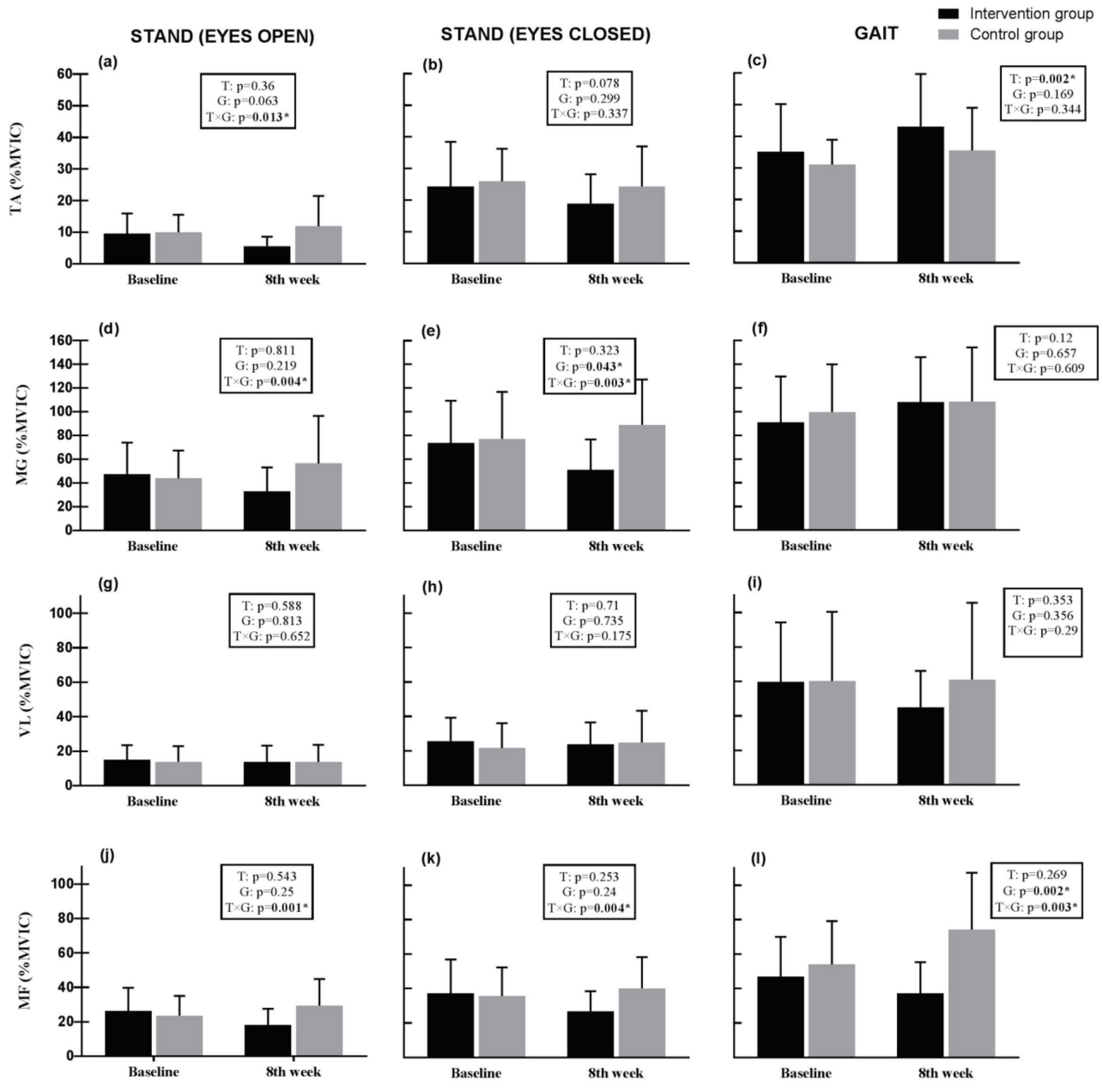

Figure 2. EMG activity of Tibialis anterior (TA), medial gastrocnemius (MG), vastus lateralis (VL) and multifidus (MF) during different task before and after 8 weeks of intervention. *: significant difference.

improve mean conduction velocity from 36.6 m/s to 39.7 m/s, 18 patients were required considering two tailed, alpha level of 0.05 and power (1-beta) of 0.85 in each group. We assumed a standard deviation of 4.1 of the response variable. Total 44 subjects were shown to be necessary including hypothesized 20% drop out.

Statistical analysis

The normality of distribution of all variables was verified using Shapiro Wilk test, skewness and histogram. Non-parametric test was used for the measures that showed non-normal distribution. Demographic characteristics and baseline measures were compared using independent t-test or Mann Whitney U test. 2×2 mixed model ANOVA was used to find out main effect (group effect and time effect) and time × group interaction. If the baseline values showed a significant difference between the groups, then 2×2 mixed ANCOVA was applied taking pre-values as covariate. All statistical analyses were carried out using SPSS version 21. Statistical significance was indicated if $p \leq 0.05$ and confidence interval

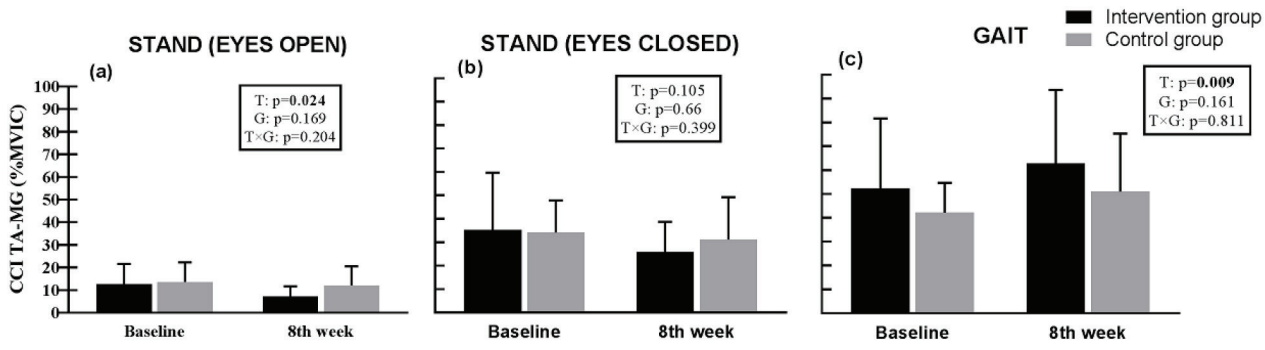

Figure 3. Co-contraction index of muscles during different task before and after 8 weeks of intervention. *: significant difference.

was set at 95%. Data are presented as mean±SD unless otherwise indicated.

Results

Demographic characteristics have been presented in Table 1. Comparison of demographic characteristics revealed no significant difference between the groups except HbA1c (p=0.017). The between-group comparison of baseline assessments found significant difference only for proprioception in front direction (p=0.029) (Table 2).

Proprioception

Repeated measures ANOVA revealed a significant time effect for proprioception in all the four directions (p≤0.016), group effect was found significant only in the front direction (p=0.002) and time×group interaction was found significant for proprioception in front (p=0.027), back (p=0.032) and left (p=0.011) directions (Table 3). The intervention group in the present study showed more improvement in front, back, left and right direction (31.38%, 32.18%, 47.26%, and 47.42%, respectively) than control group (19.29%, 2.22%, 0.2%, and 8.89%, respectively).

Nerve conduction studies

There was significant difference in the conduction velocity of the peroneal nerve for time effect (p=0.007) and time × group interaction (p=0.022) whereas a non-significant difference was found for the group effect (p>0.05). Conduction velocity of the peroneal nerve showed 6.43% increase in the intervention group whereas control group showed an increase of 0.6% only. Both within- and between-group comparisons of latency, amplitude and duration of the peroneal nerve were found to be non-significant (Table 3).

Conduction velocity for tibial nerve showed significant time effect (p<0.001) while group effect and time × group interaction were non-significant. There was an increase in conduction velocity in both groups (12.46% in the intervention group and 8.83% in the control group). Also, time × group interaction was found significant for tibial nerve latency (p=0.03). The intervention group showed decrease in the distal latency of tibial nerve by 8.54%, while the control group showed increase in the latency by 6.97%. There was no significant difference in the amplitude and duration of the peroneal nerve with respect to time or group (Table 3).

Electromyographic activity

Figures 2 and 3 present the results of EMG analysis of the muscles studied after intervention. During eyes-open stance, the time×group interaction in the muscle activity of the tibialis anterior (p=0.013), medial gastrocnemius (p=0.004) and multifidus (p=0.001) showed significant changes after the intervention, whereas only medial gastrocnemius (p=0.003) and multifidus (p=0.004) showed significant changes in eyes-closed condition after the intervention. On the other hand, treadmill walking found significant group effect (p=0.002) as well as time × group interaction (p=0.003) for multifidus muscle indicate 20.66% reduction were recorded in the intervention group, while 37.57% increase was recorded in the control group. Also, treadmill walking showed significant time effect (p=0.002) for the tibialis anterior muscle (22.8% increase in the intervention group and 14.34% increase in the control group).

Co-contraction index of tibialis anterior and medial gastrocnemius showed significant time effect during eyes open stance (p=0.024) (Figure 3(a)) (reduction of 42.93% in intervention group and 11.52% in control group) as well as during treadmill walking (p=0.009) (Figure3(c)) (an increase of 20.06% in intervention group and 20.9% in control group).

Discussion

The effect of sensorimotor and gait training on proprioception, nerve function and electromyographic activity of lower limb muscles in DPN patients were evaluated in the present study.

Proprioception

The results of our study revealed that intervention group significantly improve proprioception in front, back, left and right (closed to significant) directions which was found similar with the previous studies. Song et al. reported that balance exercises improved trunk proprioception in older adults with diabetic neuropathy[25]. Tai chi exercise has also enhanced the ankle and knee proprioception in adult and older population[40-42].

The present study included balance exercises that increase the stimulation of mechanoreceptors present in muscle spindle, golgi tendon organs and joint capsule responsible for enhancing proprioception inputs from foot, ankle and trunk[43]. Training also includes different patterns of walking comprising of small repetitive ankle and knee movement which improves proprioception. Also, a gradual increase in the difficulty of sensorimotor and gait exercises leads to enhance proprioception, as learning effect is one of the facts, which contributes to the improvement in the lower limb proprioception.

Previous studies suggest that loss of proprioception results in balance impairment experience multiple falls in older people[44]. Improvement in the proprioception decreases the risk of falls in the older population[45]. Though, the present study does not directly measure risk of falls, it indicates that improved proprioception might decrease the risk of falls in patients with DPN, thus, supporting the above findings.

Nerve conduction studies

There are few studies investigating lower limb nerve conduction in patients with diabetic neuropathy. Previous studies reported an improvement in NCV after aerobic or aerobic plus resistance exercise in diabetic population with or without neuropathy[26-28,30] which was found similar with our study. Hung et al. has also showed an increase in the NCV of the tibial nerve and median nerves after Tai chi exercise[29]. Hung et al. recruited diabetic patients without overt sign and symptoms of diabetic neuropathy[29], whereas we included diabetic patients with neuropathy, longer duration of diabetes, and higher level of HbA1C. Studies showed that NCV of the peroneal nerve can predict neuropathy-related mortality[46,47]. Moreover, a decrease in the latency of the tibial nerve was also recorded in our study after the exercise intervention.

The changes in NCV suggest partial regeneration or restoration of motor nerve function. The possible mechanisms of nerve function restoration after eight weeks of intervention are increased endoneural blood flow, decrease nitric oxide and decreased oxidative stress. Exercise induced microvascular circulation via endothelium vasodilation which increases endoneural blood flow[48], improves the abnormal perfusion and facilitates oxygen delivery to the nerve[49] reverses the chronic hypoxia of the nerves. Exercise enhanced nerve perfusion through ATP sensitive K^+ channels opening in diabetic neuropathy[50]. Decreased nitric oxide production might also be useful in preventing diabetes-induced polyol pathways that have a deleterious effect on Schwann cells and the endothelium, thereby restoring nerve function[51]. Increased antioxidant enzymes and decreased serum C-reactive protein after Tai chi exercises indicate reduction of risk of oxidative stress[52]. Training has been also shown to increase levels of Na/K ATPase activity in rat muscle cells[53]. It is therefore, speculated that exercise intervention in diabetic neuropathy could be related to improvement of Na/K ATPase activity.

Electromyographic activity

Results of our study shows reduction in the activity of tibialis anterior (41.64%), medial gastrocnemius (30.94%) and multifidus (31.07%) during eyes open and decrease in the activity of tibialis anterior (22.14% but not significant), medial gastrocnemius (30.9%) and multifidus (27.63%) during eyes closed stance on an unstable platform, suggesting enhanced postural control at the level of ankle and trunk after eight weeks of intervention. Loss or reduction of proprioception and somatosensory feedback from lower limbs leads to an increase in the activity of lower limb and trunk muscles during postural task[16]. Present study found an increase in somatosensory and proprioceptive inputs (as described) from foot, ankle and trunk after sensorimotor and gait exercises; hence it decreased the activity of muscles around the ankle and trunk. Song et al. found decrease in the trunk reposition errors in eyes-open and eyes-closed stance in stable surface and in eyes open on foam surface after eight week of exercise in diabetic neuropathy patients[25]. The present study comprised of different balance exercises like sit to stand, wobble board exercise, toe and heel raise exercise which might give beneficial effect on the trunk proprioception. Also, core stabilization program in the interventional group enhanced the sensory inputs from the trunk muscles and activation characteristics of trunk musculature[54,55]. The patients gained better sensory feedback by enhancing sensory inputs which decreased over contraction of muscle (which is compensatory strategy to gain more stability) around the joint.

Our study shows that the intervention helped in increasing the activity of tibialis anterior (22.8% in the interventional group and 14.34% in the control group) and medial gastrocnemius (18.89% in the interventional group and 8.8% in the control group) during treadmill walking, although the difference between the groups was not found to be significant. Sartor et al. results was found similar to our study; improvement in the ankle dorsiflexion and eccentric control of forefoot contact, as a function of the tibialis anterior, and increased participation of hallux and toes, as a function of medial gastrocnemius during walking[32]. Therefore, we can say that the intervention helps in increasing shock absorption during the initial contact phase of gait as contributed by the tibialis anterior and increasing push off power during heel off phase as contributed by the gastrocnemius. Technically, the skewed distribution of the data might be the reason for the statistically non-significant result. Although inconsistent, a large number of patients showed improvement in muscle

activation during walking in the intervention group in comparison with the control group. However, the patients reported better balance during walking on treadmill after the intervention and clinically found less compensatory adaptive strategy used during walking in the patients with DPN.

Interestingly, our study found reduction in the activity of multifidus during treadmill walking following the sensorimotor and gait training. Sensory integration relayed lesser motor response, therefore, multifidus activity was reduced during treadmill walking. Also, treadmill walking was challenging for the patients with lesser ankle strategy; therefore, the trunk leaned forward for maintaining balance as a compensatory strategy, consequently overloading the multifidus. After intervention better sensory feedback from foot and ankle helps proper use of ankle strategy. Thus, improvement in activity of the muscles around the ankle might have led to lesser compensation by trunk musculature with more erect trunk position, and therefore, lesser activation of the multifidus was found.

Clinical implications

Sensorimotor and gait training has revealed positive effects on proprioception, nerve function and activity of lower limb musculature. These exercises are feasible, easy and used in the clinical setup in patients with DPN. Also, the exercises may be given as home exercise protocol for patients moderately affected with DPN, due to lesser risk, better safety and exercises not requiring much supervision. However, we would like to mention the adverse events when one patient complained about aggravated pain in the leg during set of exercise intervention and another patient had hypoglycemia in only single session. The participants were offered no financial compensation, although the high compliance rate (86.36%) observed in our study suggests that the patients were satisfied with this form of therapy. These exercises should be incorporated along with glycemic control interventions, as they play an effective role as a preventive strategy for long term complications in patients with diabetic neuropathy.

Limitations and future perspective

There were several limitations to the study, including its small sample size, considering the larger variability in the parameters of the electromyographic activity. Also subjects in the control group were not controlled with home exercises during this period. Subjects recruited for the study primarily suffered from mild to moderate level of neuropathy, while those with severe neuropathy were relatively less in number, this limits the generalizability of the results to the entire population with DPN. In future, efficacy of sensorimotor and gait training should be assessed in sensory nerve function, in patients with severe diabetic neuropathy and with increase duration of exercise to see the significant changes in the electromyographic activity of the lower limb muscles.

Conclusions

Specific progressive sensorimotor and gait training improves proprioception and nerve conduction velocity. Due to better proprioceptive feedback, these interventions provide beneficial changes in the activity of muscles around the ankle and multifidus during postural control and walking in patients with DPN.

Ethical approval

Ethical approval was taken from Institutional Ethics Committee, Jamia Millia Islamia, New Delhi, reference number: 17/9/40/JMI/IEC/2015, dated-16/11/2015.

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Appendix

History (To be completed by the person with diabetes)

1. Are your legs and/or feet numb?	Yes/No
2. Do you ever have any burning pain in your legs and/or feet?	Yes/No
3. Are your feet too sensitive to touch?	Yes/No
4. Do you get muscle cramps in your legs and/or feet?	Yes/No
5. Do you ever have any prickling feelings in your legs or feet?	Yes/No
6. Does it hurt when the bed covers touch your skin?	Yes/No
7. When you get into the tub or shower, are you able to tell the hot water from the cold water?	Yes/No
8. Have you ever had an open sore on your foot?	Yes/No
9. Has your doctor ever told you that you have diabetic neuropathy?	Yes/No
10. Do you feel weak all over most of the time?	Yes /No
11. Are your symptoms worse at night?	Yes /No
12. Do your legs hurt when you walk?	Yes /No
13. Are you able to sense your feet when you walk?	Yes /No
14. Is the skin on your feet so dry that it cracks open?	Yes /No
15. Have you ever had an amputation?	Yes /No

Total:

Physical Assessment (To be completed by health professional)

1. Appearance of Feet

Right	**Left**
a. Normal Yes No	Normal Yes No
b. If no, check all that apply:	If no, check all that apply:
Deformities	Deformities
Dry skin, callus	Dry skin, callus
Infection	Infection
Fissure	Fissure
Other	Other
Specify:_____	Specify:_____

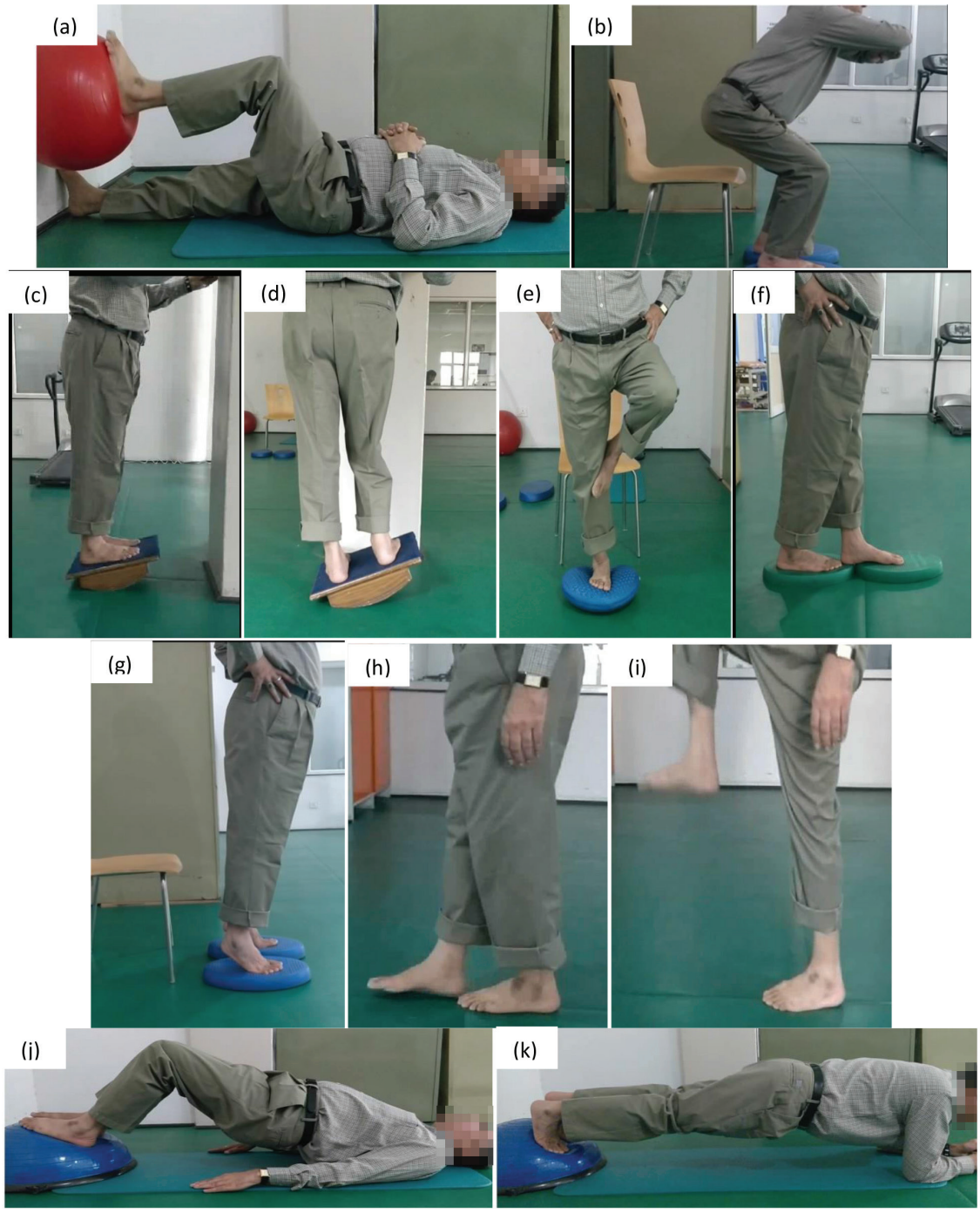
	Right			**Left**		
2. Ulceration	Absent	Present		Absent	Present	
3. Ankle reflexes	Present	Reinforcement	Absent	Present	Reinforcement	Absent
4. Vibration perception at great toe	Present	Decreased	Absent	Present	Decreased	Absent
5. Monofilament	Normal	Reduced	Absent	Normal	Reduced	Absent

Signature: Total Score:

Appendix 1. Michigan Neuropathy Screening Instrument.

Appendix 2. Description of sensorimotor and gait training program.

Exercises	Level 1	Level 2	Level 3	Level 4
Sensory training	Wall slides First 3 session: 20 reps Next 3 session: 20 reps ×2 sets	Wall slides First 3 session: 20 reps Next 3 session: 20 reps ×2 sets	Wall slides with red colour gym ball First 3 session: 20 reps Next 3 session: 20 reps ×2 sets	Wall slides with red colour gym ball First 3 session: 20 reps Next 3 session: 20 reps ×2 sets
Balance training (sensory component)	Bipedal wobble board exercise (bidirectional wobble board) First 3 session: 3mins Next 3 session: 3mins ×2 sets	Bipedal wobble board exercise (multidirectional wobble board) First 3 session: 3mins Next 3 session: 3mins ×2 sets	Unipedal wobble board exercise (bidirectional wobble board) First 3 session: 3mins Next 3 session: 3mins ×2 sets	Unipedal wobble board exercise (multidirectional wobble board) First 3 session: 3mins Next 3 session: 3mins ×2 sets
	Unipedal stance (blue oval stability trainer) First 3 session: 3mins Next 3 session: 3mins ×2 sets	Unipedal stance (grey oval stability trainer) First 3 session: 3mins Next 3 session: 3mins ×2 sets	Unipedal stance (blue round stability trainer) First 3 session: 3mins Next 3 session: 3mins ×2 sets	Unipedal stance (silver round stability trainer) First 3 session: 3mins Next 3 session: 3mins ×2 sets
	Tandem Stance (blue oval stability trainer) First 3 session: 3mins Next 3 session: 3mins ×2 sets	Tandem Stance (grey oval stability trainer) First 3 session: 3mins Next 3 session: 3mins ×2 sets	Tandem Stance (blue round stability trainer) First 3 session: 3mins Next 3 session: 3mins ×2 sets	Tandem Stance (silver round stability trainer) First 3 session: 3mins Next 3 session: 3mins ×2 sets
Balance training (motor component)	Toe and Heel raise (blue oval stability trainer) First 3 session: 10 reps Next 3 session: 10 reps ×2 sets	Toe and Heel raise (grey oval stability trainer) First 3 session: 10 reps Next 3 session: 10 reps ×2 sets	Toe and Heel raise (blue round stability trainer) First 3 session: 10 reps Next 3 session: 10 reps ×2 sets	Toe and Heel raise (silver round stability trainer) First 3 session: 10 reps Next 3 session: 10 reps ×2 sets
	Sit to stance (blue oval stability trainer) First 3 session: 10 reps Next 3 session: 10 reps ×2 sets	Sit to stance (grey oval stability trainer) First 3 session: 10 reps Next 3 session: 10 reps ×2 sets	Sit to stance (blue round stability trainer) First 3 session: 10 reps Next 3 session: 10 reps ×2 sets	Sit to stance (silver round stability trainer) First 3 session: 10 reps Next 3 session: 10 reps ×2 sets
Core training	Normal back bridging First 3 session: 10 reps Next 3 session: 10 reps ×2 sets	Back bridging on bosu ball First 3 session: 10 reps Next 3 session: 10 reps ×2 sets	Back bridging on silver stability trainer First 3 session: 10 reps Next 3 session: 10 reps ×2 sets	Back bridging on gym ball First 3 session: 10 reps Next 3 session: 10 reps ×2 sets
	Prone bridging First 3 session: 5 reps Next 3 session: 5 reps ×2 sets	Prone bridging on bosu ball First 3 session: 5 reps Next 3 session: 5 reps ×2 sets	Prone bridging on silver stability trainer First 3 session: 5 reps Next 3 session: 5 reps ×2 sets	Prone bridging on gym ball First 3 session: 5 reps Next 3 session: 5 reps ×2 sets
Gait training	Normal walk First 3 session: 5 mins Next 3 session: 5 mins ×2 sets	High march walk First 3 session: 5 mins Next 3 session: 5 mins ×2 sets	Backward walk First 3 session: 5 mins Next 3 session: 5 mins ×2 sets	High march backward walk First 3 session: 5 mins Next 3 session: 5 mins ×2 sets
	Walk on the line First 3 session: 5 mins Next 3 session: 5 mins ×2 sets	Tandem walk First 3 session: 5 mins Next 3 session: 5 mins ×2 sets	High march tandem walk First 3 session: 5 mins Next 3 session: 5 mins ×2 sets	High march tandem backward walk First 3 session: 5 mins Next 3 session: 5 mins ×2 sets
1 minute of rest between the sets; 1 minute to 3 minutes of rest between the two exercises.				



Appendix 3. Sensorimotor and gait exercises. *Sensorimotor exercises: (a) Wall slides with ball; (b) Sit to stand; (c) and (d) Bipedal wobble exercise; (e) Unipedal stance; (f) Tandem stance; (g) Toe and heel raise; Gait training: (h) Tandem walk (i) High march walk; Core training: (j) Back bridging on bosu ball (k) Prone bridging on bosu ball.*