Virtualizing the Assessment: A Novel Pragmatic Paradigm to Evaluate Lower Extremity Joint Perception in Diabetes

Gurtej Grewal^a Rashad Sayeed^a Steve Yeschek^a Robert Alexander Menzies^b
Talal K. Talal^b Lawrence A. Lavery^c David G. Armstrong^d Bijan Najafi^{a, d}

^aCenter for Lower Extremity Ambulatory Research (CLEAR), Scholl College of Podiatric Medicine, Rosalind Franklin University of Medicine and Science, North Chicago, Ill., USA; ^bDiabetic Foot and Wound Center, Department of Medicine, Hamad Medical Co., Doha, Qatar; ^cDepartment of Plastic and Reconstructive Surgery, University of Texas Southwestern, Dallas, Tex., and ^dSouthern Arizona Limb Salvage Alliance (SALSA), Department of Surgery, University of Arizona College of Medicine, Tucson, Ariz., USA

Key Words

Virtual reality • Diabetes peripheral neuropathy •
Lower extremity joint perception • Body-worn sensors •
Fall prevention • Obstacle crossing

Abstract

Background: Individuals with diabetes have a higher risk of falls and fall-related injuries. People with diabetes often develop peripheral neuropathy (DPN) as well as nerve damage throughout the body. In particular, reduced lower extremity proprioception due to DPN may cause a misjudgment of foot position and thus increase the risk of fall. **Objective:** An innovative virtual obstacle-crossing paradigm using wearable sensors was developed in an attempt to assess lower extremity position perception damage due to DPN. **Methods:** 67 participants (age 55.4 ± 8.9 , BMI 28.1 ± 5.8) including diabetics with and without DPN as well as aged-matched healthy controls were recruited. Severity of neuropathy was quantified using a vibratory perception threshold (VPT) test. The ability of perception of lower extremity was quantified by measuring obstacle-crossing success rate (OCSR), toe-ob-

stacle clearance (TOC), and reaction time (T_R) while crossing a series of virtual obstacles with heights at 10% and 20% of the subject's leg length. **Results:** No significant difference was found between groups for age and BMI. The data revealed that DPN subjects had a significantly lower OCSR compared to diabetics with no neuropathy and controls at an obstacle size of 10% of leg length ($p < 0.05$). DPN subjects also demonstrated longer T_R compared to other groups and for both obstacle sizes. In addition, TOC was reduced in neuropathy groups. Interestingly, a significant correlation between T_R and VPT ($r = 0.5$, $p < 10^{-3}$) was observed indicating a delay in reaction with increasing neuropathy severity. The delay becomes more pronounced by increasing the size of the obstacle. Using a regression model suggests that the change in T_R between obstacle sizes of 10% and 20% of leg length is the most sensitive predictor for neuropathy severity with an odds ratio of 2.70 ($p = 0.02$). **Conclusion:** The findings demonstrate proof of a concept of virtual-reality application as a promising method for objective assessment of neuropathy severity, however a further study is warranted to establish a stronger relationship between the measured parameters and neuropathy.

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Introduction

According to the National Diabetes Information Clearinghouse (NDIC) [1], 20.8 million people in the USA – at least 7% of the population – have diabetes. Diabetic peripheral neuropathy (DPN) is one of the most common complications of diabetes that affects nerve functions. It is estimated that DPN may occur in 25% of patients with 10 or more years of diabetes and up to 50% with 20 years of diabetes [2]. Among the elderly above 60 years of age with a history of diabetes, DPN can affect more than 50% of the population [3]. The result of long-term diabetes coupled with nerve damage leads to significant deficits in lower limb proprioception, touch sensation, vibration perception, and kinesthesia [4]. Patients with DPN experience a high incidence of injuries while walking and have a low level of perceived safety [5]. In certain cases the impaired judgment – mainly due to impaired proprioceptive feedback – can cause obstacle collision leading to falls and injuries [3, 4, 6–8].

The ankle inversion/eversion proprioceptive threshold for older subjects with DPN has been reported to be five times greater than age-matched subjects without DPN [9]. The reduced joint proprioception makes obstacle negotiation difficult and increases the risk of fall. During the actual phase of obstacle crossing, an individual does not have complete visual information regarding clearance between the obstacle and foot, and thus relies on proprioception for the leading limb and feed-forward mechanism for the trailing limb. Therefore, especially among subjects with degraded balance and lost proprioception of joint position, the risk of contact with obstacle would be high.

Diabetic neuropathy is known to reduce ankle muscle strength even before it is diagnosed [10]. Several studies suggest that diabetes itself may increase the risk of falling, suggesting that degradation in gait and balance may be initiated before diagnosing DPN. For example, Miller et al. [11] demonstrated that individuals with diabetes are 2.5-fold more likely to experience an accidental fall or a fall-related injury than healthy individuals. In the Women's Health and Aging Study ($n = 1,002$), Volpato et al. [12] reported persons with diabetes demonstrated a 44% increased risk of falls over 3 years through a multivariate model. In a study of osteoporotic fractures ($n = 9,249$), Schwartz et al. [13] reported a 68% increased fall risk for persons with diabetes. Interestingly, poor balance appears to describe more of the fall risk association than loss of sensation or decreased vibratory perception. Other authors have also described loss of sensation falling out of a multivariate model for conservative gait patterns in

persons with diabetes [14]. Schwartz et al. [13] reported poor balance as assessed by tandem gait and standing described 23% and 14% of the fall risk association compared with 3% and 6% for monofilament insensitivity and decreased vibration perception. Thus, identifying subtle gait and balance degradations in patients with diabetes may be helpful for early diagnosis of neuropathy and assessing the associated risk of falling, especially in challenging environments, including obstacle avoidance.

The subtle, early findings that are indicative of postural instability are difficult to accurately assess from a clinical examination, and gait laboratory assessment is not currently available or practical. Thus, unfortunately, many patients that are 'at risk for falls' are undiagnosed. The conventional methods for assessment of gait, balance, and obstacle-crossing ability have been limited to gait laboratories equipped with motion-tracking systems [15–19] which may not be suitable for a clinical environment [20–23]. In addition, assessing gait and balance in a real condition such as using an actual obstacle could be risky for DPN patients and may cause injury during the test such as hitting the obstacle.

In the current study, we implemented a virtual-reality game-based obstacle-crossing paradigm using wearable sensors for quantifying subject's ability to successfully cross a series of virtual obstacles. The implemented portable system provides real-time joint-position feedback from the lower limbs and uses virtual obstacles thereby posing minimum risk of injury to participants. The visual feedback of the joint position can be removed when desired in order to measure the feed-forward response of the participant to the approaching obstacle.

Methodology

Subject Recruitment

Sixty-seven eligible subjects, ranging in age from 38 and 75 years, were recruited from podiatry clinics in Chicago, USA and Doha, Qatar over an 8-week period. Subjects were eligible for participation if they were able to walk at least 20 m without any walking aid. Additionally, individuals were required to have the ability to cross obstacles without assistance and no restrictions on the passive ranges of motion of the knees, hips, ankles, and MTP joints. Subjects were excluded if diagnosed with cognitive, vestibular, or central neurological dysfunction, musculoskeletal abnormality, foot ulcers, Charcot's joints, rheumatic diseases, or a history of a balance disorder unrelated to DPN. Furthermore, subjects were excluded if they had previous surgeries, diseases, or disorders other than type 2 diabetes mellitus (DM) that caused nerve damage.

Patients with type 2 DM who were diagnosed by the primary physician and satisfied the above inclusion and exclusion criteria

Fig. 1. a Illustration of mounting of body-worn sensors. The shank and thigh sensors were mounted on the front side of the segments. The lower back sensor, battery, and hub were mounted on a wide custom-made Velcro belt. **b** Illustration of virtual obstacle paradigm. The motion of lower extremities was captured by mounted inertial measurement units and replicated on the laptop screen in real time as feedback for the participant.

were recruited. Healthy control subjects were matched to the recruited patients for age (± 5 years), gender and BMI. Evidence of DPN was confirmed using the criteria explained in the ADA statement [24] and defined by insensitivity of a 10-gram Semmes-Weinstein monofilament at 1–3 sites in the following locations: hallux, 1st, 3rd, and 5th metatarsal heads and vibratory perception threshold (VPT) of 25 V or higher. Severity of neuropathy was quantified by VPT. Participants were classified into three groups including: group 1: healthy, group 2: type 2 DM without DPN, and group 3: type 2 DM with DPN.

Written consent was obtained from all participants through an IRB-approved consent form. The study was approved by Hamad Medical Corp., Doha, Qatar and the Rosalind Franklin University of Medicine and Science, North Chicago, Ill., USA.

Equipment and Graphical Interface

The current research study implemented a novel obstacle-crossing paradigm with a virtual game-based interface that provides real-time joint-position information to the participant and measures various obstacle-crossing parameters. Participants were presented with a virtual interface on a laptop screen placed in front of them. Their lower extremities were represented as a stick model in the center of the screen with the body facing the right side of the screen as illustrated in figure 1. Any motion of the lower extremities (e.g. lifting the foot from the ground) was captured by five wearable inertial sensors (LegSys™; Biosensics LLC, Cambridge, Mass., USA) attached to each shank, thigh, and the subject's lower back using elastic bands (fig. 1). Each sensor has a tri-axial accelerometer, tri-axial gyroscope and a tri-axial magnetometer. The system has a built-in memory to record and transfer data in real time at a frequency of 100 Hz using a wireless connection based on WiFi protocol. A five-link biomechanical model of the human body was developed to represent each shank and thigh as well as trunk segments and estimate the position of the ankle, knee, and hip joints. The model assumed the hip as a fix joint and animates other segments around the hip joint. The

position of each joint was estimated based on the length of each segment and matrix of rotation extracted from the inertial sensors using a quaternion approach [7].

Protocol and Assessment

Before the measurement trials began the participants were explained the paradigm and allowed visualization of their limbs on the screen of the computer to become familiar with the system (fig. 2). The height of each individual was inserted to the program to estimate the length of lower body segments including each shank and thigh and estimate the height of the virtual obstacle proportionate to the length of the legs. The method of estimation of body segment length from the subject's stature was described in our previous publication [7]. This technique allows to create a realistic virtual environment for the subject. During measurement trials the stick model representing the lower extremities stood upright in the middle of the computer screen and a virtual obstacle appeared at the right end of the monitor and moved towards the participant at a speed of 0.25 m/s appropriately translated into pixels resolution of the monitor. The participants were expected to avoid the approaching virtual obstacle by lifting their foot off the ground as the obstacle approached closer. If the approaching obstacle was successfully avoided by lifting the foot to an appropriate height, the obstacle disappeared and a positive feedback sound was played. However, if the obstacle was hit, the obstacle disappeared with a negative feedback sound. A total of four blocks were performed – one practice and three assessments. Each block included ten trials of approaching obstacles and the time associated with each block was 2–3 min; a 1-min break between successive blocks was given to avoid fatigue. The obstacle height was chosen based on previously conducted research studies [15, 25]. Subjects first initiated practice with an obstacle size of 5% of their leg length to become familiar with the protocol and virtual environment, then performance of subjects in crossing virtual obstacles was examined at 10% and 20% of the subject's leg length. For all trials, a visual and audio feedback was provided as

Fig. 2. Protocol of test. Participants were presented with a virtual interface on a laptop screen placed in front of them. Their lower extremities were represented as a stick model in the center of the screen with the body facing the right side of the screen.

described above. If the participant experienced difficulty in maintaining balance during the trials, the measurements were stopped and no further data was collected.

Study Outcomes

Performance of the participant for crossing virtual obstacles was quantified by measuring obstacle-crossing success rate (OCSR), toe-obstacle clearance (TOC), and reaction time (T_R). OCSR was defined by the number of successful obstacle avoidances divided by the total number of obstacle trials multiplied by 100. TOC was defined as the vertical distance between foot and obstacle's top edge measured from the stick model and virtual obstacle presented on the laptop screen. T_R was quantified as time from lifting the foot above a defined threshold to the time the foot successfully avoided or hit the approaching obstacle. Each parameter was estimated for all ten trials at each obstacle size and then averaged for each individual.

Statistical Analysis

Independent-sample Kruskal-Wallis one-way ANOVA test and Scheffé's post-hoc test were used to examine the difference between

groups as well as between DPN and other groups. The Mann-Whitney U test (two samples) was used to compare the results between the two groups. Between-groups difference for gender and type of antidiabetic therapy was tested using the χ^2 test. Repeated measures ANOVA test was used to examine significant change in performance between different obstacle sizes. If the data was found not to be spherical, a Huynh-Feldt adjustment was used to determine significance. When a significant difference ($p < 0.05$) was found the least significance difference test was used as the post-hoc test to assess pairwise comparisons. Spearman's correlation of coefficient was used to examine whether change in obstacle clearance parameters had a significant correlation with neuropathy severity quantified by the VPT score. A linear regression model (stepwise) was used to identify significant predictors for predicting neuropathy severity. Results were expressed as means $\pm$ SD. A p value ≤ 0.05 was considered statistically significant. Statistical analyses were performed using SPSS® version 19.

Results

Recruitment and Subject Demographics

Sixty-seven participants (age 55.4 ± 8.9 , BMI 28.1 ± 5.8) were recruited. Two participants could not follow the protocol and the program crashed resulting in complete loss of data during trials for 4 different participants. Table 1 summarizes the demographic information of subjects included in data analysis for each group. Thirty percent of participants were female. No significant difference was found between groups for age, height, weight, gender, and BMI of participants ($p > 0.05$). The average history of diabetes for the non-DPN group was 10 ± 7 years and for the DPN group it was 14 ± 8 years. Average VPT was 10.5 ± 5.8 , 15.4 ± 6.5 , and 44.2 ± 17.7 V respectively for healthy, diabetes without neuropathy, and DPN groups. Hemoglobin A_{1C} level was slightly higher in the neuropathy group compared to non-neuropathy (7.0 ± 1.7 vs. $8.0 \pm 2.3\%$) but the difference was not statistically significant ($p = 0.28$, 95% CI = $[-2.6, 0.9]$).

Obstacle-Crossing Success Rate

There was no incidence of complete loss of balance during any of the trials for any participant. Table 2 summarizes obstacle-crossing performance for each group and each obstacle size. Overall, OCSR deteriorated in the DPN group compared to other groups for all obstacle sizes. However, only at an obstacle size of 10% of leg length, the difference achieved a statistically significant level (fig. 3a). At 10% obstacle size, OCSR in the DPN group was reduced 22% and 26% respectively compared to healthy ($p = 0.05$, diff. = -19% , 95% CI = $[-38.0\%]$) and diabetes without DPN groups ($p < 0.01$, diff. = -24% , 95%

Fig. 3. OCSR (a), T_R (b), and TOC (c) for healthy (group 1), diabetes without neuropathy (group 2), and diabetes with diagnosed peripheral neuropathy (group 3). * $p < 0.05$.

CI = [-42, -5.5]). OCSR at an obstacle size of 10% was negatively correlated with the age ($r = -0.33$, $p = 0.01$) and BMI ($r = -0.32$, $p = 0.02$) of participants. Interestingly, results also suggest that by increasing neuropathy severity quantified by VPT the obstacle success rate was significantly reduced ($r = -0.5$, $p < 10^{-6}$).

Reaction Time

Between-groups comparison suggests that T_R is significantly different between groups (table 2). In summary, both the DPN and non-DPN groups had slower T_R s than healthy subjects irrespective of neuropathy. On the same note, comparison between the DPN group and non-DPN group suggest that neuropathy is associated with slower T_R s. At 10% obstacle size, T_R was increased in the DPN group by 64% and 20% on average compared to group 1 (healthy) and group 2 (diabetes without DPN) respectively ($p < 0.05$). Interestingly, T_R was positively correlated with VPT ($r = 0.50$, $p < 10^{-3}$; fig. 4), suggesting that by increasing neuropathy severity, the response time to an approaching obstacle is slowing down. The correlation reached its maximum value for group 2 ($r = 0.65$, $p < 10^{-5}$). No significant correlation was found between T_R and BMI as well as the age of participants ($r < 0.1$, $p > 0.2$). The results were consistent for both obstacle sizes.

Toe-Obstacle Clearance

Figure 3c plots the TOC observed among different groups and obstacle sizes. TOC was significantly reduced in the DPN group compared to other groups for both obstacle sizes ($p < 0.01$; table 2). However, no significant difference was found between DPN and non-DPN. While TOC remained the same by doubling the obstacle size (21

Fig. 4. Relationship between VPT score and T_R of participants to approaching obstacles.

± 9 cm for 10% vs. 20 ± 10 cm for 20%), the TOC was reduced for both diabetes with and without DPN by doubling the obstacle size. In the DPN group, TOC was reduced by 16% by increasing the obstacle size from 10% to 20% ($p = 0.02$, diff. = -2.8 cm, 95% CI = [-6.3, -0.4] cm). A similar trend was identified for non-DPN subjects ($p = 0.03$, diff. = -2.8 cm (15%), 95% CI = [-6.8, -0.5] cm) suggesting that independent of neuropathy, the ability of

Table 1. Participant demographic information

Group	n	Health status	Age years	BMI	VPT V	History of diabetes years	HbA _{1C} %	Type of antidiabetic therapy, % of insulin therapy
1	13	non-diabetes control subjects	55 ± 10	27.0 ± 6.1	10.5 ± 5.8	0	–	–
2	13	diabetes without peripheral neuropathy	52 ± 7	29.3 ± 9.6	15.4 ± 6.5	10 ± 7	7.0 ± 1.7	7.7
3	35	diabetes with peripheral neuropathy, 25 V ≤ VPT ≤ 35 V	57 ± 9	28.2 ± 4.4	44.2 ± 17.7	14 ± 8	8.0 ± 2.3	14.3

Table 2. Obstacle-crossing performance

	Obstacle size % of leg length	Group 1	Group 2	Group 3	p value, comparison between groups	p value, comparison between DPN and non-DPN
OCSR, %	10	87 ± 23	92 ± 21	68 ± 29	0.01	0.001
	20	86 ± 25	86 ± 21	74 ± 43	0.44	0.15
T _R , %	10	0.83 ± 1.13	1.13 ± 0.74	1.36 ± 0.61	0.04	0.04
	20	0.77 ± 0.42	1.23 ± 0.95	1.44 ± 0.56	0.01	0.02
TOC, cm	10	21 ± 9	25 ± 9	18 ± 10	0.06	0.009
	20	20 ± 10	21 ± 11	15 ± 6	0.05	0.01

Table 3. Neuropathy severity predictors

Independent variables	Coefficient	p value
Age	0.92	0.001
BMI	0.05	0.90
T _R	6.7	0.12
TOC	–0.60	0.05
OCSR	–0.15	0.28
Δ _{TR}	14.9	0.02
Δ _{TOC}	–1.1	0.007
Δ _{OCSR}	0.06	0.39

subjects in crossing higher obstacle size is reduced in patients with diabetes. No significant correlation was observed between TOC and age, BMI, and VPT ($r < 0.1$, $p > 0.3$) for an obstacle size of 10% of the subject's leg length. However, by increasing the obstacle size to 20%, a negative correlation was observed between VPT and TOC ($r = -0.3$, $p < 0.05$) suggesting that more severe neuropathy was associated with a reduction in the ability to cross taller obstacles. Similar to the finding with tests of

an obstacle size of 10%, no significant correlation was found between TOC and age and BMI of participants for an obstacle size of 20%.

Evaluation of Neuropathy Severity

To identify significant predictors for evaluating neuropathy severity, a stepwise linear regression model was used. The dependent variable was VPT assuming a suitable predictor to evaluate neuropathy severity. The independent variables were T_R, OCSR, and TOC estimated at an obstacle size of 10%, as well as their changes from an obstacle size of 10–20% of leg length. In addition, age and BMI of participants were assumed as additional independent variables. Table 3 summarizes the results. The model can significantly predict the VPT values with a fair-to-good accuracy ($r = 0.64$, $p < 0.001$). Results suggest that age, T_R, as well as changes in T_R and TOC between obstacle sizes 10% and 20% of leg length are significant predictors for neuropathy severity. Among the study parameters, the change in T_R between obstacle sizes of 10% and 20% is the most sensitive predictor with an odds ratio of 2.69 indicating more delay in reaction when the obstacle size increases and severity of neuropathy is increasing.

Discussion

Obstacle crossing has been the focus of research for a long time, but so far the tools implemented for measuring kinematic parameters have been limited to gait laboratories equipped with a motion-tracking system [15–19, 21] which might not be suitable for a clinical environment and may also not reflect the real-world environment response of an individual [20, 23, 26]. In addition, conventional systems have other shortcomings, like the use of actual obstacles during experiments, which may increase the risk of adverse events during testing, required dedication of expensive infrastructure and a relatively large space that is not readily available for the vast majority of patients, need for expert technicians and longer time periods associated in preparation and trials. Very few studies have assessed obstacle crossing using technologically advanced wearable sensors [20] that would not require motion tracking. However, often due to heavy cost of calculation (e.g. double integration of acceleration to estimate toe clearance), these systems are incapable of real-time joint-position estimation, which is of key importance for virtual-reality application. To the best of our knowledge, our proposed technique is the first system that allows the assessment of obstacle-crossing ability using a combination of body-worn sensors and virtual reality.

The major effect of loss of joint proprioception and sensation is on gait and balance [3, 4, 6, 7, 27]. Diabetic neuropathy is known to reduce ankle muscle strength even before it is diagnosed [10]. The reduced joint proprioception makes obstacle negotiation difficult and increases the risk of falling. Studies have shown that patients with neurological disorders like diabetes, Parkinson's disease, and stroke have compromised obstacle negotiation [28, 29]. A reduction in TOC during obstacle crossing has been reported among patients with neurological disorders when compared to healthy subjects [15, 18, 29, 30]. Literature suggests that obstacle crossing even among healthy older adults is compromised causing them to adopt different strategies to avoid obstacles [16, 17, 31]. This study evaluated the proof of a concept of an innovative virtual-reality game-based system for quantifying the patient's ability to successfully avoid obstacles. The three parameters suggested to quantify obstacle-crossing ability included OCSR, T_R , and TOC. The results suggest that all three parameters were significantly different between healthy subjects, subjects with diabetic neuropathy, and subjects with diabetes and no neuropathy. Additionally, the results suggest that subjects with more severe neuropathy had an increased response delay to an

approaching obstacle. On the same note, the subject's reaction to an approaching obstacle was delayed more by increasing the size of the obstacle and increasing the neuropathy severity.

The findings of reduced TOC among DPN were consistent with recent literature [15]. It seems that the combination of loss of joint proprioception coupled with reduced ankle muscle strength would likely cause reduction in TOC ability and OCSR in the DPN group. However, delay in T_R , in particular by increasing the obstacle size, may be explained by the delay in sensory response due to neuropathy, given the fact that the highest correlation was observed only between T_R and VPT scores.

Lower rates of obstacle-crossing success in patients with DPN is consistent with previous studies suggesting a high risk of falling in the DPN group compared to healthy and diabetics without DPN [5]. Our results also suggest that reaction time to an approaching obstacle in subjects with diabetes (with or without neuropathy) was longer than in healthy subjects. This observation is consistent with recent studies suggesting that diabetes is an independent risk factor for falling [11, 12]. An additional study is needed to explore whether quantification of obstacle-crossing performance could be used as a more sensitive predictor for risk of falling in patients suffering from diabetes.

There are several limitations in this study. First, since real-time joint-position visual feedback was provided during assessment, it may have aided somewhat towards an increased obstacle success rate. This in turn may reduce the effect size for recognizing potential damage in joint perception due to DPN. However, based on the significant differences observed between groups, the authors would like to conclude that the proposed paradigm of virtual obstacle avoidance was a successful attempt towards assessment of joint proprioception. Second, an additional study is required to validate whether the observed deteriorations in virtual obstacle-crossing performance due to diabetes and DPN are associated with the risk of falling. Third, using vibration perception testing alone may not be an accurate method to quantify neuropathy severity. Additional measures of sensory and autonomic neuropathy may help to assess neuropathy. Finally, the age of the study participants (55.4 ± 8.9 years) is rather young from a geriatric point of view. Although the chronologic age of our population is slightly younger, the chronic medical condition of diabetes and associated comorbidities results in an effective clinical situation where this population is physiologically and functionally

more consistent with an older population. For example, Reistetter et al. [32], by studying 79,526 persons with a first-time hip fracture, demonstrated that younger patients with diabetes had poorer outcomes (e.g. length of stay in the medical rehabilitation unit or hospital) than patients with no diabetes. Their results also suggest that the difference between diabetes and non-diabetes in recovery outcomes after hip fracture is more pronounced in younger subjects than older subjects. This may suggest that fall prevention should be addressed in diabetics at an earlier age than non-diabetic subjects.

An early diagnosis of DPN would be of value in providing a change towards foot care before further complications arise. However, conventional modalities such as monofilament and VPT tests often diagnose neuropathy at a late stage and are subjective. A gait laboratory-based system can be used for an accurate and objective assessment of gait and balance deterioration due to reduce joint proprioception caused by neuropathy. However, these techniques are very expensive, they are not reimbursed by insurers and they are not suitable for busy clinics and routine clinical assessment. Additionally, it could be risky to examine patients who are vulnerable to trauma (such as diabetes) in a real condition, since even a small accident (e.g. hitting a real obstacle) could cause a serious adverse event such as diabetic foot ulcer, which is difficult to heal. The proposed technique based on virtual reality can replace the assessments performed in a gait laboratory without imposing any risk to patients and without requirement of expensive motion analyzer systems and/or devoting a big gait laboratory space, which is often unaffordable for many small clinics. Additionally, the developed technique could be used by diabetics at home for assessing their motor function deterioration caused by diabetes and neuropathy, which in turn may help to prevent falls and other associated traumas caused by progression in neuropathy severity.

Finally, the paradigm presented can also be implemented as a training tool for obstacle avoidance/crossing

in a virtual environment. Such a motor learning-based virtual-reality paradigm would be of greater benefit for patients than conventional balance training programs, especially in a clinical environment. The visual information plays a significant role on foot elevation in feed-forward control of lower limbs locomotion during obstacle crossing [19]. Significant improvements in gait parameters and foot obstacle clearance using virtual obstacle and real-time feedback have been demonstrated in post-stroke patients with hemiplegia [33]. During the actual phase of obstacle crossing, an individual does not have complete visual information regarding clearance between the obstacle and the foot, thus they rely on proprioception of the leading limb and feed-forward mechanism of the trailing limb. Therefore, it stands to reason that providing visual feedback during obstacle crossing may be used as a motor learning paradigm to improve feed-forward performance (improvement in accuracy of prediction) via intact sensory feedbacks (e.g. visual, muscles, ligaments, etc.).

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Disclosure Statement

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute of Diabetes and Digestive and Kidney Diseases or the National Institutes of Health or the Qatar National Research Foundation. The authors have no further conflicts of interest to disclose.

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