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An altered spatiotemporal gait adjustment during a virtual obstacle crossing task in patients with diabetic peripheral neuropathy

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Obstacle avoidance, Virtual reality, Anticipatory, Gait, Diabetes

ABSTRACT

This study investigates spatiotemporal gait adjustments that occur while stepping over virtual obstacles during treadmill walking in people with/without diabetic peripheral neuropathy (DPN). Eleven adults with Type 2 diabetes mellitus, ten DPN, and 11 age-matched healthy adults (HTY) participated in this study. They stepped over forthcoming virtual obstacles during treadmill walking. Outcomes such as success rate, spatiotemporal gait characteristics during obstacle crossing, and correlations between these variables were evaluated. The results partially supported our hypotheses that when comparing with HTY and DM, people with DPN adopted a crossing strategy which decreased obstacle crossing success rate and maximal toe elevation, and increased stride time and stance time during virtual obstacle crossing. This might be due to the compromised somatosensory functions of their lower extremity which may increase the risk of falling. This study also found an inter-leg relationship which may be applied to future stepping or obstacle crossing training that incorporates both legs as a means for improving outcomes of the trailing leg during daily obstacle negotiation.

1. Introduction

Ranked as the seventh leading cause of death resulting in approximately 250 thousand deaths in the U.S., diabetes mellitus (DM) impacts over 30 million American adults with the estimated prevalence rate of 12%.[1] Approximately 50% of DM patients are affected by diabetic peripheral neuropathy (DPN), a disease which damages patients' sensory and motor nerve fibers because of uncontrolled high blood sugar (i.e., hyperglycemia).[2-4] In addition to the nature of delayed afferent nerve sensory inputs or efferent motor outputs,[5] DPN results in poor postural control, loss of position and tactile sensation in the feet when compared to healthy individuals.[6] DPN also leads to higher spatiotemporal gait variability and increases the incidence of falling/tripping accidents due to the compromised sensory feedback.[7-9] Several studies pointed out an altered gait pattern in DPN patients which results in a shortened step length, wider step width, increased double support time, and increased step-to-step variability.[10–12] These gait alterations, due to potential somatosensory feedback deficit during walking, are also associated with a high risk of falling.[8,9,11–16]

Stepping over obstacles or performing an obstacle crossing task (OCT) requires people to be proactive in adjusting their spatiotemporal gait characteristics before reaching the obstacle.[17,18] In a study on cats, an increased discharge of motor cortical cell was observed when stepping over an obstacle on the treadmill, confirming that the central nervous system (CNS) played a role during OCT.[19] In human locomotion, McFayden et al rendered a term “anticipatory locomotor adjustments” to depict the preluded voluntary modification at the supraspinal level when confronting an obstacle.[20] They further suggested that OCT could also be controlled at the cortical level below the CNS. Next, stepping over obstacles consists of the consecutive movement of two legs in which the trailing leg usually demonstrated lowered OCT success rate than the leading leg.[17,21–23] Chou & Draganich indicated that the absence of visual contact during OCT makes a difference on the trailing leg.[17] Specifically, previous studies addressed that two independent control mechanisms of leading and trailing leg (i.e., vision-dependent and memory-dependent, respectively) in healthy adults during OCT,[21,22,24] and which could contribute to the difference of OCT success rate between two legs. As a result, a well-coordinated and adapted limb movement driven by the CNS is necessary to maintain balance during OCT. However, it is unclear how the leading and trailing leg coordinate during OCT in people with DPN. Even though different lower extremity trajectories and joint kinematic/kinetic patterns between DPN patients and healthy controls during OCT were observed,[25] evidence regarding the changes of DPN's gait adjustments that occur during OCT remains unknown.

Given the required proactivity and bipedal movement of motor control, OCT provides a means to examine the changes in spatiotemporal gait characteristics that are influenced by anticipatory locomotor adjustments (e.g., feedforward control) as well as inter-leg coordination. With the assistance of current virtual reality technology that enables real-time visual information and presets the upcoming task, the control of lower

extremity while stepping over obstacles can be examined. Therefore, this study aimed to investigate the impact of DPN and leg on the spatiotemporal gait adjustments that occur while stepping over forthcoming virtual obstacles during treadmill walking. We hypothesized that, when comparing to age-matched healthy controls and DM, DPN would show lower OCT success rate along with altered spatiotemporal gait characteristics. We also hypothesized that the coordination of these spatiotemporal gait characteristics between leading and trailing legs would be present among the successful OCT trials.

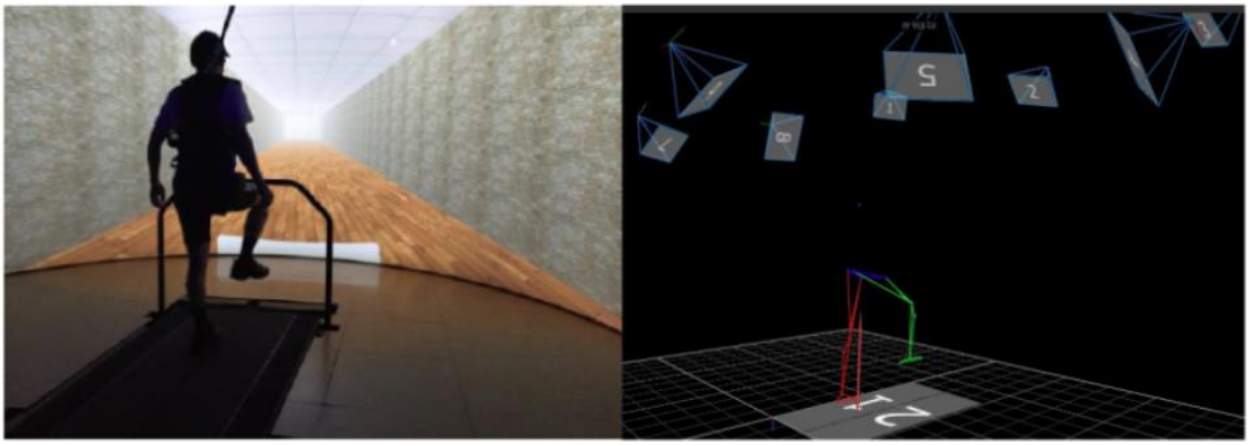

Fig. 1. The experimental set-up of virtual OCT (left) and task synchronized in Vicon (right).

2. Subjects, materials & methods

2.1. Participant eligibility

Participants with Type 2 DM were recruited from the Nebraska Medicine Diabetes Center, while DPN patients were recruited from the clinics of the Department of Neurological Sciences at UNMC. The age-matched healthy participants were recruited through flyers in surrounding communities. DPN was defined as the presence of either motor or sensory symptoms in the lower extremities or abnormalities seen in quantitative sudomotor axon reflex testing (QSART), quantitative sensory testing (QST) or through electrophysiological tests. Large fiber peripheral neuropathy was confirmed through electrophysiological tests (i.e., abnormal peroneal, tibial or sural nerve conduction and corresponding changes in the needle electromyography) while small fiber neuropathy was defined by QSART, QST, and electrophysiological test.[26] Participants' lower extremity muscles were examined to reach Grade 5 of manual muscle testing[27] to ensure they were capable of walking on a treadmill independently for at least 5 min. Additionally, an eye chart was used to ensure participants' vision acuity was normal or adjusted with at least of 20/40, to well-perceive the visual information during the test. The exclusion criteria were peripheral arterial disease, recent lower extremity fracture (less than six months), diabetic foot deformity (i.e., Charcot foot), foot ulcers/amputation, Type 1 DM, current pregnancy, unable to perceive the visual

information due to visual impairments and other illness that lead to postural instability such as neurovascular disease and vestibular disorders.

2.2. Instrumentations

This study used the GRAIL system (Motekforce Link, the Netherlands) in the Virtual Reality Laboratory of the Biomechanics Research Building at UNO. The GRAIL system consists of 1) a 3D motion capture system equipped with eight high-resolution Vicon T160 cameras along with the Nexus software suite (Vicon Motion Systems, Oxford, UK) that acquires and processes the kinematic data of markers from lower extremities at 100 Hz; 2) a motorized fully instrumented treadmill (Bertec Corp., Columbus, Ohio); 3) the D-Flow software (Motekforce Link, the Netherlands) which generates virtual scenarios and integrates signals simultaneously. The virtual scene was projected on a cylindrical screen ahead by three fore-mounted projectors. To ensure the safety during treadmill walking, subjects were protected by wearing the harness-like vest with straps attached on a ceiling-mounted track system (Solo-Step, Inc., North Sioux City, SD; Fig. 1).

2.3. Experimental protocol

All participants completed the informed consent forms approved by the Institutional Review Board at UNMC. Following that, they reported their demographic information such as date of birth, leg dominance, height, weight, race, most current hemoglobin A1C (i.e., the average blood glucose level over the last two months (Table 1). To evaluate functional balance performance, all participants completed the Berg Balance Scale (BBS)28 which consists of 14 sub-items of functional balance test, and each scores 0–4 with a total score of 56.

Table 1
The demographics by group of this study (N = 32).

	HTY (n = 11)	DM (n = 11)	DPN (n = 10)	*p* value
Age (years)	55.18 ± 7.99	55.82 ± 11.7	60.9 ± 9.42	0.44
Height (cm)	170.29 ± 7.97	169.49 ± 11.08	168.66 ± 10.52	0.88
Weight (kg)	76.78 ± 11.38	91.84 ± 19.45	91.23 ± 16.70	0.08
BMI (kg/m^2)	26.43 ± 3.21	31.83 ± 5.20	31.85 ± 3.76	<0.01[a]
A1C (%)	–	7.53 ± 1.37	7.68 ± 0.99	0.21
15% leg length (mm)	125.86 ± 8.86	123.00 ± 8.19	123.90 ± 8.56	0.51

BMI (Body-Mass Index, where <18.5, 18.5–24.9, 25–29.9 and >30 are defined as underweight, normal, overweight, and obese, respectively).
[a] One-way ANOVA was adopted to compare the group difference where DM and DPN showed significantly higher BMI than that in HTY.

Participants wore a singlet to ensure that all reflective markers were well-affixed on the bony landmarks. The modified Plug-In Gait marker set of lower extremity with 17 reflective markers was adopted (the seventh cervical vertebrae, left/right anterosuperior iliac spine, posterosuperior iliac spine, lateral thigh, knee, shank, ankle, toe, and heel).[29,30] The marker-based human model established using Nexus software was further synchronized to the GRAIL system through D-Flow for participants to interact with the VR environment. Next, participants practiced an overground OCT by stepping over an actual object 30 times. Considering the appropriate height of obstacle from previous studies (i.e., 10–30% of leg length),[20–22,25,31] we set the obstacle height at 15% of participants' leg length (i.e., the length between the greater trochanter and lateral

ankle) and was stepped over first using dominant leg as the leading leg. After the last five trials were recorded, participants were instructed to walk on the treadmill with their self-selected comfortable speed while the virtual hallway moved toward them with the same perceived speed (Fig. 1). Meanwhile, a series of forthcoming virtual obstacles with dimensions of 45 cm (width) ∗ 5 cm (depth) ∗ 15% of the participant's leg length (height) were shown at the end of the hallway and moved toward the participants on the cylindrical screen.[30] Participants also stepped over the virtual obstacles using their dominant leg as leading leg given the instruction of “To pretend to step over the obstacle as you practiced before, and do not contact it as it is an actual one.” (Fig. 1) The collision events were defined as any contact that occurred between right/left virtual toe markers and virtual obstacle through D-Flow, and were marked as failures of virtual OCT. Only the variables of successful virtual OCT were used for further analysis.

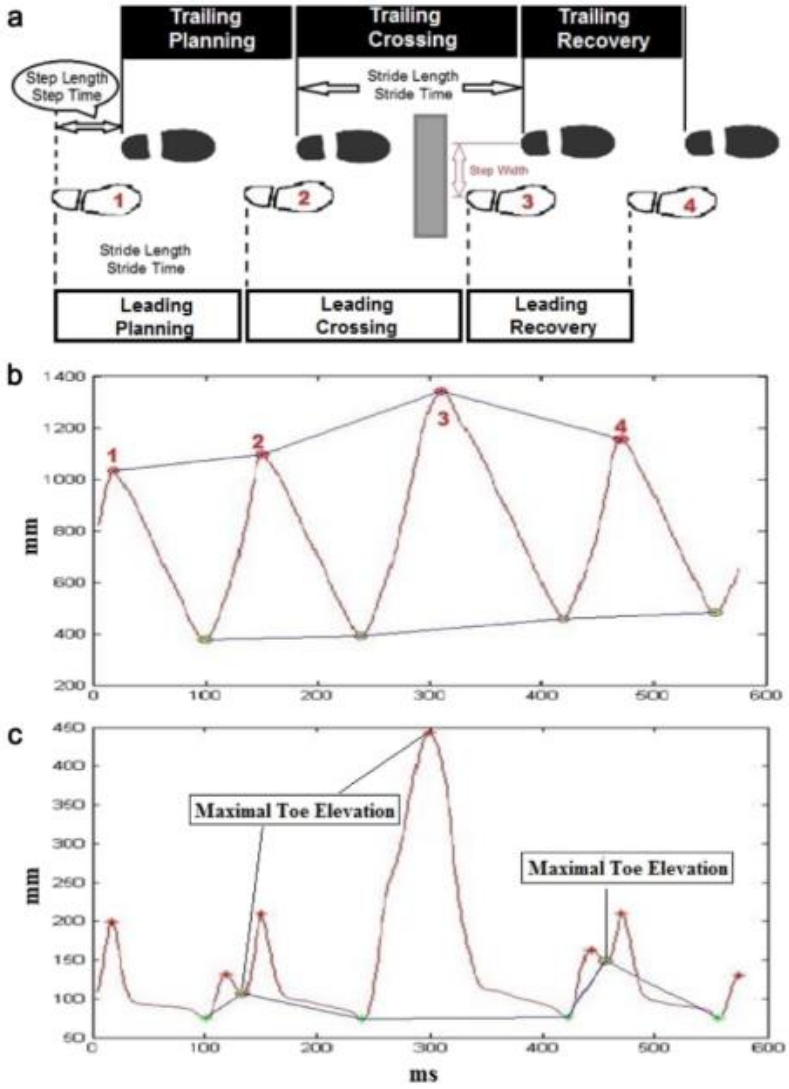

Fig. 2. a) The crossing phase is defined by the stride length while stepping over the virtual obstacle; b) heel marker displacement over time in anteroposterior direction where each number represents the moment of heel contact in Panel a; c) toe marker displacement over time in vertical direction (i.e., maximal toe elevation, MTE). Note the MTE before, during and after OCT were remarked.

2.4. Data reduction & analysis

All data were filtered using a 6 Hz zero-lag low-pass Butterworth filter.[32] The spatiotemporal gait characteristics including maximal toe elevation (MTE; the distance between the highest toe position and that at baseline.) during crossing were calculated using MATLAB (MathWorks, Inc., Natick, MA),[33] and the definitions of each gait characteristic are described in the Appendix Table. Obstacle crossing phase was determined as the period when participant's leading or trailing leg stepped over the virtual obstacle (i.e., stride time; Fig. 2.a).

2.5. Sample size justification & statistical analysis

The minimal sample size of eight in each group was calculated according to the previous published data using the G*Power 3.0 software with the acceptable power rate of 85% and 0.05 alpha-error probability.[30,34] All data were first screened for normality using the Shapiro-Wilk test, and all data fit the assumption of normal distribution. For comparing the differences between groups, dependent variables that were not leg-dependent during crossing (i.e., step length, step width, step time and their CVs) were analyzed using a one-way Analysis of Variance (ANOVA). To evaluate the interaction between the groups and the legs during crossing, a two-way ANOVA with one-between (i.e., group effect) and one-within (i.e., leg effect) factor was applied to examine the changes in the remaining gait characteristics (i.e., MTE, stride length, stride time, stance time, and swing time) and the virtual OCT success rate. The multiple comparisons with Bonferroni corrections were adopted if a significant main effect was found. Pearson's correlation coefficient (r) was adopted to examine the relationships among success rate of virtual OCT, DM/DPN's A1C, and spatiotemporal gait characteristics. The significant levelof all statistical analyses was set at $\alpha = 0.05$.

Table 2
The outcome measures among three groups during obstacle crossing (presented as mean and standard deviation in parenthesis).

Outcomes \ Group / Leg	HTY (male : female = 6:5)		DM (male : female = 4:7)		DPN (male : female = 6:4)	
	Leading	Trailing	Leading	Trailing	Leading	Trailing
BBS (0-56)	55.78 (0.44)		55.11 (1.17)		48.63 (12.51)	
Walking speed (m/s)	0.84 (0.11)		0.81 (0.10)		0.70 (0.23)	
OCT success rate	0.86 (0.17)	0.52 (0.26)	0.76 (0.17)	0.39 (0.25)	0.71 (0.35)	0.42 (0.27)
MTE (mm)†	410.09 (76.76)	346.82 (120.78)	306.90 (64.99)	288.90 (105.96)	355.00 (61.02)	291.38 (60.22)
Step length (mm)	821.00 (172.77)		768.91 (122.21)		883.22 (173.31)	
Step width (mm)	144.27 (68.04)		175.64 (45.50)		156.22 (65.95)	
Stride length (mm)†	1242.45 (206.29)	1464.00 (202.22)	1186.90 (136.48)	1410.60 (193.69)	1285.25 (202.44)	1628.50 (203.69)
Step time (ms)	542.27 (419.46)		322.45 (248.92)		335.67 (247.28)	
Stride time (ms)†	1371.00 (241.16)	1505.91 (219.19)	1365.70 (145.57)	1557.80 (173.14)	1496.75 (182.71)	**1898.75** (438.63)
Stance time (ms)†	720.82 (174.76)	913.00 (139.67)	749.09 (78.38)	910.27 (102.24)	765.78 (95.87)	1189.78 (415.94)
Swing time (ms)†*	649.45 (89.64)	605.36 (81.41)	629.60 (75.94)	605.50 (75.65)	728.25 (123.04)	694.50 (86.27)

*: Main effect of group was observed in which the DPN was significantly higher than DM; †: main effect of leg was observed; bold: a significant interaction following significant multiple comparisons between HTY and DPN was observed.
BBS: Berg Balance Scale; OCT: obstacle crossing task; MTE: maximal toe elevation.

3. Results

A total of 32 participants consisted of 11 DMs, 10 DPNs, and 11 age-matched healthy adults (HTY), participated in this study (mean age = 57.19 ± 9.85 years; 16

females; Table 1) in which DM and DPN's BMI were significantly higher than HTY (31 vs. 26; p b 0.01). Next, DPN demonstrated a non-significantly lowered walking speed when compared with HTY and DM (Table 2). Overall, a higher OCT success rate was observed at the leading leg versus the trailing leg during crossing, and DPN's leading and trailing legs showed lower OCT success rates (71% and 41%, respectively) when compared with HTY (86%/52%) and DM (76%/39%), but did not reach statistical significance (p N 0.3).

3.1. Impacts of group and leg on spatiotemporal gait characteristics

The Group analysis results showed that DPN significantly increased their stride time and swing time as compared with HTY (p = 0.04; F = 3.68) and DM (p = 0.04; F = 3.5), respectively. DPN demonstrated a non-significantly decreased MTE when compared with HTY and an increased stride time when compared with DM. Additionally, an increased MTE variability was observed in DPN's trailing leg when compared with HTY and DM, but it did not reach statistical significance (p = 0.07; F = 3.73).

The Leg analysis results indicated the significantly increased MTE (p b 0.01; F = 9.26) and swing time (p = 0.02; F = 6.46) at the leading leg while the significantly increased stride length (p b 0.01; F = 59.49), stride time (p b 0.01; F = 38.98), and stance time (p b 0.01; F = 33.43) at the trailing legs during the virtual OCT. A significant interaction between Groups and Legs was also found (p = 0.03; F = 4.06) for the trailing leg in DPN had an increased stride time than the HTY (p = 0.02). However, the DPN's trailing leg revealed a non-significant increase in stride time than DM (p = 0.05). In spatiotemporal gait variability (Table 3), there is an increasing trend of trailing leg's MTE variability across HTY, DM, and DPN. Also, the Leg analysis results showed that the stride time and stance time variabilities were significantly lowered at the trailing leg during virtual OCT (p b 0.01; F = 250.77 and 291.65, respectively). Concerning inter-leg coordination, significant correlations were found between leading and trailing legs' OCT success rate (r = 0.47; p b 0.01), MTE (r = 0.61; p b 0.01), stride length (r = 0.58; p b 0.01), stride time (r = 0.71; p b 0.01), and swing time (r = 0.74; p b 0.01).

Table 3
The changes of spatiotemporal gait variability (coefficient of variation) of three groups during obstacle crossing (presented as mean and standard deviation in parenthesis).

Group / Leg / Outcomes	HTY (male : female = 6:5)		DM (male : female = 4:7)		DPN (male : female = 6:4)	
	Leading	Trailing	Leading	Trailing	Leading	Trailing
MTE	0.15 (0.09)	0.17 (0.13)	0.15 (0.07)	0.18 (0.12)	0.11 (0.03)	0.19 (0.16)
Step length	0.13 (0.05)		0.12 (0.08)		0.09 (0.05)	
Step width	0.30 (0.14)		0.20 (0.11)		0.29 (0.22)	
Stride length	0.13 (0.04)	0.13 (0.08)	0.11 (0.06)	0.10 (0.08)	0.15 (0.10)	0.08 (0.03)
Step time	0.81 (0.58)		0.63 (0.56)		0.48 (0.49)	
Stride time†	0.16 (0.04)	0.10 (0.05)	0.14 (0.06)	0.09 (0.06)	0.16 (0.06)	0.08 (0.03)
Stance time†	0.21 (0.05)	0.15 (0.05)	0.16 (0.09)	0.13 (0.05)	0.20 (0.06)	0.14 (0.06)
Swing time	0.17 (0.05)	0.10 (0.04)	0.13 (0.06)	0.07 (0.04)	0.17 (0.11)	0.09 (0.07)

†: Main effect of leg was observed.
MTE: maximal toe elevation.

3.2. Relationship between clinical examination and OCT

The A1C inversely correlated with the maximal toe elevation (MTE) of leading and trailing legs (r = −0.43/p = 0.01 and r = −0.3/p = 0.1, respectively) and the success rate of virtual OCT at the leading leg (r =−0.31; p = 0.2). Additionally, BBS significantly correlated with both leading and trailing success rate (r = 0.68/p b 0.01 and r = 0.49/p = 0.01, respectively). The walking speed was significantly associated with BBS (r = 0.80, p b 0.01), OCT success rate at the leading (r =0.60, p b 0.01) and trailing leg (r = 0.45, p = 0.01).

4. Discussion

This study aimed to investigate the impact of diabetes on spatiotemporal gait adjustments while stepping over forthcoming virtual obstacles during treadmill walking. Overall, the results of this study partially supported our hypotheses that DPN patients adopted a different strategy of crossing when compared to others which demonstrated the least OCT success rate, decreased walking speed, and the altered spatiotemporal gait characteristics such as the decreased maximal toe elevation (MTE) and increased stride time/swing time.

4.1. Effect of group on virtual OCT

MTE is a crucial variable of detecting a success or failure of crossing during OCT. As the reduced MTE was documented in previous OCT-related studies, such as in healthy adults with distracted attentions,[17,23] elder adults[35] and patients with neurological illness,[31,36–38] it caused the failure of obstacle clearance and sequentially led to trips and falls.[39,40] Even though the difference of MTE between groups (i.e., HTY, DM and DPN) was not statistically significant, in line with the previous study,[25] the decreased MTEs in DM and DPN reflected the nature of reduced OCT success rate of this study. Specifically, patients with DPN have a higher risk of falling/tripping when compared to others, and this can be observed by a trend of decreasing OCT success rate of leading (HTY, DM, DPN: 86%, 76%, 71%) or trailing leg (52%, 39%, 42%) in the current study. Consistently, the tread was also documented (86%, 86%, 74%) in a previous study in which participants were instructed to step over forthcoming virtual obstacles presented on a screen while standing.[38] The negative correlation between leading MTE and A1C referred to the fact that a higher A1C level (i.e., DPN) correlates with a lowered MTE, which increases the risk of tripping during OCT.[25] Additionally, the severity of DM and DPN (i.e., 6–10.8% A1C) was inversely associated with the success rate of virtual OCT in both leading and trailing legs (92–38%). Even though the BMI in DM and DPN was significantly higher than that in HTY and is thought to be a factor that leads to lower reduced success rate, the non-significant correlation between BMI and success rate fails to explain this interpretation. Alternatively, the somatosensory deficit in DPN that compromises neuromuscular control during virtual OCT may be one of the factors that causes reduced success rate in DPN. For instance, DM and DPN at the early stage of illness have been identified as deficits of distal joint position sense (i.e.,

ankle joint) during weight-bearing condition.[41] As a result, the compromised somato-sensory at ankle joint during virtual OCT (which is categorized as a weight-bearing condition) can lead to misjudgment of MTE, and further decrease success rate of crossing.[25]

The walking speed varies by groups in which DPN walked the slowest following by DM and HTY, and similar results have been noted in studies of overground walking in DM/DPN.[2,42,43] The rigidity of ankle joint and affected muscle activation (i.e., gastrocnemius) in DM/DPN during mid-stance/terminal-stance of gait cycle have been indicated to reduce walking speed.[42,43] In addition, a trend toward decreased BBS and walking speed was observed during virtual OCT (Table 2), and walking speed presented a strong correlation with BBS, and a mild-to-moderate positive correlation with the OCT success rate. These supporting findings not only indicated that walking speed highly relates to functional balance performance, but also inferred that increasing DM/DPN's functional walking speed correlates with the reduced likelihood of tripping or stumbling over objects during overground walking.

Consistent with the findings from previous study,[2] both non-significant increased stride time and stance time were observed in the current study. Specifically, this study demonstrated that DPN lengthened the stride time at trailing leg during virtual OCT by increasing the swing time. A previous study has indicated a slightly increased swing phase of the gait cycle in DPN when compared to DM and HTY during overground walking.[43] In addition, Sawacha et al illustrated a significantly increased trunk movement in the sagittal plane (i.e., flexion/extension) of DPN across swing phase of gait cycle.[42] This profound trunk movement was also documented during OCT in which DM demonstrated a significantly increase in pelvic tilt than that of HTY.[25] Taken together, the increased swing time in DPN may attribute to the need of adjusting trunk kinematics during the virtual OCT. This result also implies that DPN requires more time (i.e., increased stride time and swing time) to step over a virtual obstacle, and the increased swing time of leading leg requires increased stance time of trailing leg accordingly during virtual OCT. Notably, this extended moment of obstacle crossing (i.e., single leg stance) could expose DPN under a situation of imminent instability and falling.

The non-significant changes in spatiotemporal gait variability between groups did not support our hypothesis which may be due to the insufficient sample size in each group.

4.2. Effect of leg on virtual OCT

The effect of leg impacts crossing behavior significantly, and this study showed that the OCT success rate of leading leg was higher than that of trailing leg (77% vs. 44%). This finding was consistent with the previous study in which the leading leg demonstrated more successes than the trailing leg (91% vs. 53%) when stepping over an imaginary obstacle without given any visual cue.[22] But when comparing OCT success rate with Heijnen et al,[22] the major factors that lead to a lower OCT success

rate of this study can be attributed to age (22 vs. 57 years) and healthy condition (Healthy vs. DM/DPN). Additionally, the overall leading leg OCT success rate of healthy group was low (i.e., 86%) when compared to previous studies incorporating a real OCT (i.e., 99%).[21,22] This difference may be due to the continuous moving belt of treadmill that is contrary to the moment of stepping over a real obstacle during overground walking. Also, the lack of presenting real-time location of toe marker (i.e., exproprioceptive visual information) in the given VR environment failed to provide participants with obstacle-leg representation and might increase the failure during OCT.[24]

The significant changes in spatiotemporal gait characteristics were identified between leading and trialing leg during virtual OCT in this study. Specifically, participants cautiously stepped over the obstacle while crossing their leading leg (i.e., increased MTE and swing time) and accordingly lengthened stride time and stance time of trailing leg. The different control mechanisms between leading and trailing legs (i.e., limb independence) during virtual OCT can be attributed to the fundamental phenomenon in which leading leg is vision-dependent while trailing leg is memory-dependent.[21,22,24] Our previous work also supported this concept of limb independence by illustrating an increased success rate of trailing leg given VR-induced visual information when compared to no visual information condition.[30]

This study suggested the leg independence during virtual OCT could be coordinated and influenced by the other. For example, a mild correlation was found between leading and trailing leg's OCT success rate. Collectively, several significant moderate-to-strong correlations of leading and trailing leg's MTE, stride length, stride time, and swing time were also observed. Lajoie et al illustrated that the movement of trailing leg during OCT could be regulated through the neural representation of obstacle properties (i.e., the experience and memory from leading leg).[24] It is also documented that the adaptation changes of MTE gained by leading leg can be transferred to trailing leg.[44] Furthermore, Lu et al compared the outcomes between leading and trailing legs while stepping over obstacles and demonstrated a similar pattern of inter-joint coordination.[45] As a result, DPN's affected trailing leg performance during OCT (i.e., decreased success rate, MTE, increased stride time and stance time) might be positively adjusted through leading leg given a future stepping or OCT exercise which incorporates both legs.

4.3. Interaction between groups and legs

The increased stride time and stance time of DPN's trailing leg during crossing has been noted. A previous study depicted that DPN showed a longer reaction time of lower extremity from lifting toe to successfully avoid an approaching target,[38] and the increased stride time of trailing leg of this study can be inferred that DPN needs more time to process and organize their feedforward stepping strategy.[20] The stance time (i.e., stance phase of gait cycle) of trailing leg is an important element of maintaining stability for leading leg to step over obstacles.[40] However, the increased stance time of

trailing leg implies that DPN could encounter higher imminent instability and expose themselves under the risk of falling given the higher BMI and deficit of distal joint sense during single leg stance of trailing leg.[41] These findings supported our hypothesis that DPN took more time than HTY did during crossing and can be possibly due to the sensorimotor deficits that prolonged the process of judging the upcoming event they perceived.[40]

To reduce the occurrence of falling/tripping accidents, the top-down feedforward control is needed to execute an accurate movement for maintaining balance during walking. This feedforward control communicates with CNS and rapidly forms the basis for computing necessary motor output by predicting or correcting errors of event information brought by the bottom-up feedback control.[46,47] Taken together, given a preset virtual OCT, DPN patients adopted a crossing strategy with a decreased walking speed, increased stride time, stance time, and decreased MTE, which leads to the lowest OCT success rate when compared to others and may be an indicator of future falling incidence. To further identify the impact of feedforward control on lower extremity movements in diabetes, future studies that focus on changes of lower extremity muscle activations, joint kinematics, and the cortical control are warranted. Additionally, the present inter-limb correlation of this study suggested that the trailing leg performance (i.e., success rate) of DPN may be positively influenced by leading leg through a stepping or an obstacle crossing training that incorporates both legs.[45]

4.4. Limitations

There are several limitations in this study. First, the performance of virtual OCT may not be equivalent to an actual OCT. Future studies are recommended to verify the similarity/equivalence of virtual and actual OCT by examining biomechanical changes (e.g., joint kinematics and kinetics). Next, the small sample size of each group may not reveal the clinical or statistical significances. Future studies that enroll more participants in each group are warranted. Last, the fixed-speed treadmill may influence participants' gait pattern as they usually walk and step over obstacles. As mentioned in the previous study,[33] the adoption of a self-paced treadmill which accommodates each participant's walking speed should be considered in the future studies.

Conflict of interest

The authors have no conflict of interest to disclosure in this study.

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Appendix A

Appendix Table
The definition of spatiotemporal gait characteristics of this study.[33]

Gait characteristics	Definition
Maximal toe elevation (mm)	The distance between the highest toe position and that at baseline.
Step length (mm)	The distance between right and left heel markers in anteroposterior direction.
Stride length (mm)	The distance between two consecutive heel markers of the same foot in anteroposterior direction.
Step width (mm)	The distance between right and left heel markers in mediolateral direction.
Step time (ms)	The duration of right and left heel contact.
Stride time (ms)[a]	The duration of two consecutive heel contacts of the same foot.
Stance time (ms)	The duration of heel contact to the following toe-off of the same foot.
Swing time (ms)	The duration of toe-off to the following heel contact of the same foot.

[a] Stride time consists of stance time and swing time.

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