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ORIGINAL ARTICLE

Role of sensory feedback in postural control of the patients with diabetic neuropathy

Alireza Reisi[1] · Alireza Hashemi-Oskouei[1] · Mohammed N. Ashtiani[2] · Farid Bahrpeyma[2]

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Abstract

Background/Purpose Impaired balance is prevalent in patients with type II diabetes mellitus (T2DM). The aim of the current study was to evaluate the role of sensory information in these patients.

Methods Stabilogram-diffusion analysis was utilized to categorize the balance into local and central control modes based on the center of pressure (CoP) data acquired from quiet standing tests of 36 patients with T2DM and 20 healthy individuals. Local control was considered the efforts of muscles to stiffen the joints. Central control was the mode in which sensory information is used. Open- and closed-eye conditions were added to detect other sensory sources during the standing. Traditional linear measures of stability were also calculated for anterior–posterior and mediolateral directions.

Results Results showed that sway area, pathlength, and maximum velocity of the CoP are higher in the T2DM group ($p < 0.001$) in open-eye condition, but they did not change in eyes closed ($p > 0.158$). Both the local and central control mechanisms can cause postural instability in AP direction in patients with T2DM ($p < 0.017$). Contrarily, diabetes had no effect on the ML direction ($p > 0.051$). Patients with T2DM had a significant delay (about 225 ms greater than the controls) in the use of sensory information reflected in the AP direction outputs ($p < 0.009$).

Conclusion The patients with T2DM had poorer stability due to the delayed use of the sensory information. Diabetic postural stability was not fully provided in comparison with the healthy people even with using the sensory information. Elimination of the visual feedback led to reduced postural balance in these patients.

Keywords Diabetes mellitus · Peripheral neuropathy · Postural control · Sensory feedback · Stabilogram-diffusion analysis

Introduction

Type II diabetes mellitus (T2DM) causes several problems regarding the control of posture. About one-third of the older diabetic persons with peripheral neuropathy (PN) have at least one falling experience in the year [1]. The well-documented literature on postural stability acknowledges that T2DM impairs the visual and somatosensory systems [2, 3]. The T2DM, also, adversely affects the muscles' strength to exacerbate the standing instabilities [4]. Some researchers stated that the balance behavior of the patients with T2DM is compromised in comparison with their age-matched healthy individuals. However, these studies used different measurement methods such as body or center of mass sways [5], trunk inclinations [6], and the center of pressure (CoP)-related parameters of stability like sway range, velocity, area, variability, and time-to-boundary measures [7–12].

It was overlooked for a long time that the central processing of the feedback afferents may be impaired by the T2DM with peripheral neuropathy (PN) [13]. However, recent studies emphasized the effects of diabetes on the brain by indicating cerebral microvascular lesions [14], cortical atrophy [15, 16], and also the loss of neuroplasticity in animal models [17]. Because the normal postural control postulates motor and sensory coordination during standing, it is crucial to focus on the integration and use of sensory information for the motor responses. Meanwhile, several neuroimaging outcomes have shown decreased function of the motor and sensory cortices in patients with T2DM [18–21]. These findings complete the previous information about the motor behavior deficiency like posture instabilities and gait impairments in patients with

✉ Farid Bahrpeyma
bahrpeyf@modares.ac.ir

[1] Faculty of Biomedical Engineering, Sahand University of Technology, Tabriz, Iran

[2] Department of Physiotherapy, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran

T2DM [11, 12, 22, 23]; however, the correlation between the central and peripheral impairments has been rarely inspected using a single analytic method.

The maintenance of balance may have two modes of control: the local control, which is defined based on the efforts of muscles to stiffen the joints without using sensory information, and the central control, which is defined as the mode in which the sensory information is used. The discrimination between these two modes by means of routine postural measures like the CoP data has been suggested by Collins and Deluca (1993). They developed the stabilogram-diffusion analysis (SDA) based on the principles of statistical mechanics, which presumes the nature of random walk for the parameter of interest like the CoP. The SDA method calculates the squared-mean values for the desired parameter to correlate it to the time intervals by a linear constant called diffusion coefficient, representing the average stochastic activity of the posture analogous to a random walk movement [24]. Figure 1 graphically shows the details of this method. The first linear region in the SDA indicates the postural control without the use of sensory information, i.e., the local control mode, and the second linear behavior reveals the central mode of the control of posture by using sensory information [25, 26]. The SDA method has been widely used to determine the postural strategies among several pathological groups like diabetes [25], Parkinson's diseases [27], aging [28, 29], vertigo [30], etc. Toosizadeh et al. (2015) investigated the central versus local control of the posture in patients with diabetes and healthy controls using the SDA method applied on the center of mass (CoM) excursions [25].

The present study aimed to assess the role of type II diabetes mellitus with PN in central and local strategies during the control of posture in comparison with healthy age-matched individuals in terms of the CoP data. It was hypothesized that (i) the T2DM reduces the stability during standing; (ii) the central control of the posture in the patients with T2DM is affected more than the local control; (iii) patients with T2DM have more postural instabilities in the absence of visual information; and (iv) patients with T2DM have delay in use of sensory feedback.

Materials and methods

Participants

Thirty-six patients with type II diabetes mellitus (16 females, average age: 58.8 ± 7.3 years, BMI: 27.8 ± 4.9 kg/m2, duration of T2DM: 10.0 ± 3.9 years) and 20 healthy age-matched control subjects (6 females, average age: 52.1 ± 3.4 years, BMI: 27.3 ± 3.2 kg/m2) participated in this cross-sectional observational study. The participants entered the T2DM group if their age was between 40 and 75 years and had diabetes for 5 to 15 years, fasting glucose between 120 and 250 mg/dl, blood pressure between 100/60 and 140/90 mmHg, HbA1c between 6.5 and 9%, minimum visual acuity of 20/40, and should be able to

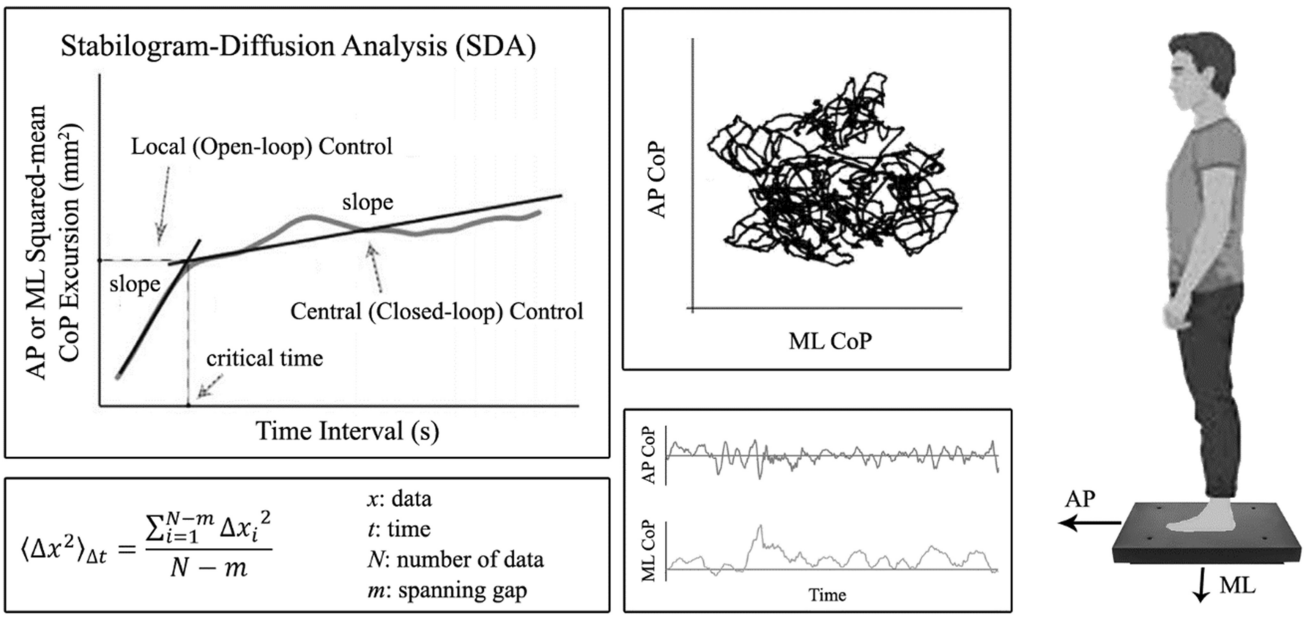

Fig. 1 Schematic representation of the test condition, raw CoP data in both AP and ML directions, data analysis to calculate critical time, local and central stability metrics in the SDA method

walk and stand without any aiding device. The PN of the patients has been evaluated by the Valk neuropathy score greater than 2 and also a recorded nerve conduction velocity less than 40 m/s for the peroneal tibial nerve. Exclusion criteria for these patients were suffering from cardiac disorders, vein thrombosis, CNS dysfunctions, vestibular dysfunctions, musculoskeletal disorders, foot wounds that prevent long-term standing, edema in the lower extremities, and any locomotive limitations. The participants in both groups received verbal and written explanations about the tests and signed the consent form. The ethical committee of the university approved this study.

Procedure

Both groups (T2DM and Ctrl) were asked to stand for 30 s on a force platform for 5 trials with a 2-min rest between the trials. They were barefoot with arms along the body with eyes open and closed using a blindfold.

Data acquisition and analysis

A force platform (Kistler, type 9286AA, Winterthur, Switzerland) measured the movement of the center of pressure during standing with a sampling rate of 100 Hz. Linear metrics of the postural stability were sway area (the area of an ellipse that encloses at least 95% of the CoP data), pathlength (the total length that the CoP travels during the task), maximum velocity, and the root mean square of the CoP data. The latter three metrics were calculated for both anterior–posterior (AP) and mediolateral (ML) directions. Nonlinear metrics of the postural stability were calculated based on the stabilogram-diffusion analysis including the critical time interval, local (open-loop) stability, and central (closed-loop) stability metrics (see Fig. 1). Details of this technique were presented in references [24, 26].

Statistical analysis

The normality of the data distribution was analyzed using the Kolmogorov–Smirnov test. One-way analysis of variance (ANOVA) was utilized to assess the roles of T2DM and vision on the linear conventional and the SDA metrics of postural stability. The significance level for all analyses was considered 5%.

Results

There was no significant different between the demographic data of age ($p = 0.611$) and BMI ($p = 0.798$). The distributions of all linear and SDA metrics were normal.

Table 1 shows the mean (SD) of the linear metrics for control and T2DM participants in open- and closed-eye conditions and the statistical measures. The sway area for patients with T2DM was significantly greater than the healthy controls ($F = 21.6$, $p < 0.001$). In the AP direction, the path length ($F = 65.4$, $p < 0.001$), maximum velocity ($F = 54.1$, $p < 0.001$), and RMS ($F = 83.2$, $p < 0.001$) of the CoP excursions were significantly increased in the participants with T2DM. In the ML direction, on the other hand, only the maximum velocity ($F = 23.0$, $p < 0.001$) and the RMS ($F = 25.1$, $p < 0.001$) were increased significantly in comparison to the healthy control subjects. The ML CoP path length was not changed between two groups ($F = 0.7$, $p = 0.408$).

The removal of visual feedback had no effect on all CoP-related linear metrics of stability ($p > 0.05$).

Table 2 also presents the mean (SD) values of SDA metrics for the test conditions. In AP direction, all SDA parameters, i.e., critical time interval ($F = 7.1$, $p = 0.009$), local ($F = 5.9$, $p = 0.017$), and center stability ($F = 15.7$, $p < 0.001$) were significantly higher in the patients with T2DM rather than the healthy ones. However, these SDA metrics in the ML direction were not different for the participants with T2DM ($F < 3.9$, $p > 0.051$).

Table 1 Linear variables of standing for healthy control (Ctrl) and type II diabetes mellitus (T2DM) participants and the related statistical results

	Ctrl		T2DM		Group *p*-value	Vision *p*-value
	EO	EC	EO	EC		
Sway area (cm^2)	1.3 (0.7)	1.5 (0.8)	4.3 (3.3)	5.4 (5.6)	**< 0.001**	0.293
AP direction						
Pathlength (cm)	15.8 (4.7)	16.6 (6.1)	27.1 (8.3)	30.3 (9.3)	**< 0.001**	0.219
Max velocity (cm/s)	2.8 (1.6)	2.5 (0.7)	4.6 (1.5)	5.3 (2.0)	**< 0.001**	0.392
RMS (cm)	0.3 (0.2)	0.4 (0.2)	1.6 (0.9)	1.9 (1.0)	**< 0.001**	0.332
ML direction						
Pathlength (cm)	16.3 (10.2)	17.8 (12.5)	15.8 (4.7)	16.6 (6.1)	0.408	0.158
Max velocity (cm/s)	2.5 (1.3)	2.5 (1.1)	3.3 (0.9)	3.9 (1.4)	**< 0.001**	0.175
RMS (cm)	0.6 (0.3)	0.7 (0.3)	0.4 (0.2)	0.4 (0.2)	**< 0.001**	0.751

The bold-faced values denote statistically-significant effects of the group and vision i.e. $p < 0.05$

Table 2 Nonlinear variables of standing for healthy control (Ctrl) and type II diabetes mellitus (T2DM) participants and the related statistical outputs whose main effects are presented in the last two columns but pairwise comparisons are developed by superscript letters noted below

	Ctrl		T2DM		Group *p*-value	Vision *p*-value
	EO	EC	EO	EC		
AP direction						
Critical time interval (s)	0.94 (0.40)	0.88 (0.39)	1.15 (0.43)	1.12 (0.47)	**0.009**	0.640
Local stability (cm^2/s)	0.41 (0.24)	0.40 (0.28)	0.49 (0.35) [a]	0.94 (0.57) [a]	**0.017**	**0.024**
Central stability (cm^2/s)	0.07 (0.06)	0.07 (0.07)	0.14 (0.10) [b]	0.27 (0.20) [b]	**< 0.001**	**0.017**
ML direction						
Critical time interval (s)	1.02 (0.48)	0.86 (0.46)	1.12 (0.47) [c]	0.82 (0.43) [c]	0.747	**0.005**
Local stability (cm^2/s)	0.52 (0.23) [d,e]	0.87 (0.50) [d]	0.82 (0.52) [e,f]	1.25 (0.67) [f]	0.051	**0.015**
Central stability (cm^2/s)	0.19 (0.28)	0.21 (0.24)	0.12 (0.11) [g]	0.49 (0.43) [g]	0.830	0.071

a: significantly diferrent ($F=6.7$, $p=0.012$); b: significantly diferrent ($F=7.3$, $p=0.009$); c: significantly diferrent ($F=8.0$, $p=0.006$); d: significantly diferrent ($F=7.7$, $p=0.008$); e: significantly diferrent ($F=5.6$, $p=0.021$); f: not significant ($F=3.2$, $p=0.077$); g: significantly diferrent ($F=5.9$, $p=0.018$)

The bold-faced values denote statistically-significant effects of the group and vision i.e. $p < 0.05$

The effect of vision was roughly significant for the SDA metrics. In particular, the local stability metric in the AP direction was significantly increased for the T2DM group ($F=6.7$, $p=0.012$), whereas not different for the healthy participants ($F=0.019$, $p=0.892$). The same results existed for the central stability metric, which is significantly increased for the T2DM group by elimination of visual feedback ($F=7.3$, $p=0.009$), and not changed for the healthy ones ($F=0.000$, $p=0.996$). The vision's main effects were significant for local and central stability metrics ($F=5.3$, $p=0.024$ and $F=0.9$, $p=0.017$, respectively). The critical time interval in the AP direction was not changed due to the closure of the eyes ($F=0.2$, $p=0.640$). In the ML direction, the critical time interval was significantly reduced during the closure of the eyes in the T2DM group ($F=8.0$, $p=0.006$), while not changed in the healthy group ($F=1.1$, $p=0.297$). The vision's main effect on the ML critical time was significant ($F=8.4$, $p=0.005$). The ML local stability metric was also increased significantly by the removal of visual feedback ($F=6.1$, $p=0.015$). The ML central stability was not changed due to closure of the eyes ($F=3.3$, $p=0.071$). But merely among the patients, the ML central stability was significantly higher in closed-eyes condition ($F=5.9$, $p=0.018$).

Discussion

The present study investigated the effects of type II diabetes mellitus on central and local control of the posture. For this purpose, stabilogram-diffusion analysis was utilized to discriminate two motor behaviors of the patients with T2DM with and without the sensory information. The main questions addressed in this study were (i) diabetes causes more postural instability in comparison with the healthy group, (ii) patients with T2DM have more instable central control than the local control, (iii) the removal of visual feedback has a destabilizing effect on balance, and (iv) patients with T2DM have delayed use of sensory information.

Effects of the diabetes

In terms of the linear measures of stability (Table 1), the patients with T2DM had considerably reduced stability during quiet standing for 30 s. Regardless of the visual condition, the healthy individuals had lower sway areas of the CoP, which indicates a higher stability level. The CoP pathlength that may reflect the amount of energy expenditure during the provision of stability was also lower in the healthy group. This outcome shows more optimal standing in comparison to the patients with T2DM. The maximum velocity was also two times greater in the patients than that of the healthy individuals. This parameter indicates the dexterity of postural control, which was impaired in the patients with T2DM. The higher velocity of the CoP may be originated by uncoordinated co-contractions of the muscles specifically acting on the ankle joint. Previous studies also developed similar results. For instance, sway area [31–35], path length [35, 36], and sway velocity [7] all showed greater values in the patients with diabetes in comparison with the healthy controls. The RMS of the antero-posterior CoP excursions was higher in the patients indicating farther CoP travels. This larger distance creates a larger moment arm for the ground reaction force, i.e., larger flexory/entensory moment about the ankle joint, which should be counterbalanced by the ankle muscles. Normally, the somatosensory afferent signaling would inform the CNS about the creation of such a large moment; nevertheless, the SDA time intervals of referring to the sensory information in patients with T2DM were

significantly greater in the AP direction (see Table 2). It was shown that the human and rodent models with diabetes have slower conduction velocity of upper motor neurons [37–39], maybe due to neuronal loss or demyelination [31, 40–42]. Abbruzzese et al. measured motor-evoked potentials in diabetic and healthy people and found that the central motor conduction times in upper and lower muscles are prolonged due to the diabetes seemingly independent from the PN [37]. The same results have been reported by Moglia et al. who investigated a larger population of the participants and found no correlation between the conduction time delays in the diabetic patients and their disease duration and also existence of the PN [38]. In the current study, the time delay in the use of sensory information may interfere with an effective feedback data processing in control of the posture.

In the T2DM patients, local (open-loop) instability is significantly increased, specifically in the AP direction when the vision was eliminated. Providing the local stability may be the result of the collaboration between different muscles of the lower extremity, which often uses a stiffening strategy while standing [25]. Decrease of muscle strength in the ankle [43], knee [4, 44], and the upper extremity [45, 46] due to diabetes (even without the PN) can lead to instabilities in the local control of posture among the patients with T2DM. The SDA local stability measure has been used as a discriminative index of human balance in many studies that employed the SDA method to differentiate between a variety of disorders, aging, or challenging conditions during standing. In most of the mentioned studies, the local stability indices were lower in the control group, which means a more stable condition. This local index has been generalized to the total stability in standing position. The researchers believed that if the short-term response is not stable enough, further endeavors cannot compensate this defect even after using the sensory information in the central response. But in two studies, the central stability (i.e., with the usage of sensory information) was unexpectedly greater in the control groups [25, 47]. This finding has been interpreted as a kind of adaptation to compensate for the unstable local-control mode.

It seems the interpretation of SDA results needs to consider study protocols. Collins et al. (49) applied the SDA method to the CoP data of young and elder people while Toosizadeh et al. (25) applied this method to the CoM of patients with neuropathic diabetes. The compensation in providing stability argued by Toosizadeh et al. (2015) might be originated from the somatosensory. In contrast, the literature confirmed that diabetes, specifically with the PN, has adversely affected the sensitivity and functionality of the muscle spindles in diabetic humans and mice [48–50]. Although the use of sensory information in the central control of the posture ameliorated the balance in both groups, the patients' central stability was still lower than the healthy individuals. Using a synchronized electromyographic analysis along the posturography during the standing task may elucidate the role of reduced muscle strength in diabetic patients [4, 43, 51, 52]. Furthermore, Toosizadeh et al. applied the SDA method to the CoM excursions, which have been considered non- or weakly chaotic behavior [53, 54]; hence, from a practical point of view, the assumption of the random walk motion for the CoM movements is not necessarily justifiable. The results of the current study did not confirm the outputs of the latter study, noting the application of the SDA to the CoP data here. The central stability of the patients with T2DM was significantly reduced in comparison with the healthy control individuals. It implies the deteriorative effect of diabetes on the anterior–posterior postural stability even during the existence of the sensory information. In fact, the CNS was faced to limitations in integration and processing of the the sensory information.

Effects of the vision

The linear measures of stability showed no significant effect of the vision on balance. Removal of the visual feedback whose role in the control of diabetic people's posture is highly emphasized by the literature [7] did not affect the linear measures of stability. But in contrast, the nonlinear SDA metrics showed a significant difference between open- and closed-eye conditions (see Table 2). The ML critical time interval, i.e., the parameter that quantifies the intervals of using the sensory data, was reduced by the elimination of visual feedback only in the diabetic patients. It implied that in the absence of vision, the CNS has relied on the other sources of information (here probably the vestibular system due to the PN) more frequently than when the eyes were open. Previous studies have shown that the stability in the ML direction is more dependent on the vestibular function [55]. Since the participants in this study had no symptomatic dysfunction in their vestibular systems, referring to the vestibular data as the only available and reliable feedback source in the ML direction was accelerated by the CNS. Individuals are often better able to maintain their balance in the ML than in the AP direction. The base of support is elongated in the ML direction between the feet so that the CoP has a wider area to travel far away from the margins of the base of support. In contrast, the base of support in the AP direction is narrower, and the probability of the CoP nearness to the base of support margin is higher.

The critical time interval of the healthy individuals changed neither in the AP nor in the ML direction by closure of the eyes. This highlighted the role of somatosensory feedback information in the healthy people and its defects in the patients with T2DM. The visual feedback also locally and centrally stabilized the posture in these patients especially in the AP direction.

The results of this study can shed light on the prospective treatments that would be designated for the improvement of posture in patients with T2DM. Since it was highlighted that the sensory information, which plays crucial roles in posture, is adversely affected by T2DM, exercise programs should consider proprioception. The goal of these exercises should be an improvement in proprioceptive acuity. For instance, Santos et al. (2016) proposed a set of circuit exercises with 13 stations to stimulate the proprioceptive sensation of women with diabetes [56]. From the outcomes of the present study, it could also be suggested as well that the physical therapies should comprise sensory stimulations of the feet soles, calf muscles, tibialis anterior/posterior, and peroneus longus/brevis.

Conclusion

In conclusion, the stabilogram-diffusion analysis could assess the balance in two segregated local and central modes of postural control in patients with T2DM. But it is necessary to note that the parameter of interest should vary like a random walk motion. The overall stability revealed in the linear metrics showed instable standings for these patients especially in the AP direction. These instabilities were more crucial in the central control of posture, i.e., with usage of the sensory information as the feedback, although the local, i.e., without sensory feedback control mode was instable too. Therefore, no compensation strategy was observed in the patients. The removal of visual feedback adversely affected the balance in the diabetic people. The patients with T2DM had a delayed use of the sensory information.

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Data Availability The data are available from the corresponding author.

Declarations

Conflict of interests The authors declare no competing interests.

Ethical clearance The Ethical Committee of Tabriz University of Medical Sciences approved the study (code: IR.TBZMED.REC.1397.655). All procedures were performed according to the Declaration of Helsinki. All participants signed informed consent forms before participating in the study.

Informed Consent was obtained from all participants included in the study.

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