Доклади на Българската академия на науките
Comptes rendus de l'Académie bulgare des Sciences

Tome 75, No 6, 2022

MEDICINE

Clinical medicine

EFFECTS OF DIABETIC NEUROPATHY ON THE POSTURAL STABILITY OF ADULTS WITH TYPE 2 DIABETES MELLITUS

Mariya Irikeva, Katerina Kirilova, Dorina Petrova*, Georgi Angov, Katerina Stambolieva#**

Received on November 21, 2019
Presented by P. Vassileva, Member of BAS, on December 17, 2019

Abstract

Diabetic peripheral neuropathy (DPN) is one of the most common complications, which occurs in 50–70% of people with Type 2 diabetes mellitus (T2DM). The disease usually affects the peripheral nerves and can cause loss of sensation in the feet, leading to impaired body equilibrium during quiet stance and gait, and elevated risk of falls. A total of 38 non-insulin-dependent T2DM adults (mean age 53.21±7.74 years) – 18 with DPN and 20 without DPN, and 20 age- and sex-matched controls took part in the study. The DPN group was selected with standard clinical criteria and a Bulgarian version of the Michigan neuropathy screening instrument. Postural stability was evaluated with static posturography under two visual conditions (eyes open and eyes closed) on firm and soft support. Both diabetic groups exhibited significantly higher postural instability compared with the healthy controls, as well as stronger visual dependence. While standing on firm support, subjects with DPN exhibited significantly higher postural instability than those without DPN in the closed eyes condition only, whereas when standing on soft support, their postural stability was significantly more impaired compared with the diabetic subjects without

#Corresponding author.

This work was partially supported by the Bulgarian Ministry of Education and Science under the National Research Programme "Young scientists and postdoctoral students", approved by DCM # 577/17.08.2018.

DOI:10.7546/CRABS.2022.06.13

DPN in both experimental conditions (open and closed eyes). A better understanding of the changes in postural stability in persons with T2DM would contribute to early diagnostics, rehabilitation and prevention of DPN.

Key words: diabetic neuropathy, postural stability, posturography

Introduction. Poor glycaemic control and persisting high blood sugar levels in people with Type 2 diabetes mellitus (T2DM) increase the risk of complications such as diabetic neuropathy. Diabetic peripheral neuropathy (DPN) most often affects the distal ends of the long nerve fibres with large diameter which innervate the lower limbs. That usually causes disruption and delay in the proprioceptive information from the muscle spindles, the tendon, joint and cutaneous mechanoreceptors. The result is decreased sensation in the feet and reduced sense of position in the ankle leading to postural instability during stance and gait, and thus increased risk of falls, especially in the elderly population [1,2].

Static posturography is the most commonly used method for postural stability evaluation. Measurements of postural sway are based on the displacements of the centre of pressure (COP) under the feet in both anterior-posterior (AP) and medial-lateral (ML) directions. Several stabilographic parameters such as mean amplitude, sway path, sway velocity and sway area are used for quantitative estimation of postural stability [3]. A number of studies using static posturography have reported high postural instability during quiet stance in T2DM adults with DPN in comparison with healthy controls. There is evidence that subjects with DPN have larger sway area, larger sway velocities and larger COP range during stance with open and closed eyes [4–8]. Whether adults with T2DM but not DPN have impaired postural stability is still under debate. Several authors have reported significant instability of persons with diabetes compared to healthy controls [9,10], while others have not found differences in the postural sway parameters [5,11].

The purpose of this study is to evaluate the effects of DPN on postural stability in adults with T2DM and pinpoint specific conditions and parameters that could serve as early predictors of this pathological complication.

Subjects and methods. Thirty-eight persons, aged between 45 and 60 years with clinically diagnosed T2DM and desease history from 5 to 10 years, without insulin dependence and 20 age- and sex-matched controls took part in this study. All participants with T2DM were treated with oral medicines to maintain the blood sugar level at about 7.5–10 mmol/l. About 30% of the subjects and 17% of the healthy controls had hypertension and had been taking medicines for blood pressure regulation. The exclusion criteria for the study were: age under 45 or over 60 years, comorbidities such as: part or complete foot amputation, neurological disorders, musculoskeletal impairments, arthritis, acute sciatica, excessive hypertension, vitamin B12 or thyroid deficiency, major vascular complications, autonomic neuropathy or retinopathy. All subjects underwent a neurotological

examination prior to participation. Persons with spontaneous, latent or positional nystagmus (detected by Frenzel glasses and electronystagmography) were not included in the study. The participants were divided in 3 groups: 20 diabetic subjects without DPN, 18 subjects with clinically diagnosed DPN and 20 healthy controls. Participants' characteristics are presented in Table 1. All subjects were volunteers and gave their signed informed consent to participate in the study, in accordance with the ethical standards of the Helsinki declaration and the local Ethics Committee.

All persons with T2DM were tested with a Bulgarian version of the Michigan neuropathy screening instrument (MNSI) [10], applying the modified criteria of Herman et al. [13] for DPN identification, where abnormal scores are ≥ 4 for MNSI questionnaire and > 2.5 for the MNSI neurological examination. Maximal scores are 13 for MNSI questionnaire and 8 for MNSI examination, corresponding to the highest gravity of DPN [12, 13]. The neurological examination included: examination of the feet for deformities, perception of vibration (produced by a 128 Hz vibrating fork, located on the interphalangeal joint of the great toe), Achilles reflex (in kneeling position), graded 0–4 [14].

Postural stability during quiet stance was evaluated by the Static Posturographic System previously described [15]. Postural sway was registred in four experimental conditions: stance with eyes open and eyes closed on firm support and on a foam pad with dimensions $400 \times 400 \times 150$ mm, density – 77.5 kg/m^3, and elastic modulus – 74.9 N/m^2. The duration of each trial was 30 s and the rest period between trials was 2 min. Participants were instructed to stand upright with 3 cm heel to heel distance and feet splayed at an angle of 30°. Sway amplitudes and sway velocities in both directions – anterior-posterior (AP) and medial-lateral (ML), were calculated for each subject in the four experimental conditions.

Statistica 7.0 (Stat Soft Inc., USA, 2004) was used for statistical evaluation. Continuous data were evaluated for normal distribution by the Kolmogorov–Smirnov test. The Mann–Whitney test was used to evaluate the independent variables without normal distribution, and the Fisher exact test was applied for the evaluation of categorical data (%). A $p \leq 0.05$ was accepted as the level of statistical significance.

Results. There were no significant differences among the groups in the main characteristics of the participants (Table 1).

MNSI questionnaire mean score of the subjects with DPN was 5.6±2.1, which was significantly higher than the mean score of subjects with T2DM without DPN: 2.8 ±1.6 (Mann–Whitney U test, $p < 0.05$). No deformities or surface changes in the soles were observed in either of the two diabetic groups. All healthy controls had good vibration perception (100%) and Achilles reflex (grade 3–4). For 80% of the diabetic persons without DPN vibration perception was normal. For 70% of those subjects a weak Achilles reflex in both legs was registred (grade 1–2), for

Table 1

Participants' main characteristics

Variables	T2DM ($n = 20$)	T2DM with DPN ($n = 18$)	Control group ($n = 20$)
Age (years)	52.1 ± 8.4	56.7 ± 6.7	55.2 ± 5.3
Gender (Male/ Female)	7/13	8/10	7/13
Height (cm)	167.4 ± 12.5	165.9 ± 10.3	165.3 ± 14.1
Body mass index	28.4 ± 3.1	31.2 ± 4.6	29.8 ± 2.7
Duration of T2DM (years)	7.5 ± 3.8	10.2 ± 4.1	—
Duration of DPN (years)	—	4.7 ± 2.6	—
HbA_{1C} (%)	7.2 ± 1.3	7.9 ± 1.8	—
Systolic blood pressure [mm Hg]	130 ± 12.3	135.3 ± 9.1	125.5 ± 7.1
Diastolic blood pressure [mm Hg]	80.8 ± 6.4	82.1 ± 10.3	78.7 ± 3.2

Data are presented as mean values ± standard deviation or number of subjects. T2DM – type 2 diabetes mellitus, DPN – diabetic peripheral neuropathy, control group – healthy adults

20% weak positive response of the Achilles reflex was registred when the Jendrassik maneuver was applied and for 10% it was absent. Vibration perception and Achilles reflex were impaired in all persons with DPN. Their vibration perception was decreased (delay in vibration perception was about 15–20 s), the Achilles reflex was absent in 95% of the DPN persons and it was very weak in the remaining 5% when the Jendrassik maneuver was applied.

The mean amplitudes (MA) of postural sway of the two diabetic groups (with and without DPN) were significantly higher in both directions (AP and ML) than the healthy controls' (Mann–Whitney U-test, $p < 0.05$), except for the MA in the ML direction during stance on firm support with open eyes, where significant differences were not observed (Mann–Whitney U-test, $p = 0.08$) (Fig. 1). The MA of both diabetic groups increased with increasing task difficulty. Significant differences between the two diabetic groups were observed in the AP direction during stance on firm support with closed eyes and in the ML direction during stance on foam support with open and closed eyes (Mann–Whitney U-test, $p = 0.08$) (Fig. 1).

The increase of the MA in the control group during stance with closed eyes (in comparison with open eyes) was less than 35% (firm support: AP = 34%, ML = 22%; foam support AP = 19%, ML = 23%). The persons with DPN had the highest increase: about 50% for standing on firm support (AP = 54%, ML = 47%) and even higher on foam support (AP = 63%, ML = 79%). The MA of the diabetic group without DPN increased less with closed eyes (firm support: AP=40%, ML = 24%; foam support: AP = 41%, ML = 49%) but their MA

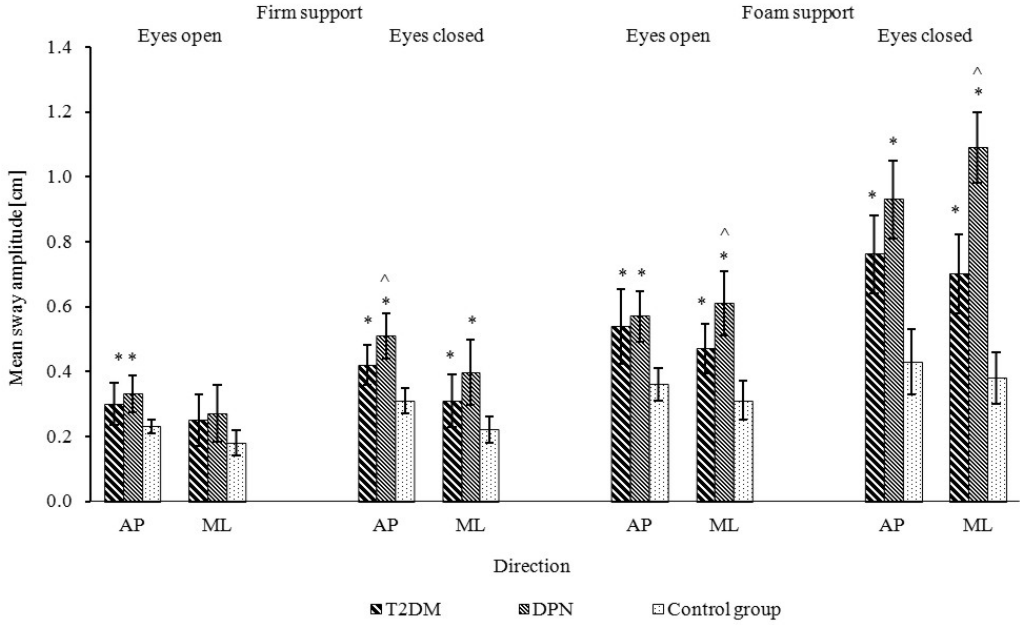

Fig. 1. Mean amplitudes of the centre of pressure displacements in the anterior-posterior (AP) and medial-lateral (ML) directions in 4 experimental conditions for the three investigated groups: T2DM – diabetic adults, without polyneuropathy, DPN – diabetic adults with polyneuropathy, Control group – healthy adults. Differences between groups are shown: $*$ – in comparison with the control group, $\wedge$ – differences between the two diabetic groups (Mann–Whitney U test, level of significance $p < 0.05$)

increase was still greater than the controls', except for the ML direction, where difference was not observed.

The mean sway velocities (MV) in the four experimental conditions are presented in Fig. 2. Significant differences between the diabetic adults and the control group were found in the stance on firm support with closed eyes and in both conditions (open and closed eyes), during stance on foam support for both directions (AP and ML), where the diabetic subjects demonstrated higher MV than the healthy controls (Mann–Whitney U-test, $p < 0.05$). Significant difference between the two diabetic groups was observed in the stance with closed eyes on firm support in the ML direction only, where the adults with DPN showed higher MV than the T2DM subjects without DPN (Mann–Whitney U-test, $p < 0.05$) (Fig. 2). The healthy subjects demonstrated relatively weak visual dependence. Their postural sways increased during stance with closed eyes less than 20% (firm support: AP=18%, ML = 10%; foam support: AP = 3%, ML = 10%). Both diabetic groups showed strong visual dependence, especially during stance on foam support. The changes were as follows: for T2DM – stance on firm support AP = 60%, ML = 61%, on foam support AP = 82%, ML = 96%, and for the DPN

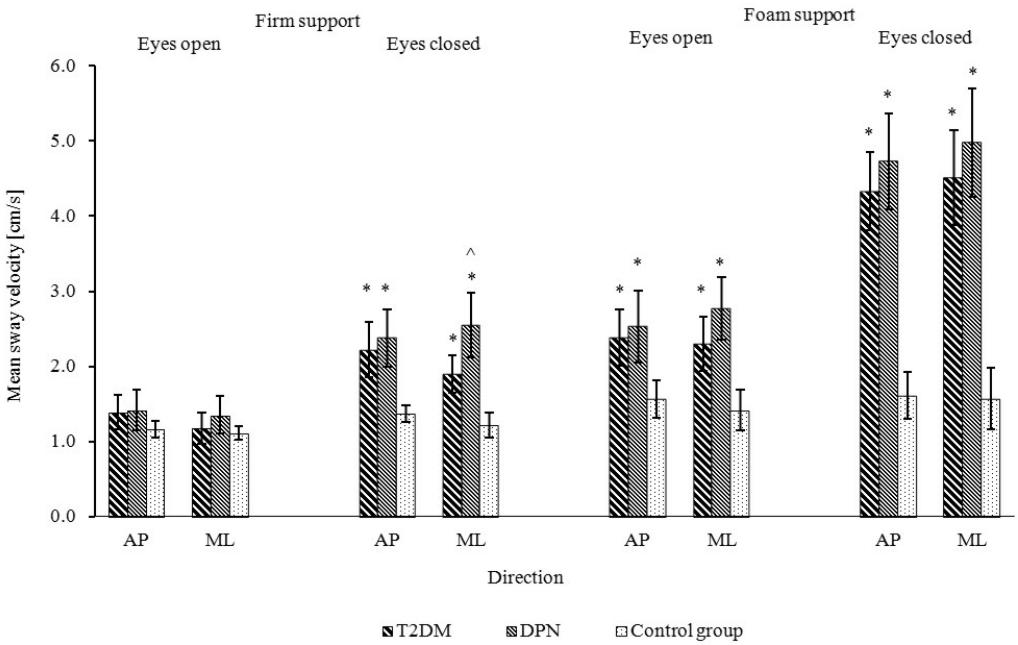

Fig. 2. Mean velocities of the centre of pressure displacements in the anterior-posterior (AP) and medial-lateral (ML) directions in 4 experimental conditions for the three investigated groups: T2DM – diabetic adults, without polyneuropathy, DPN – diabetic adults with polyneuropathy, Control group – healthy adults. Differences between groups are shown: $*$ – in comparison with the control group, $\wedge$ – differences between the two diabetic groups (Mann–Whitney U test, level of significance $p < 0.05$)

subjects – stance on firm support AP = 68%, ML = 89%, on foam support AP = 87%, ML = 79%.

Discussion. The visual, vestibular, and propriceptive systems and their integration in the CNS are essential for maintaining postural balance in upright stance. When one of these sensory inputs is damaged or becomes dysfunctional, the compensatory mechanisms of sensory reorganization are put in action for maintaining balance [16]. The decreased leg proprioception in DPN subjects puts them in a state of permanent sensory conflict and thus disturbed equilibrium, which makes postural instability one of the major characteristics of DPN [1, 2, 4].

During stance on firm support with open eyes – when the afferent information from the three sensory systems actively participates in postural control, the ankle strategy was observed for all investigated subjects (AP sway dominated over the ML sway). In this experimental condition both diabetic groups showed significantly elevated MA of sway in the AP direction only, while significant differences with the controls in the ML direction was not observed. That suggests that the interaction between the visual and vestibular systems offsets the proprioceptive dysfunction in adults with T2DM (with and without DPN). That is in accordance

with the stronger visual dependence for postural stability that we found in both diabetic groups when compared with the healthy controls.

The elevated MV of COP displacements in DNP subjects during stance with provoked sensory conflict is in line with previous reports [7,8]. In those experimental conditions (eyes closed or/and foam support) both diabetic groups showed a significant increase in the MA and MV of postural sway in comparison with the healthy controls. We suggest that the higher MA and MV of subjects with T2DM without DPN are probably due to the fact that T2DM has a long pre-clinical progression before reaching the stage of neuropathy. Long-term elevated blood sugar in adults with T2DM causes a decrease of the peripheral microcirculation, followed by local disruption of blood supply in the nerve fascicules which is the basis for random demyelination, progressing later to the axonal degeneration in DPN.

On the other hand, the maintanance of postural stability is tightly related to activation of the sole mechanoreceptors and the ankle torque. The additionally provoked sensory conflict – by deprivation of vision or stance on soft support, highlights the differences between the two diabetic groups, especially during stance on foam support when the proprioceptive information is additionally altered by the support. The foam support leads to reduced effectiveness of the ankle torque for postural stabilization and provokes changes in the postural control mechanisms and strategy (switching from ankle to hip strategy) [17]. In both diabetic groups that led to increased MA and MV of the postural sway in the ML direction, even during stance with open eyes.

Petrovic et al. [18] established structural abnormalities within the Achilles tendon of diabetic individuals leading to stiffness and inability to apply ankle torque for effective postural control. These structural and functional changes could explain the similarities in postural behaviour that we observed in the two diabetic groups, reflected by increased MV in the ML direction and changes in the postural control strategy for maintaining equilibrium.

Conclusion. A better understanding of the changes in postural stability of persons with T2DM would contribute to the establishment of training programmes for reducing the risk of unexpected falls, especially in the geriatric population.

REFERENCES

[1] Ahmmed A. U., I. J. Mackenzie (2003) Posture changes in diabetes mellitus, J. Laryngol. Otol., **117**, 358–364.

[2] El Bardawil M., M. Abd El Hamid, N. A. El Sawy, M. H. Megallaa, W. S. El Emary (2013) Postural control and central motor pathway involvement in type 2 diabetes mellitus: dynamic posturographic and electrophysiologic studies, Alexandria Journal of Medicine, **49**(4), 299–307.

[3] Prieto T., R. Hoffmann, E. Lovett, M. Myklebust (1996) Measures of Postural Steadiness: Differences between Healthy Young and Elderly Adults, IEEE Transaction on Biomedical Engineering, **43**(9), 956—966.
[4] Giacomini P. G., E. Bruno, G. Monticone, S. DiGirolamo, A. Magrini et al. (1996) Postural rearrangement in IDDM patients with peripheral neuropathy, Diabetes Care, **19**, 372–374.
[5] Emam A. A., A. M. Gad, M. M. Ahmed, H. S. Assal, S. G. Mousa (2009) Quantitative assessment of posture stability using computerized dynamic posturography in type 2 diabetic patients with neuropathy and its relation to glycaemic control, Singapore Med. J., **50**, 614–618.
[6] Fioretti S., M. Scocco, L. Ladislao, G. Ghetti, R. A. Rabini (2010) Identification of peripheral neuropathy in type-2 diabetic subjects by static posturography and linear discriminant analysis, Gait Posture, **32**, 317–320.
[7] Boucher P., N. Teasdale, R. Courtemanche, C. Bard, M. Fleury (1995) Postural stability in diabetic Polyneuropathy, Diabetes Care, **18**, 638–645.
[8] Uccioli L., P. Giacomini, P. Pasqualetti, S. Di Girolamo, P. Ferrigno et al. (1997) Contribution of central neuropathy to postural instability in IDDM patients with peripheral neuropathy, Diabetes Care, **20**, 929–934.
[9] Simoneau G. G., J. S. Ulbrecht, J. A. Derr, M. B. Becker, P. R. Cavanagh (1994) Postural instability in patients with diabetic sensory neuropathy, Diabetes Care, **17**, 1411–1421.
[10] Vaz M. M., G. C. Costa, J. G. Reis et al. (2013) Postural control and functional strength in patients with type 2 diabetes mellitus with and without peripheral neuropathy, Arch. Phys. Med. Rehabil., **94**(12), 2465–2470.
[11] Yamamoto R., T. Kinoshita, T. Momoki, T. Arai, A. Okamura et al. (2001) Postural sway and diabetic peripheral neuropathy, Diabetes Res. Clin. Pract., **52**, 213–221.
[12] Feldman E. L., M. J. Stevens, P. K. Thomas, M. B. Brown, N. Canal et al. (1994) A practical two-step quantitative clinical and electrophysiological assessment for the diagnosis and staging of diabetic neuropathy, Diabetes Care, **17 (**11), 1281–1289.
[13] Herman W. H., R. Pop-Busui, B. H. Braffett, C. L. Cleary, P. A. Albers et al. (2012) Use of the Michigan Neuropathy Screening Instrument as a measure of distal symmetrical peripheral neuropathy in Type 1 diabetes: results from the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications, Diabet. Med., **29**(7), 937–944.
[14] Weiner W. J., C. G. Goetz, R. K. Shin, S. L. Lewis (2010) Neurology for the Non-Neurologist, Lippincott Williams & Wilkins, pp 499–502.
[15] Stambolieva K. (2011) Fractal properties of postural sway during quiet stance with changed visual and proprioceptive inputs, J. of Physiol. Sci., **61**, 123–130.
[16] Massion J. (1994) Postural control system, Curr. Opin. Neurobiol., **4**, 877–887.
[17] Shumway-Cook A., F. Horak (1986) Assessing the influence of sensory interaction on balance, Phys. Ther., **66**, 1548–1559.
[18] Petrovic M., C. N. Maganaris, K. Deschamps, S. M. Verschueren, F. L. Bowling et al. (2018) Altered Achilles tendon function during walking in people with diabetic neuropathy: implications for metabolic energy saving, J. Appl. Physiol., **124**, 1333–1340.

Department of Cognitive Psychophysiology
Institute of Neurobiology
Bulgarian Academy of Sciences
Akad. G. Bonchev St, Bl. 23
1113 Sofia, Bulgaria
e-mail: mariya_kav@yahoo.com
kat_kirilova@abv.bg
katerina_stambolieva@yahoo.com

[*] *Department of Neurology*
National Transport Hospital "Tzar Boris III"
108 Knyaginya Mariya-Luiza Blvd
1233 Sofia, Bulgaria

[**] *Clinic of Neurology*
UMHAT "Alexandrovska"
Medical University
1 St. Georgy Sofiiski St
1431 Sofia, Bulgaria
e-mail: g_angov@yahoo.com