ELMER PRESS

Original Article

J Neurol Res. 2023;13(1):50-55

Measurement of Electrophysiology, Sexual Dysfunction, and Cognitive Impairment in Patients With Diabetes Referred for Neuropathy Symptoms: A Case-Control Study

Leila Simani[a], Muhanna Kazempour[b], Mahtab Ramezani[c, d], Faezeh Maghsudloo[c], Hasan Kazazi[e], Sahar Abedi[c], Zahra Fatehi[e], Fatemeh Ghorbani[a], Ehsan Karimialavijeh[d, f, g]

Abstract

Background: The association between diabetic neuropathy, cognitive impairment, and sexual dysfunction together in patients with diabetes mellites (DM) is not assessed in prior studies. This study aimed to investigate the association between all these microvascular complications of DM.

Methods: A cross-sectional study was conducted on 162 participants (110 diabetic patients and 52 non-diabetic subjects). Neuropathy was evaluated by neuropathy disability score (NDS) and neuropathy symptom score (NSS). Nerve conduction study (NCS), sural and radial sensory nerve action potential, sural/radial nerve amplitude ratio (SRAR), and tibial compound muscle action potential were measured. Participants underwent cognitive and sexual assessments by Montreal cognitive assessment (MoCA), Beck depression score, female sexual function index, and the male sexual function index questionnaires.

Results: Both groups showed a decline in cognitive functions; however, diabetic patients had a significantly lower score in MoCA compared to the non-diabetic group (mean ± standard deviation: 20.98 ± 5.07, 23.17 ± 4.47; P value < 0.001). No statistical difference was observed regarding sexual activity (P value = 0.12 and 0.39 for female and male sexual function index), and Beck score (mean ± standard deviation: 8.56 ± 6.47, 8.96 ± 4.74; P value = 0.451) between the two groups. The NCS parameters were notably different in both groups. There were no differences between NCS, NDS, and NSS findings and sexual function.

Conclusions: Our data suggest that NCS parameters, even SRAR, do not necessarily correlate with cognitive performance and sexual function. Sexual dysfunction was not correlated with diabetic neuropathy, but clinical findings of NDS and NSS showed a modestly negative correlation with cognitive function.

Keywords: Diabetes mellitus; Neuropathy; Sexual dysfunction; Cognition; Nerve conduction study

Manuscript submitted April 1, 2023, accepted May 13, 2023
Published online August 8, 2023

[a]Skull Base Research Center, Loghman Hakim Hospital, Shahid Beheshti University of Medical Science, Tehran, Iran
[b]Department of Rheumatology, Loghman Hakim Hospital, Shahid Beheshti University, Tehran, Iran
[c]Brain Mapping Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[d]Tehran University of Medical Sciences, Tehran, Iran
[e]School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[f]Khoula Hospital, Ministry of Health, Muscat, Oman
[g]Corresponding Author: Ehsan Karimialavijeh, Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran. Email: e-karimi@tums.ac.ir

doi: https://doi.org/10.14740/jnr752

Introduction

Diabetes mellitus (DM) is a common metabolic disorder worldwide and has been rising rapidly, especially in low- and middle-income countries [1]. Diabetic patients frequently develop microvascular complications such as nephropathy, retinopathy, peripheral neuropathy (PN), and sexual and cognitive disorders due to capillary dysfunction and metabolic disturbances [2]. All of these can affect the quality of life and impose a considerable social burden. Up to 50% of people with diabetes have some form of PN. Diabetic sensorimotor polyneuropathy (DSPN) is the most common type, which can lead to significant disability [3]. A large number of screening and diagnostic tools are introduced to diagnose DSPN, including electrophysiological studies and standard questionnaires [4]. The findings of the nerve conduction study (NCS) provide objective data for confirmation and diagnosis of diabetic neuropathy [5].

The sexual health of diabetic patients has often been overlooked. Sexual dysfunction (SD) could be a result of central nervous system dysfunction, autonomic or peripheral nerve damage, psychogenic causes, medications, or a combination of these factors [6]. SD in male and female patients with DM is reported in various studies [6, 7]. In addition, anxiety and depression are prevalent among patients with SD [8].

Cognitive dysfunction (CD) is one of the major comorbidities in diabetic patients, which may reflect microvascular brain damage as a consequence of diabetes [9]. People with type 2 diabetes mellitus (T2DM) have approximately 60%

greater risk of development of cognitive problems compared with non-diabetes equivalents [10]. Prior data have shown that multiple cognitive domains including psychomotor speed, memory, executive function, and attention are impaired in T2DM patients [11].

No study has assessed the association between diabetic neuropathy, cognitive impairment, and SD together. we aimed to investigate the association between electrophysiological findings of neuropathy and CD and SD.

Materials and Methods

Participants

In this observational study, patients with diagnosed T2DM, who were referred to our university-affiliated electrodiagnostic (EDx) laboratory for the investigation of polyneuropathy between September 2021 and August 2022, were recruited. All patients above 45 years with a minimum of 5 years of education (primary school - secondary school - high school - university) were included in this study. Patients with a history of head trauma, cerebral palsy, intellectual disability, dementia or neurodegenerative disease (such as epilepsy, multiple sclerosis, and Parkinsonism), malignancy, previously documented psychiatric and sleep disorders, those who had an acute systemic disease (endocrine disorder, fluid-electrolyte imbalance, and infection), users of medications (neuroleptics, benzodiazepine, and antidepressant) that may cause cognitive impairment, severe hearing and visual problems, substance and alcohol users, pregnant women and lactating women were excluded. Non-diabetic individuals matched for age and sex who were referred to the EDx study served as a comparison group.

Clinical examination and laboratory measurements

All patients completed a self-administered questionnaire, which addressed diabetes duration, a history of hypertension, ischemic heart disease and medications including neuroleptics, benzodiazepine, and antidepressant. A research nurse calculated the body mass index (BMI) and blood pressure of participants in a sitting position for 10 min. Peripheral venous blood was sent for routine laboratory tests including hemoglobin A1C (HbA1C) under fasting conditions.

Neurological assessment

The neuropathy symptom score (NSS) questionnaire [12] that is an assessment of four major items that measures the presence, localization, time of appearance, and improvement of neuropathy symptoms, was completed by all participants. The total score ranges from 0 to 10, and the score of 3 - 4, 5 - 6, and 7 - 10 serve as mild, moderate, and severe neuropathy symptoms, respectively. The neuropathy disability score (NDS) questionnaire was completed by an expert neurologist. The NDS grades neuropathy from 0 (no neuropathy) to 28 (severe neuropathy) [13]. A score of 0 - 2 was defined as "no neuropathy," score of 3 or more were considered as "neuropathy".

An experienced neurologist performed EDx studies in a quiet room while the participants skin temperature was stabilized to approximately 31 °C. A system from Negar Andishgan Ltd®. EMG/NCV/EP 5000Q was used for electromyographic measurements of the nerve conduction velocity (NCV). Sensory nerve action potential (SNAP) was antidromically recorded from bilateral sural and superficial radial nerves. The mean amplitude of both sides and sural/radial nerve amplitude ratio (SRAR) was measured for all subjects. Additionally, compound muscle action potential (CMAP) was documented from both tibial nerves recording abductor hallucis brevis muscle, and the mean tibial conduction velocity (CV), mean tibial distal latency (DL) and mean amplitude were calculated.

Cognitive assessment

Montreal cognitive assessment (MoCA) is a widespread and concise screening tool for the assessment of cognitive impairment that has had a significant impact on the evaluation of age-related cognitive decline. The MoCA is a 30-item test that allows healthcare providers to discover cognitive impairment. The test checks language, memory, visual, and spatial thinking, reasoning, and orientation skills and the scores range from 0 to 30. A score of 26 and higher is considered normal. In the initial study data, normal controls had an average score of 27.4. People with mild cognitive impairment (MCI) scored an average of 22.1. People with Alzheimer's disease had an average score of 16.2 [14].

Beck depression inventory (BDI) is a 21-question multiple-choice self-report inventory, one of the most widely used instruments for measuring the severity of depression. A value of 0 to 3 is assigned for each answer and then the total score is compared to the key score to determine the depression's severity. The standard cutoffs are as follows: (0 - 10) normal, (11 - 16) mild mood disturbance, (17 - 20) borderline clinical depression, (21 - 30) moderate depression, (31 - 40) severe depression, over 40 extreme depressions.

Sexual activity assessment

We used the female sexual function index (FSFI) and the male sexual function index (MSFI) questionnaires for evaluating SD in both patients and control groups. The FSFI is a 19-item self-report questionnaire assessing the six domains of sexual function in women including desire, arousal, lubrication, orgasm, satisfaction, and pain; and the MSFI is a 16-item self-report questionnaire evaluating five domains containing desire, arousal, erection, orgasm, and satisfaction over the previous 30 days. The full-scale score range is between 2 - 36 [15].

Statistical analysis

Statistical analyses were performed using SSPS version 22.0

Table 1. Clinical Features of Study Participation

Variables	Neuropathy diabetes (n = 110)	Non-diabetic controls (n = 52)	P value
Sex			
Male/female, n (%)	57 (51.8)/53 (48.2)	20 (38.5)/32 (61.5)	0.112
Comorbidity			
Hypertension, n (%)	53 (48.6)	8 (15.4)	0.001
IHD, n (%)	23 (21.1)	2 (3.8)	0.001
Age	57.96 ± 9.75	55.57 ± 10.53	0.158
BMI (kg/m^2)	31.2 ± 5.4	30.1 ± 6.2	0.2
Duration of disease	10.51 ± 7.17	-	-
Beck score	8.56 ± 6.47	8.96 ± 4.74	0.451
MoCA	20.98 ± 5.07	23.17 ± 4.47	0.001
Sexual activity			
FSFI	11.03 ± 8.13	14.05 ± 9.46	0.122
Desire	3.23 ± 1.32	3.05 ± 1.44	0.438
Arousal	2.27 ± 2.02	2.86 ± 2.30	0.119
Lubrication	1.19 ± 1.27	1.47 ± 1.34	0.341
Orgasm	1.76 ± 1.75	2.15 ± 1.85	0.338
Satisfaction	2.23 ± 1.84	2.36 ± 1.87	0.667
Pain	1.23 ± 1.57	1.41 ± 1.50	0.609
MSFI	15.10 ± 8.05	17.2 ± 12.5	0.395
Desire	3.23 ± 1.23	3.05 ± 1.44	0.438
Arousal	2.27 ± 2.02	2.86 ± 2.30	0.119
Erection	1.96 ± 1.68	1.75 ± 1.68	0.636
Orgasm	2.23 ± 1.84	2.36 ± 1.87	0.667
Satisfaction	3.17 ± 2.26	3.60 ± 2.36	0.275

Data were expressed as n (%) or mean ± standard deviation. IHD: ischemic heart disease; BMI: body mass index; MoCA: Montreal cognitive assessment; FSFI: female sexual function index, MSFI: male sexual function index.

(SPSS, Inc., Chicago, IL, USA). To compare the diabetic patients with non-diabetic controls, basic characteristics, including frequency of males and females and frequency of comorbid diseases (hypertension and ischemic heart disease), were analyzed using the Chi-square test. For numerical variables including age, duration of disease, Beck score, MoCA, FSFI, MSFI, and NCS parameters, mean ± standard deviation was calculated, and the Kolmogorov-Smirnov test was used to confirm the normal distribution of the data. Then, values were compared between the two groups using the independent *t*-test. Finally, to assess the correlation between SRAR, NSS, and NDS values, the Pearson correlation coefficient and Spearman rank coefficient were applied. A P value < 0.05 was considered statistically significant.

Ethics approval

The study was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences, Tehran, Iran (ethics committee number: IR.SBMU.RETECH.RCE.1399.641). The study was conducted in compliance with the ethical standards of the responsible institution on human subjects as well as with the Helsinki Declaration.

Results

Demographic and clinical data for the subjects included in the study are shown in Table 1. A total of 110 patients with diabetes, 57 men and 53 women with a mean age of 58.57 ± 9.64 years, were included in the study. The comparison group consisted of 52 non-diabetic subjects, 20 men and 32 women with 55.73 ± 10.46 years on average. No differences were found between patients and non-diabetic controls for age, sex, as well as Beck depression score. The patients had a significant vascular risk factor including hypertension and ischemic heart disease compared with non-diabetic subjects. The mean ± standard deviation of HbA1c (%) among patients with diabetes was 7.5 ± 1 and only 12 (10.9%) patients had HbA1C level > 7%.

Table 1 shows the cognitive performance and sexual activity in diabetic patients compared to the comparison group. Although our findings revealed that both groups had low cog-

Table 2. NCS Parameters

Variables	Patients	Non-diabetic controls	P value*
NSS	5.83 ± 2.40	1.72 ± 1.96	0.001
NDS	4.11 ± 2.45	0.43 ± 1.02	0.001
SRAR	0.27 ± 0.19	0.56 ± 0.1	0.001
Mean tibial conduction velocity	35.00 ± 16.04	44.75 ± 3.55	0.001
Mean tibial distal latency	5.12 ± 0.92	4.42 ± 0.68	0.001
Mean tibial CMAP amplitude	10.32 ± 14.89	5.34 ± 1.84	0.001
Mean sural amplitude	6.75 ± 5.75	15.32 ± 4.5	0.001
Mean radial sensory amplitude	20.82 ± 8.35	27.02 ± 7.33	0.001

Data are expressed as mean ± standard deviation. *P < 0.05. NCS: nerve conduction study; NSS: neuropathy symptom score; NDS: neuropathy disability score; SRAR: sural/radial nerve amplitude ratio; CMAP: compound muscle action potential.

nitive scores in MoCA, the patients had a significantly lower level of cognitive performance compared to the control group (P < 0.001). In the patients with diabetes, 55 patients (50%) were with MCI and 32 (29.1%) with mild dementia compared to 25 (48.1%) with MCI and nine (17.3%) with mild dementia in the control subjects. No differences were observed between the two groups for sexual activity.

As demonstrated in Table 2, there was a significant difference between scores of NCS in both groups (P = 0.001). Since hypertension and ischemic heart disease can be linked to neuropathy and CD, we conducted analysis of covariance (ANCOVA) to determine the possible confounding effects of hypertension and ischemic heart disease on variables of NCS and MoCA. This analysis demonstrated similar results, even after considering hypertension and ischemic heart disease as confounding factors.

According to our results in overall population, there was a significant reverse association between SRAR and severity of NSS and NDS, also a reverse association in each group was observed (Table 3). There was no significant association between MoCA and SRAR. Among patients, a weak negative correlation was observed between NDS, NSS, and MoCA score (r: -0.219; P = 0.02, r: -0.252; P = 0.01, respectively). We found no statistical differences between NCS parameters and sexual function.

Discussion

Microvascular complications of DM are prevalent despite advances in diabetes prevention and treatment. The present study attempted to identify associations between clinical findings of SD and CD and quantitative aspects of axonal loss in T2DM patients.

Our findings showed that diabetic patients have a significantly lower score on MoCA compared with non-diabetic subjects, but we found no correlation between CD based on MoCA score and objective NCS findings. CD in individuals with DM can manifest as MCI and dementia [16]. A growing body of evidence has linked diabetes with CD [16-18], We expect that DM with PN to be more associated with CD than DM alone. However, the information about the association of PN and CD is different. A retrospective cohort study containing 94 diabetic participants revealed that diabetic people have poorer cognitive performance, but the CD is not correlated with the severity of neuropathy based on NSS and NDS scores [19]. A recent study demonstrated that although cognitive scores are lower in patients with diabetes, the presence of PN adds no more cognitive decline. The PN is assessed by questionnaire and EDx findings of median, ulnar, and peroneal nerves [20]. Lin et al in their cross-sectional study of 828 participants using neurofilament examination of both feet, showed that the severity of PN is significantly negatively correlated with cognitive performance [21]. This result indicates that CD in patients with diabetes may not be limited to microvascular damage of the brain [22]. In fact, recent data strongly imply that both vascular and neurodegenerative pathologies are associated with cognition in diabetic individuals [9, 23].

In the current study, we analyzed the severity of neuropathy using diabetic neuropathy questionnaires as well as quantitative data of NCS together to increase the sensitivity of results. According to previous research sural SNAP amplitude and the SRAR are probably useful parameters for differentiating normal subjects from those with distal polyneuropathy,

Table 3. Correlation Between SRAR and NSS and NDS

	SRAR					
	Total		Patients		Comparison	
	r	P*	r	P*	r	P*
NSS	-0.848	0.001	-0.811	0.001	-0.398	0.012
NDS	-0.856	0.001	-0.795	0.001	-0.44	0.005

*P < 0.05. NSS: neuropathy symptom score; NDS: neuropathy disability score; SRAR: sural/radial nerve amplitude ratio.

especially when age adjustment is performed [24, 25]. Moreover, we observed a negative correlation between NDS, NSS, and MoCA scores; however, this correlation is weak, which implies increasing in sample size is warranted.

Although our findings show diabetic patients do have a worse cognitive function, the control group obtained lower scores as well. Since there was no statistical difference in Beck depression scores between the two groups, this finding may be due to mood disorders or aging effect on cognition [26].

Also, our results indicate no correlation between NCS parameters and sexual function in DM patients. Prior data showed reverse results based on evaluating neuropathy by physical examination. A recent cross-sectional analysis of 1,213 men (206 men with diabetes), assessing erectile dysfunction and PN by a single question self-interview and 10-g monofilament testing, respectively, showed decreased lower extremity sensation is a risk factor for erectile dysfunction in both diabetes and non-diabetes people [27]. A similar study in Japan demonstrated a positive correlation between diabetic neuropathy and severe erectile dysfunction [28]. Moreover, our different results may be as a consequence of small fiber neuropathy-induced sexual impairment, which preserved large fibers and NCS findings [29].

We found no differences regarding SD between the two groups. This finding may be a result of a low Beck depression score in all participants, which is in agreement with previous studies [30].

Our study has several limitations: first, our limited sample size prevented further psychological and neurocognitive evaluations in a different subgroup of DM patients. Future studies should pay particular attention to possible confounding factors such as current life stress and ensure a sufficiently large sample size to take large inter-individual variance into account. Second, although cognitive impairment is not considered a specific feature in patients with DM, a complete neuropsychological assessment is lacking. Third, our hospital is in an area of the city that covers a population with low socio-economic status and lower levels of education, and this might have affected the results of their cognitive performance test. Finally, HbA1C reflects the glycemic status within the last 3 months, to correlate the effect of glycemic control on the NCV findings and overall symptoms in patients with diabetes, we need to conduct a prospective study and check HbA1c in several time points to get a broader view of the glycemic status of the patients.

Conclusions

This study showed that NCS measures of nerve fiber functions, even SRAR, do not necessarily correlate with cognitive performance and sexual function. However, clinical assessments of neuropathy, including NDS and NSS, were negatively correlated with cognitive function.

Acknowledgments

We would like to extend our gratitude to all the staff at the Neurology Clinic of Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran for their cooperation during conducting this research. We also thank the Clinical Research Development Unit (CRDU) of Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences Tehran, Iran for their assistance in this research.

Financial Disclosure

This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

Conflict of Interest

The authors have declared that there is no conflict of interest.

Informed Consent

Consent to publish is obtained from the participants of this study through informed written consent.

Author Contributions

LS and MK: conceptualization, methodology, project administration, supervision. MR: data curation, formal analysis, methodology, validation, editing. FM and SA: data collection, writing the original draft. ZF, FG, and HK: data collection. EK: final revision, review and editing.

Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

References

1. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. Nat Rev Endocrinol. 2018;14(2):88-98. doi pubmed
2. Ogurtsova K, da Rocha Fernandes JD, Huang Y, Linnenkamp U, Guariguata L, Cho NH, Cavan D, et al. IDF Diabetes Atlas: Global estimates for the prevalence of diabetes for 2015 and 2040. Diabetes Res Clin Pract. 2017;128:40-50. doi pubmed
3. Feldman EL, Callaghan BC, Pop-Busui R, Zochodne DW, Wright DE, Bennett DL, et al. Diabetic neuropathy. Nature Reviews Disease Primers. 2019;5(1):1-18.
4. Petropoulos IN, Ponirakis G, Khan A, Almuhannadi H, Gad H, Malik RA. Diagnosing diabetic neuropathy: something old, something new. Diabetes Metab J. 2018;42(4):255-269. doi pubmed pmc
5. Zochodne D, Malik R. Electrophysiologic testing in diabetic neuropathy. Diabetes and the Nervous System.

2014:235.
6. Rahmanian E, Salari N, Mohammadi M, Jalali R. Evaluation of sexual dysfunction and female sexual dysfunction indicators in women with type 2 diabetes: a systematic review and meta-analysis. Diabetol Metab Syndr. 2019;11:73. doi pubmed pmc
7. Kouidrat Y, Pizzol D, Cosco T, Thompson T, Carnaghi M, Bertoldo A, Solmi M, et al. High prevalence of erectile dysfunction in diabetes: a systematic review and meta-analysis of 145 studies. Diabet Med. 2017;34(9):1185-1192. doi pubmed
8. Cooper S, Leon N, Namadingo H, Bobrow K, Farmer AJ. "My wife's mistrust. That's the saddest part of being a diabetic": A qualitative study of sexual well-being in men with Type 2 diabetes in sub-Saharan Africa. PLoS One. 2018;13(9):e0202413. doi pubmed pmc
9. Biessels GJ, Despa F. Cognitive decline and dementia in diabetes mellitus: mechanisms and clinical implications. Nat Rev Endocrinol. 2018;14(10):591-604. doi pubmed pmc
10. Chatterjee S, Peters SA, Woodward M, Mejia Arango S, Batty GD, Beckett N, Beiser A, et al. Type 2 diabetes as a risk factor for dementia in women compared with men: a pooled analysis of 2.3 million people comprising more than 100,000 cases of dementia. Diabetes Care. 2016;39(2):300-307. doi pubmed pmc
11. Kim HG. Cognitive dysfunctions in individuals with diabetes mellitus. Yeungnam Univ J Med. 2019;36(3):183-191. doi pubmed pmc
12. Veves A, Manes C, Murray HJ, Young MJ, Boulton AJ. Painful neuropathy and foot ulceration in diabetic patients. Diabetes Care. 1993;16(8):1187-1189. doi pubmed
13. Yang Z, Chen R, Zhang Y, Huang Y, Hong T, Sun F, Ji L, et al. Scoring systems to screen for diabetic peripheral neuropathy. Cochrane Database Syst Rev. 2018;2018(7):CD010974.
14. Bosco A, Caffo AO, Spano G, Lopez A. Beyond the cut-offs: A Bayesian approach to the use of the Montreal cognitive assessment as a screening tool for mild cognitive impairment and dementia. Diagnosis and Management in Dementia: Elsevier. 2020. p. 395-410.
15. Rosen R, Brown C, Heiman J, Leiblum S, Meston C, Shabsigh R, Ferguson D, et al. The Female Sexual Function Index (FSFI): a multidimensional self-report instrument for the assessment of female sexual function. J Sex Marital Ther. 2000;26(2):191-208. doi pubmed
16. Xue M, Xu W, Ou YN, Cao XP, Tan MS, Tan L, Yu JT. Diabetes mellitus and risks of cognitive impairment and dementia: A systematic review and meta-analysis of 144 prospective studies. Ageing Res Rev. 2019;55:100944. doi pubmed
17. Brognara L, Volta I, Cassano VM, Navarro-Flores E, Cauli O. The association between cognitive impairment and diabetic foot care: role of neuropathy and glycated hemoglobin. Pathophysiology. 2020;27(1):14-27. doi pubmed pmc
18. Umegaki H, Kawamura T, Umemura T, Kawano N. Factors associated with cognitive decline in older adults with type 2 diabetes mellitus during a 6-year observation. Geriatr Gerontol Int. 2015;15(3):302-310. doi pubmed
19. Moreira RO, Soldera AL, Cury B, Meireles C, Kupfer R. Is cognitive impairment associated with the presence and severity of peripheral neuropathy in patients with type 2 diabetes mellitus? Diabetol Metab Syndr. 2015;7:51. doi pubmed pmc
20. Elsharkawy RE, Abdel Azim GS, Osman MA, Maghraby HM, Mohamed RA, Abdelsalam EM, Ebrahem EE, et al. Peripheral polyneuropathy and cognitive impairment in type ii diabetes mellitus. Neuropsychiatr Dis Treat. 2021;17:627-635. doi pubmed pmc
21. Lin YJ, Kao TW, Chen WL. Relationship between peripheral neuropathy and cognitive performance in the elderly population. Medicine (Baltimore). 2021;100(20):e26071. doi pubmed pmc
22. Ba-Tin L, Strike P, Tabet N. Diabetic peripheral microvascular complications: relationship to cognitive function. Cardiovasc Psychiatry Neurol. 2011;2011:723434. doi pubmed pmc
23. Frison E, Proust-Lima C, Mangin JF, Habert MO, Bombois S, Ousset PJ, Pasquier F, et al. Diabetes Mellitus and Cognition: Pathway Analysis in the MEMENTO Cohort. Neurology. 2021;97(8):e836-e848. doi pubmed pmc
24. Papanas N, Trypsianis G, Giassakis G, Vadikolias K, Christakidis D, Piperidou H, Efstratiadis G, et al. The sural sensory/radial motor amplitude ratio for the diagnosis of peripheral neuropathy in type 2 diabetic patients. Hippokratia. 2010;14(3):198-202. pubmed pmc
25. Guo Y, Palmer JL, Brown XS, Fu JB. Sural and Radial Sensory Responses in Patients with Sensory Polyneuropathy. Clin Med Rev Case Rep. 2015;2(3):049. doi pubmed pmc
26. Murman DL. The Impact of Age on Cognition. Semin Hear. 2015;36(3):111-121. doi pubmed pmc
27. Hicks CW, Wang D, Windham BG, Selvin E. Association of Peripheral Neuropathy with Erectile Dysfunction in US Men. Am J Med. 2021;134(2):282-284. doi pubmed pmc
28. Furukawa S, Sakai T, Niiya T, Miyaoka H, Miyake T, Yamamoto S, Maruyama K, et al. Diabetic peripheral neuropathy and prevalence of erectile dysfunction in Japanese patients aged <65 years with type 2 diabetes mellitus: The Dogo Study. Int J Impot Res. 2017;29(1):30-34. doi pubmed
29. Dhage S, Ho JH, Ferdousi M, Kalteniece A, Azmi S, Adam S, Marshall A, et al. Small fibre pathology is associated with erectile dysfunction in men with type 2 diabetes. Diabetes Metab Res Rev. 2020;36(3):e3263. doi pubmed
30. Thakurdesai A, Sawant N. A prospective study on sexual dysfunctions in depressed males and the response to treatment. Indian J Psychiatry. 2018;60(4):472-477. doi pubmed pmc