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Relationship between Diabetic Peripheral Neuropathy and Cognitive Functions

AHMED H. MOKHTAR, M.Sc.*; NAWAL A. ABU SHADY, Ph.D.*; ASHRAF A. DARWESH, PhD.*; AMIRA A. LABIB, M D.**; HEBA R. AHMED, MD.*** and LAMIS S. MUBARAK, MD.***

The Department Neurology, Faculty of Physical Therapy, Cairo University, Department of Clinical Neurophysiology**, Faculty of Medicine, Cairo University and The National Institute of Diabetes & Endocrinology in Cairo, Egypt****

Abstract

Background: Diabetic neuropathy (DN) is a sensorimotor polyneuropathy that is symmetrical and length-dependent and is caused by metabolic and microvascular alterations due to prolonged exposure to hyperglycemia and concomitant cardiovascular risk factors. Diabetes is associated with cognitive disorders, including reductions in cognitive function and an increased risk of dementia.

Aim of Study: This study aims to investigate the relationship between diabetic peripheral neuropathy and cognitive functions.

Subjects and Methods: 50 patients with diabetic peripheral neuropathy were recruited from the National Institute of diabetes and Endocrinology and outpatient clinic of Neurology, Faculty of Physical Therapy, Cairo University. The recruitment included both genders in the sample. Various assessments and measurements were conducted, including the use of a general and specific neurological evaluation sheet to gather comprehensive neurological information. Cognitive functions were assessed using the Montreal Cognitive Assessment (MoCA). Additionally, a neurophysiological study involving motor (Rt. Ulnar and Rt. Common peroneal) and sensory (Rt. Sural and Rt. Ulnar) conduction studies was performed to obtain objective measurements of nerve conduction velocity, amplitude and distal latency, contributing to the assessment of neuropathy.

Results: The results revealed a significant positive strong correlation between sensory nerve parameters, including amplitude and conduction velocity, and MoCA scores. Aslo, there was a negative strong correlation between sensory nerve peak latency and MoCA scores. Additionally, a strong positive correlation was observed between motor nerve parameters, such as amplitude and conduction velocity, and MoCA scores. Also, there was a negative strong correlation between motor nerve distance latency and MoCA scores.

Conclusion: Findings indicate that higher sensory and motor nerve function, as measured by amplitude and conduction velocity, are associated with better cognitive performance, while longer peak latency and distance latency are linked to poorer cognitive function, Moreever the long duration of illness of diabetic neuropathy is associated with the impairment of cognitive function.

Key Words: *Diabetic neuropathy — Electrophysiological study — Cognitive functions.*

Correspondence to: Dr. Ahmed H. Mokhta,
E-Mail: Dr.ahmedmokhtar95@gmail.com

Introduction

DIABETES is a long-term metabolic condition characterized by high levels of blood glucose, which can lead to serious damage to the heart, blood vessels, eyes, kidneys, and nerves over time. The most common form is type 2 diabetes, typically occurring in adults, where the body either becomes resistant to insulin or doesn't produce enough insulin **[1].**

Diabetic neuropathy (DN) is a type of nerve damage that occurs as a result of prolonged exposure to high blood sugar levels and associated cardiovascular risks. It is described as a symmetric, length-dependent sensorimotor polyneuropathy caused by metabolic and microvascular changes [2].

DN primarily affects the feet and legs in a chronic, progressive manner, typically presenting as a distal, symmetrical, sensory polyneuropathy. It affects up to 50% of diabetic patients and is considered the most common complication of diabetes it is estimated that approximately 40% to 50% of individuals with diabetes will develop detectable DN within 10 years of diagnosis [3].

Cognition refers to the mental process of acquiring knowledge, and cognitive disorders (CDs) encompass a range of mental health conditions that primarily impact cognitive functions. This category

includes disorders such as dementia, amnesia, and motor skill impairments **[4].**

Diabetes mellitus is associated with a decline in cognitive function and changes in brain structure. Individuals with both type 1 and type 2 diabetes have been found to exhibit mild to moderate reductions in cognitive function compared to those without diabetes, as measured by neuropsychological tests. Type 2 diabetes (T2DM) has also been linked to a 50% increased risk of developing dementia **[5].**

Electrodiagnostic (EDX) testing can be performed to understand the etiology, severity, prognosis, and possible treatment options for peripheral neuropathy. It can identify the primary characteristics of the neuropathy as axonal, demyelinating, sensory, motor, multifocal, or diffuse; however, there is often overlap **[6].**

Material and Methods

Study design:

This is a cross sectional observational study conducted to investigate the relationship between diabetic peripheral neuropathy and cognitive function. This study was carried out in national institute of diabetes and endocrinology Cairo, in the period from December 2022 to May 2023. This study protocol was approved by the Research Ethics Committee of the Faculty of physical therapy, Cairo University, Giza, Egypt (approval number: No:P.T.REC/012/004385), this study was conducted between December 2022 to May 2023. All participants were thoroughly explained the study's methods and objectives, and they were asked to provide informed legal consent to participate in the study.

Sample size:

Sample size calculation was selected on the basis of a previous study of A sample size of 50 would achieve 95% power and Correlation Coefficient *(r)* = 0.516 and Coefficient of Determination *(r^2):* 0.266 with a significance level (a) of 0.05 using a two-tail exact correlation bivariate normal model. Sample size calculation was done using G Power and Sample Size Calculations software, version 3.0.11 for MS Windows (William D. Dupont and Walton **D.,** Vanderbilt University, Nashville, Tennessee, USA).

Participants:

This study involved fifty adult patients of both genders, aged between 40 and 60 years, who had been diagnosed with diabetic peripheral neuropathy and had had diabetes for more than 10 years. The patients were assessed using a Montreal Cognitive Assessment (MoCA) Scale and Neurophysiological study, and only those who were independently ambulant and medically stable with controlled diabetes mellitus were included in the study. The patients were excluded if they have Patients <10 years having diabetes, musculoskeletal deformities, psychiatric disorders or seizures. Patients with visual and auditory impairment, Patients with Radiculopathy Additionally, all patients provided their consent by signing a consent form before participating in the study.

Assessment procedures:

The age of the patients, duration of illness of diabetic neuropathy and BMI were recorded. Cognitive impairment was assessed by using the Montreal Cognitive Assessment. Additionally, a Neurophysiological studies involving motor (Rt. Ulnar and Rt. Common peroneal) and sensory (Rt. Sural and Rt. Ulnar) conduction studies was performed to obtain objective measurements of nerve conduction velocity, amplitude and distal latency were conducted by using Surpass LT EMG / EP device.

The Montreal Cognitive Assessment (MoCA) was developed as a brief screening instrument to detect Mild Cognitive Impairment. It is a paper-and-pencil tool that requires approximately 10 min to administer, and is scored out of 30 points. The MoCA assesses multiple cognitive domains including attention, concentration, executive functions, memory, language, visuospatial skills, abstraction, calculation and orientation **[7].**

Statistical analysis:

The statistical analysis involved using descriptive statistics to calculate the mean, standard deviation, and percentage of change in the collected data. Quantitative variables were summarized using mean and standard deviation, while categorical variables were summarized using frequencies and percentages. Pearson Correlation Coefficient was conducted to determine the correlation between the findings of electrophysiological studies and cognitive functions. p-value equal or less than 0 05 indicated non-significant results, while p-value greater than 0 05 indicated significant results. All statistical measures were performed using R, a language and environment for statistical computing and graphics.

Results

All demographic data including age, gender, weight, height, and BMI and the duration of illness are presented in Table (1).

The relationship between baseline characteristics and the MoCA score was examined.

The results showed a low, non-significant negative correlation between age and MoCAscore Similarly, there was a low, non-significant positive correlation between BMI and MoCA score. However, a significant and strong negative correlation was found between the duration of illness and MoCA

score, indicating that patients with longer illness durations had more severe cognitive impairments as measured by the MoCA score. The relationship between age, BMI, duration of illness, and MoCa score using Pearson's product-moment correlation. Results indicated a negative, statistically non-significant, and small correlation between age and MoCa score (r=-0.15, 95% CI [-0.41, 0.14], p=0.302). Additionally, there was a positive, statistically non-significant, and small correlation between BMI and MoCa score (r=0.20, 95% CI [-0.09, 0.45], p=0.169). However, a significant negative and very large correlation was observed between the duration of illness and MoCa score (r=-0.77, 95% CI [-0.86, -0.63], p<.001). The negative correlation implies that patients with longer illness durations are more likely to exhibit more severe cognitive impairments as measured by the MoCa score.

Table (1): Descriptive statistics of patients baseline characteristics including their age, sex, weight, height, BMI, and duration of illness.

Characteristic	N = 50
Age (Years):	
Range	46.0-59.0
Mean (±SD)	51.6 (±3.5)
Median (IQR)	52.0 (48.0, 53.8)
Sex:	
Female	26 (52.0%)
Male	24 (48.0%)
Weight (Kg):	
Range	60-107
Mean (±SD)	88 (±10)
Median (IQR)	89 (83, 94)
Height (Cm):	
Range	154-180
Mean (±SD)	167 (±8)
Median (IQR)	168 (162, 174)
BMI ($KgIm^2$):	
Range	23.90-34.70
Mean (±SD)	31.07 (±2.34)
Duration of illness (Years):	
Range	10.00-24.00
Mean (±SD)	15.54 (±3.05)
Median (IQR)	15.00 (13.00, 18.00)

The relationship between Right sensory ulnar nerve and MoCA score was examined:

The results showed that there was a positive but not statistically significant correlation between ulnar nerve amplitude and MoCA score. Similarly, the correlation between ulnar nerve conduction velocity and MoCA score was positive but not statistically significant. However, there was a significant negative correlation between ulnar nerve peak latency and MoCA score, indicating that longer peak latencies were associated with lower cognitive scores. (Fig. 1).

The relationship between Right sural nerve and MoCA score was examined:

For the right sural nerve, there were 8 cases that showed no response in the neurophysiological studies indicating pathological conduction block. There were positive and statistically significant correlations between sural nerve amplitude and conduction velocity with MoCA score. Also, a negative and statistically significant correlation was found between sural nerve peak latency and MoCA score. These results suggest that higher amplitude and conduction velocity in the sural nerve are associated with better cognitive function, while longer peak latency is associated with poorer cognitive function.

The relationship between Right motor common peroneal nerve and MoCA score was examined:

the right common peroneal nerve analysis revealed a non-significant negative correlation between nerve amplitude and MoCA score. However, there was a significant positive correlation between common peroneal nerve conduction velocity and MoCA score, indicating that higher conduction velocity was associated with better cognitive function. Additionally, a significant negative correlation was found between common peroneal nerve distance latency and MoCA score, indicating that longer distance latencies were associated with lower cognitive scores. (Fig. 2).

The relationship between Right motor ulnar nerve and MoCA score was examined:

For the right ulnar nerve, significant positive correlations were observed between ulnar nerve amplitude, conduction velocity, and MoCA score, indicating that higher amplitude and conduction velocity were associated with better cognitive function. Conversely, a significant negative correlation was found between ulnar nerve distance latency and MoCA score, indicating that longer distance latencies were associated with lower cognitive scores.

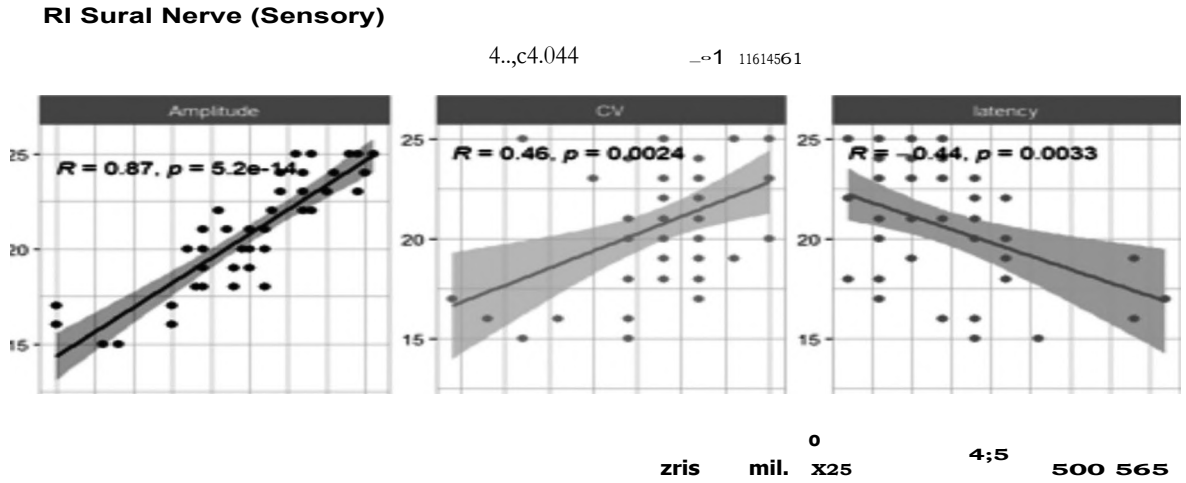

Fig. (1): Demonstrates the correlation between the neurophysiological measurements of the right sural nerve (Amplitude, conduction velocity (CV), And distal latency) and MoCA score.

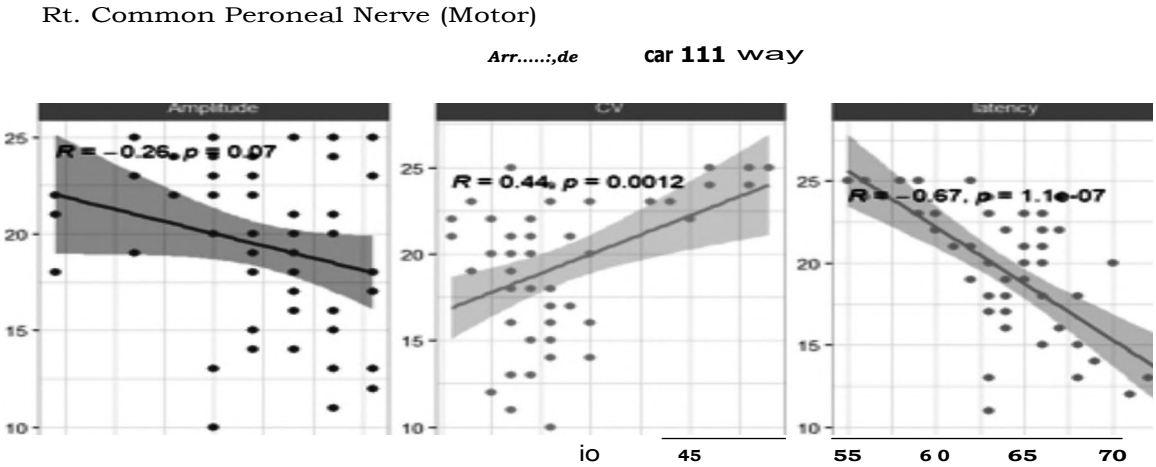

Fig. (2): Demonstrates the correlation between the neurophysiological measurements of the right common peroneal nerve (Amplitude, conduction velocity (CV), And distal latency) and MoCA score.

Discussion

Alterations in cognition with DPN and the associations of neuropathy parameters with cognition and olfaction found that memory had a positive association with the motor conduction velocity (MCV) and sensory conduction velocity (SCV) of the ulnar nerve.

Hamid, et al., **[8]** found a weak and non-significant correlation between age and MoCA score, indicating that age may not have a strong influence on cognitive function in individuals with DPN. However, the sample size and other factors may have affected the results. On the other hand, a significant and negative correlation was observed between the duration of illness and MoCA score, suggesting that longer illness durations are associated with more severe cognitive impairments. This finding aligns with previous studies demonstrating the negative impact of diabetes duration on nerve conduction velocity and neuropathy severity.

The underlying mechanisms linking DPN, and cognitive function are not fully understood. Oxidative stress and vascular factors may contribute to this association, as oxidative stress can lead to neuronal damage and vascular complications are common in diabetes Iqbal et al., Hamid et al., **[8,9].** our result supported by the study explored the relationship between neuropathy parameters and cognitive function. Positive but statistically non-significant correlations were found between ulnar nerve amplitude and conduction velocity, as well as sural nerve amplitude and conduction velocity, and MoCA score. However, a negative and significant correlation was observed between sural nerve peak latency and MoCA score.

The study examined the relationship between common peroneal and ulnar nerve parameters and MoCA score. Common peroneal nerve amplitude showed a non-significant negative correlation, while conduction velocity exhibited a significant positive correlation with MoCA score. Ulnar nerve param-

eters showed significant positive correlations with MoCA score, except for ulnar nerve distal latency, which had a significant negative correlation. These findings were consistent with previous studies on cognitive function and neuropathy in individuals with diabetes.

Diabetic peripheral neuropathy is one form of diabetic neuropathy that affects almost half of all adults with diabetes over the course of their lifetime. This type of neuropathy can result in significant morbidity, including foot ulcers, pain, and even lower limb amputation.

Conclusion:

Our results indicated that age may not have a significant influence on cognitive function in individuals with DPN, while longer illness duration was associated with more severe cognitive impairments. Nerve findings indicate that higher sensory and motor nerve function, as measured by amplitude and conduction velocity, are associated with better cognitive performance, while longer peak latency and distance latency are linked to poorer cognitive function.

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Disclosure:

No financial interest or benefit has been gained from this research.

Conflict of interest:

No conflict of interest has been declared by the authors of the current research.

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References

1- BARZILAY, SEYDAHMET A. and OZCAN K.: Relationship between diabetic neuropathy and sarcopenia. Prim Care Diabetes, 13: 521-8, 2019.

2- SPALLONE V., MAIELLO M.R., MORGANTI R., MANDICA S. and FRAJESE G.: Usefulness of ambulatory blood pressure monitoring in predicting the presence of autonomic neuropathy in type I diabetic patients. J. Hum. Hypertens, 21: 381-386, 2007.

3- DYCK P., CARTER R., YAGIHASHI and LITCHY W.: Modeling nerve conduction criteria for diagnosis of diabetic polyneuropathy. Muscle Nerve, 44: 340-345, 2011.

4- TRIVEDI J.K.: Cognitive deficits in psychiatric disorders: Current status. Indian Journal of Psychiatry, 48 (1): 10-20, 2006.

5- CHATTERJEE S., PETERS SA. and WOODWARD M.: 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. Diab. Care, 39: 300-307, 2016.

6- ENGLAND J., GRONSETH G.S. and FRANKLIN G.: Distal symmetric polyneuropathy: A definition for clinical research: Report of the American Academy of Neurology, the American Association of Electrodiagnostic Medicine, and the American Academy of Physical Medicine and Rehabilitation. Neurology, 64 (2): 199-207, 2005.

7- NASREDDINE Z.S., PHILLIPS NA., BEDIRIAN V., et al.: The Montreal Cognitive Assessment, MoCA: A brief screening tool for mild cognitive impairment. J. Am. Geriatr. Soc., 53: 695-699, 2005.

8- HAMID N., ZARAHN E., ANDERSON K.E., et al.: Cognitive reserve modulates functional brain responses during memory tasks: A PET study in healthy young and elderly subjects. Neuroimage., 19 (3): 1215-1227. [PMC free article] [PubMed] [Google Scholar], 2021.

9- IQBAL and TEJADA-VERA B.: Dementia mortality in the United States, 2000-2017. Natl. Vital Stat. Rep., 68: 01-29, 2018.

العلاقة بين التهاب الاعصاب الطرفية السكرى والوظائف الأدراكية

الخلفية: مرض السكرى من النوع الثانى هو مرض مزمن يتميز بارتفاع مستويات الجلوكوز فى الدم مما يؤدى إلى تلف في مختلف الأعضاء، يعد اعتلال الاعصاب السكرى احد الأثار الشائعة للمرض ويصل معدل حدوثها حتى ٥٠٪ فى مرضى السكرى، وتؤثر بشكل أساسى على القدمين والساقين ويترافق السكرى مع اضطرابات إدراكية، بما فى ذلك الاختلالات فى وظائف الادراك وزيادة خطر الإصابة بالخرف.

الأهداف: تهدف هذه الدراسة إلى التحقق من العلاقة بين أعراض اعتلال الأعصاب السكرى والوظائف الإدراكية.

خطه الدراسة: تم اختيار ٥٠ مريضاً يعانون من الأعراض الطرفية لأعراض الأعصاب الطرفية الناتجة عن مرض السكري من عيادات الأمراض العصبية والطب الباطنى ووحدة علم الأعصاب فى مستشفيات قصر العينى وعيادة أمراض الأعصاب فى كلية العلاج الطبيعى بجامعة القاهرة. تم تضمين كلا الجنسين فى العينة. تم إجراء تقييمات وقياسات مختلفة، بما فى ذلك استخدام ورقة تقييم عصبى عام ومحدد لجمع معلومات عصبية شاملة. تم قياس وزن وطول جميع المرضى باستخدام ميزان لتحديد مؤشر كتلة الجسم. تم تقييم الوظائف العقلية باستخدام تقييم الوعى الإدراكى لمونتريال تم أيضًا إجراء دراسة عصبية للوظيفة العصبية المحركة (العضلية) والحسية للحصول على قياسات موضوعية لسرعة توصيل الأعصاب وتأخر الإشارة العصبية المحلية، مما يساهم فى تقييم حالة الأعراض الطرفية للأعصاب.

النتائج: أظهرت الدراسة وجود ارتباط إيجابي بين معلمات الأعصاب الحسية، بما فى ذلك الشدة وسرعة التوصيل العصبى، ودرجات الاختبار المعرفى. وعلى العكس، كان هناك ارتباط سلبى بين قمة التأخير الحسي العصبى ودرجات الاختبار المعرفى. وبالإضافة إلى ذلك، لوحظ وجود ارتباط إيجابى قوى بين معلمات الأعصاب الحركية، مثل الشدة وسرعة التوصيل العصبى، ودرجات الاختبار المعرفى. وعلى العكس، كان هناك ارتباط سلبى بين مسافة التأخير الحركى العصبى ودرجات الاختبار المعرفى.

الاستنتاج: تشير النتائج إلى أن وظيفة الأعصاب الحسية والحركية الأعلى، كما يتم قياسها من خلال الشدة وسرعة الاستقطاب، مرتبطة بأداء إدراكى أفضل، فى حين أن فترة الذروة الحسية وفترة الذروة الحركية البعيدة ترتبط بأداء إدراكى أضعف.