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Electrodiagnostic Findings of Median Nerve Motor and Sensory Conduction in Neurologically Asymptomatic Newly Diagnosed Patients with Hypothyroidism

Ilija Zdravkov[1*], Hristijan Kostov[2], Elena Kostova[3]

[1]Department of Neurology, City General Hospital "8th September", Skopje, Republic of North Macedonia; [2]University Clinic for Traumatology, Orthopaedic Diseases, Anaesthesia, Reanimation, Intensive Care and Emergency Center, Skopje, Republic of North Macedonia; [3]Department of Preclinical and Clinical Pharmacology with Toxicology, Faculty of Medicine, Ss. Cyril and Methodius University, Skopje, Republic of North Macedonia

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***Correspondence:** Ilija Zdravkov. Department of Neurology, City General Hospital "8th September", Skopje, Republic of North Macedonia. E-mail: i_zdravkov@yahoo.com
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Abstract

BACKGROUND: The influence of thyroid hormones on peripheral nervous system has still not been thoroughly studied. Neurographic studies, which measure motor and sensory nerve conduction along with F-wave, have an important role in diagnosing diseases of the peripheral nerves since electrophysiological sings of neuropathy can be detected even in subclinical cases.

AIM: The aims of this study were to assess the neurophysiological parameters of the median nerve by electrodiagnostic measurements using electromyoneurogaphy (EMNG) in the region of radiocarpal joint in patients with newly diagnosed and medically untreated primary hypothyroidism who had no symptoms and signs of peripheral nerve injury. Furthermore, it was our aim to make an insight of the possible early detection of the latent damage of peripheral nervous system in untreated hypothyroidism.

MATERIAL AND METHODS: This was a prospective clinical study that comprised 78 subjects according to inclusion criteria, divided into two groups: one with primary hypothyroidism and the other group involving euthyroid subjects. Thyroid status was examined in each subject; anthropometric parameters were analyzed, and electromyoneurographic imaging (EMNG) of hand median nerve was realized.

RESULTS: Of the total number of 78 subjects included in the study, 58 (74.36%) had hypothyroidism and 20 were euthyroid subjects (25.64%). The calculated mean levels of thyroid status parameters in hypothyroid patients, TSH, aTPO and FT4, were 6.19±1.85 mIU/L, 872.22±296.66 U/mL and 0.78±0.11 ng/dL, respectively. In euthyroid patients, the mean levels of TSH, aTPO and FT4 were 0.27±0.08 mIU/L, 31.2071±5.65 U/mL and 1.31±0.25 ng/dL, respectively. Statistically significant differences were obtained between hypothyroid and euthyroid subjects regarding: age (p=0.0147, r=0.3239), body weight (p=0.0441, r= -0.531), body mass index (p=0.0050, r= -0.301), WHO classification for BMI (p=0.0032, r= -0.250), TSH (p<0.0001, r=-0.309), aTPO (p<0.0001, r=0.5554) and FT4 (p<0.0001, r= -0.317). In the group of 58 hypothyroid subjects, 38 (65.52%) were women and 20 (34.48%) were men. A strong correlation and significant statistical difference were registered in EMNG pathological findings in patients with pathologic BMI and with mild predilection for the sensory part of the median nerve. Of the 58 hypothyroid patients, EMNG pathologic findings were present in 18 that, in terms of their features, indicated a distal lesion of the median nerve. These 18 subjects had an increased body mass index (30.83±5.65 kg/m2).

CONCLUSIONS: Discovery, definition and explanation of etiopathogenic nodes in peripheral nervous system diseases will require extensive and multidisciplinary strategies in the next decades. These complex conditions, in our opinion, will claim a steady/a step-by-step/ approach to the problems, as well as consistency and symmetry in the design and methodology of the research procedures.

Introduction

The influence of thyroid hormones on peripheral nervous system has still not been thoroughly studied/examined, but new studies have indicated that thyroid receptors are expressed in Schwann cells. These receptors are inactive throughout life and become activated when peripheral nerve lesion occurs, pointing to the fact that thyroid hormones participate in the process of peripheral nervous system regeneration [1].

The pathogenesis of hypothyroid neuropathy has not been completely clarified, with variable pathological descriptions including presence of mucopolysaccharide-protein complexes in the

endoneurium and perineurium, a reduction of a large number of myelinated fibers with segmental demyelination and remyelination, aggregates of glycogen granules, mitochondria, lipid drops, lamellar bodies and axonal degeneration with decrease of axons and disorders of neurotubules and neurofilaments [2]. Studies that measure motor and sensory nerve conduction along with the F-wave can play an important role in diagnosing peripheral neuropathy since electrophy-siological sings of neuropathy can be detected even in subclinical cases.

In light of the large scientific and technological achievements in medicine, carpal tunnel syndrome remains to be a clinical diagnosis [3], [4] Carpal tunnel syndrome is a common finding in the general population and it is estimated that in 41% occurs with concomitant systemic diseases such as thyroid dysfunction, diabetes and arthritis [5], of which 29% are due to hypothyroidism [6]. In addition, it is one of the most common mononeuropathies in entrapment syndromes [7], and electromyoneurography (EMNG) is an important diagnostic procedure in its evaluation [8].

The aims of this study were to assess the neurophysiological parameters of the median nerve by electrodiagnostic measurements using electromyoneurogaphy (EMNG) in the region of the radiocarpal joint in patients with newly diagnosed and medically untreated primary hypothyroidism who had no symptoms and signs of peripheral nerve injuries. Furthermore, it was our aim to make an insight of the possible early detection of the latent damage of peripheral nervous system in untreated hypothyroidism.

Material and Methods

A prospective clinical study was conducted in PHI City General Hospital “8th September”, Skopje, North Macedonia, during a period of one year (2021-2022). For its realization, ethics approval was obtained from the Ethics Committee of the City General Hospital and Ethics Committee for Research involving Human Participants of the Faculty of Medicine, Ss. Cyril and Methodius University in Skopje. The study included 78 subjects, of which 58 hypothyroid and 20 euthyroid patients. They all gave their written informed consent for participation in the study. Inclusion criteria were: age from 30 to 60 years, positive medical history, clinical findings and biochemical results indicating manifested or subclinical hypothyroidism, duration of endocrinological history one year at most prior to diagnosis, negative history of symptoms and signs of peripheral nervous system lesion, standard neurological examination for excluding sings of focal neurological deficits and/or presence of irritating phenomena, normal serum levels of vitamin B12 and folates. Exclusion criteria were: existence of family medical history for peripheral nervous system disorders, medical history of previous symptoms and signs of peripheral nervous system injuries (including the childhood period), patients with other endocrinopathies, pregnant and breast-feeding women, patients with liver and kidney disorders/diseases and patients exposed to toxic metals/substances and those receiving chronic therapy with neurotoxic drugs. Thyroid status was defined in the following range levels:

- TSH, thyroid stimulating hormone (0.4-4.0 mIU/mL),
- FT4, thyroxin (0.89-1.76 ng/dL)
- aTPO, antithyroperoxidase antibodies (< 60 U/mL).

The following anthropometric variables were analyzed: age, gender/sex, nationality, body weight/kg (BW), body height/cm (BH), body mass index (BMI), and WHO classification for BMI [9], [10], [11], [12], [13] encompassing:

1. < 16 kg/m^2 – severe underweight
2. 16 -17 kg/m^2 – moderate underweight
3. < 18.5 kg/m^2 – mild underweight
4. 18.5 to < 25 kg/m^2 – normal range of weight
5. 25.0 to <30 kg/m^2 – overweight
6. 30.0 to < 35 kg/m^2 – obese class I
7. 35.0 to < 40 kg/m^2 – obese class II
8. 40 kg/m^2 or above – obese class III (severe obesity).

Neurological evaluation consisted of 4 phases. Firstly, each subject was tested whether he had met all the inclusion criteria. In the second phase, the included subjects independently completed the questionnaire for self-evaluation of symptoms and signs of the nervous system disorders using the Michigan neuropathy screening instrument. In the third phase, a targeted and focused neurological anamnesis was taken by employing a standardized questionnaire for assessment of neurological symptoms. Finally, in the last phase of the stratification, a neurological examination was made according to a standardized protocol by using: Neurological Disability/Impairment Scale, muscle mass examination according to the principle of manual muscle testing recommended by the Medical Research and Evaluation Council of Muscle Stretch Reflexes.

EMNG imaging was realized in the EMG laboratory of the City General Hospital with an EMG machine (Natus). A protocol recommended by the American Association of Neuromuscular and Electrodiagnostic Medicine was used in order to obtain standardization and uniformity.

The following electrophysiological characteristics were measured on the patient’s dominant hand:

- Distal motor latency (DML)
- Peak latency (PL, sensory nerves),
- Compound Motor Action Potential (CMAP),

- Sensory Nerve Action Potential (SNAP),
- Conduction velocity (CV) of each motor and sensory nerve,
- Minimal F-wave latency of motor nerves.

Procedure of neurographic recording of n. medianus motor portion

Median nerve was recorded from m. abductor pollicis brevis. The active electrode was placed on the muscle body on the vertical median axis/line from the first metacarpophalangeal bone. The reference electrode was placed slightly distal from the first metacarpophalangeal joint. Distal stimulation was ended in the area between the tendon of m. flexor carpi radialis and m. palmaris longus, and the distance between the cathode and the midline of active electrode was 8 cm. Proximal stimulation was done in the area of fossa cubitalis medially from the pulse of a. brachialis.

Procedure of neurography recording of n. medianus sensory portion (antidromic method). Recording was done over the nerves of the middle finger/3rd digit. The active electrode was placed slightly distal from the second metacarpophalangeal joint, and the reference electrode was 4 cm distal from the active one. Stimulation was done in the area between the tendon of m. flexor carpi radialis and m. palmaris longus, and the distance between the cathode and the midline of the active electrode was 14 cm.

Statistical analysis

The statistical analysis was made by the following statistical programs that are mainly used and adjusted for biomedical statistical analyses:

1. © 2023 Minitab, LLC. All rights reserved. (https://www.minitab.com/)

2. MedCalc Statistical Software version 14.8.1 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2014)

3. Addinsoft (2021) XLSTAT statistical and data analysis solution, New York, USA, https://www.xlstat.com

According to international standards for biomedical sciences, in all statistical tests the degree of probability for confirming the null hypothesis is 0.05 and 0.001. The correlation is considered to be significant if it is closer to 1 (positive correlation) or closer to -1 (negative correlation).

Results

Of the total number of 78 subjects included in the study, 58 (74.35%) had hypothyroidism and 20 (25.64%) subjects were euthyroid. In the group of 58 hypothyroid subjects, 38 (65.52%) were females and 20 (34.48%) were males (Table 1).

Table 1: Distribution of subjects according to gender and nationality

Parameter	Hypothyroid subjects	Euthyroid subjects
Gender	20 men (34.48%) 38 women (65.52%)	8 men (40%) 12 women (60%)
Nationality	44 Macedonian (75.86%) 9 Albanian (15.52%) 1 Turkish (1.72%) 4 Roma (6.9%)	16 Macedonian (80%) 4 Roma (20%)

Table 2 illustrates the mean values and standard deviation (mean value ± SD), correlation coefficient and significance in difference of anthropometric and biochemical parameters between hypothyroid and euthyroid subjects. The age of hypothyroid and euthyroid subjects ranged from 30 to 60 years, mean age 44.12 ± 8.36 and 39.21 ± 4.6, respectively.

Table 2: Anthropometric and biochemical parameters in hypothyroid and euthyroid subjects (mean value ± SD, significance in differences-p and correlation coefficient-r)

Parameter	Hypothyroid subjects Mean value ±SD	Euthyroid subjects Mean value ±SD	r	p
Age	44.12 ± 8.36	39.21 ± 4.62	0.3239	**0.0147***
BH/cm	166.45 ± 7.64	167.55 ± 8.12	-0.139	0.5859
BW/kg	75.69 ± 11.03	70 ± 9.722	**-0.531**	**0.0441***
BMI (kg/m2)	27.18 ± 3.31	24.86 ± 2.33	**-0.301**	**0.0050***
BMI/WHO clas.	4.00 ± 0.73	3.45 ± 0.60	-0.250	**0.0032***
TSH (mIU/L)	6.19 ± 1.85	0.27 ± 0.08	-0.309	**<0.0001****
aTPO (U/mL)	872.22 ± 296.66	31.2071 ± 5.65	**0.5554**	**<0.0001****
FT4 (ng/dL)	0.78±0.11	1.31 ± 0.25	**-0.317**	**<0.0001**

* = significant differences (p-value<0.05); ** = highly significant differences (p-value<0.001), NS = non-significant differences (p-value >0.05).

Body height (BH) was evaluated in hypothyroid and euthyroid subjects, and the mean values were 166.45 ± 7.64 cm and 167.55 ± 8.12, respectively. The mean values of the evaluated body weight (BW) were 75.69 kg ± 11.03 and 70 ± 9.722. BMI mean values in hypothyroid and euthyroid subjects were 27.18 ± 3.31 kg/m^2 and 24.86 ± 2.33. In terms of WHO classification for BMI, hypothyroid subjects were overweight, with the mean level of 4.00 ± 0.73, and in euthyroid subjects the calculated mean level was 3.45 ± 0.60, that is, they were with healthy weight.

The analyzed mean levels of thyroid status parameters (TSH, aTPO and FT4) in hypothyroid subjects were 6.19 ± 1.85 mIU/L, 872.22 ± 296.66 U/mL and 0.78 ± 0.11 ng/dL, respectively. The mean levels of TSH, aTPO and FT4 in euthyroid subjects were 0.27 ± 0.08 mIU/L, 31.2071 ± 5.65 U/mL and 1.31 ± 0.25 ng/dL, respectively.

Table 3: Statistical significance of gender with analyzed anthropometric and thyroid parameters in hypothyroid subjects

Parameter	Gender/sex of hypothyroid subject	
	Female	**Male**
Age	0.9937	0.9999
BH/cm	0.5739	0.9999
BW/kg	0.8372	0.9216
BMI (kg/m2)	1.0000	1.0000
BMI/WHO class.	0.2754	0.0863
TSH (mIU/L)	0.9913	0.9997
ATPO (U/mL)	<0.001	0.0005
FT4 (ng/dL)	0.9991	0.9977

Values close to 1 show a high significance.

Our study did not detect significant statistical differences between gender and body height as well as

between gender and thyroxin level in the group of hypothyroid patients. There were no statistically significant differences between gender and body height, body weight and BMI in the control group of subjects. No statistically significant difference was obtained between nationality and thyroxin levels in hypothyroid patients. Furthermore, no statistically significant difference was registered in the control group of subjects only between nationality and thyroid-stimulating hormone. Regarding all other analyzed parameters, statistically significant differences were found comparing gender and nationality (Table 3).

Table 4: Electrodiagnostic findings of median nerve in hypothyroid and euthyroid subjects (mean value ± SD, significance in difference and coefficient correlation)

Euthyroid subjects n. medianus (motor conduction)			Hypothyroid subjects n. medianus (motor conduction)
Parameter	**Mean value ± SD**	**p r**	**Mean value ± SD**
DML (ms)	4.12 ± 0.39	0.0960 0.3826	4.18 ± 0.44
CMAP (mV)	6.56 ± 1.43	<0.0001** 0.8173	6.0914 ± 1.3857
BS (m/s)	53.76 ± 2.27	<0.0001 0.8173	53.07 ± 2.42
F lat (ms)	27.42 ± 1.94	0.2428 0.2738	28.59 ± 2.06
Euthyroid subjects n. medianus (sensory conduction)			**Hypothyroid subjects n. medianus (sensory conduction)**
Parameter	**Mean value ± SD**	**p r**	**Mean value ± SD**
PL (ms)	3.40 ± 0.37	<0.0001** 0.7804	3.60 ± 0.43
SNAP (mV)	19.84 ± 5.97	0.0062* 0.5902	16.1966 ± 5.66
BS (ms)	54.22 ± 1.71	0.0288* 0.4886	52.89 ± 1.92

* = significant differences (p-value<0.05). ** = highly significant differences (p-value<0.001), NS = non-significant differences (p-value >0.05).

Statistically significant differences were registered between hypothyroid and euthyroid subjects regarding: age (p=0.0147, r=0.3239), body weight (p=0.0441, r= -0.531), r=0.3239), body mass index (p=0.0050, r= -0.301), WHO classification for BMI (p=0.0032, r= -0.250), TSH (p<0.0001, r=-0.309), aTPO (p<0.0001, r=0.5554) and FT4 (p<0.0001, r= -0.317).

Statistically significant differences and positive statistically significant correlation in terms of conduction velocity (CV) and compound motor action potential (CMAP) of the median nerve were detected between hypothyroid and control subjects. Also, there were significantly high statistical differences and positive statistically significant correlation of peak latency (PL), that is, latency along the longest length of the axons (pointing to continuity of axon architecture of the median nerve) between the group of hypothyroid patients and the control group of patients. Statistically significant differences and positive statistically significant correlation were also noted between both groups of examined patients regarding sensory nerve action potential (SNAP) and conduction velocity (CV) (Table 4).

Our investigation on median nerve motor conduction showed significant differences and negative significant correlation: between compound motor action potential (CMAP) and minimal F-wave latency of motor nerves (F lat), between conduction velocity (CV) and minimal F-wave latency of motor nerves (F lat), between conduction velocity (CV) and age of hypothyroid subjects, between conduction velocity (CV) and WHO classification for BMI, as well as between conduction velocity (CV) and body mass index in the examined hypothyroid patients. Highly significant differences and positive significant correlation were found: between conduction velocity (CV) and compound motor action potential (CMAP), between distal motor latency (DML) and WHO classification for BMI, between minimal F-wave latency of motor nerves (F lat) and patients' age, minimal F-wave latency of motor nerves (F lat) and WHO classification for BMI, minimal F-wave latency of motor nerves (F lat) and body mass index, minimal F-wave latency of motor nerves (F lat) and age of hypothyroid patients (Table 5).

Table 5. Significance in difference and correlation coefficient of parameters of median motor nerve conduction and the other analyzed parameters in hypothyroid patients

r p	DML	m CMAP	m BS	m F lat	BMI (kg/ m2)	BMI/ WHO class.	Age	TSH	aTPO	FT4
DML		-0.448 0.0004	-0.462 0.0003	0.334 0.0105	0.356 0.0065	0.449 0.0004	0.330 0.0113	-0.084 0.5331	0.580 0.0116	0.215 0.1049
m CMAP	-0.448 0.0004		0.715 <0.0001	-0.390 0.0025	-0.454 0.0004	-0.468 0.0002	-0.588 <0.0001	0.087 0.5139	-0.360 0.1428	-0.069 0.6071
m BS	-0.462 0.0003	0.715 <0.0001		-0.457 0.0003	-0.451 0.0004	-0.470 0.0002	-0.592 <0.0001	-0.027 0.8390	-0.358 0.1452	-0.146 0.2757
m F lat	0.334 0.0105	-0.390 0.0025	-0.457 0.0003		0.58 4 <0.0001	0.498 0.0001	0.390 0.0024	0.170 0.2023	0.158 0.5323	-0.180 0.1760
BMI (kg/ m2)	0.356 0.0065	-0.454 0.0004	-0.451 0.0004	0.584 <0.0001		0.919 <0.0001	0.216 0.1062	0.144 0.2842	0.124 0.6235	-0.243 0.0684
BMI/ WHO class.	0.449 0.0004	-0.468 0.0002	-0.470 0.0002	0.498 0.0001	0.919 <0.0001		0.121 0.3639	0.089 0.5079	0.192 0.4449	-0.150 0.2617
Age	0.330 0.0113	-0.588 <0.0001	-0.592 <0.0001	0.390 0.0024	0.216 0.1062	0.121 0.3639		-0.107 0.4252	-0.079 0.7562	0.132 0.3228
TSH	-0.084 0.5331	0.087 0.5139	-0.027 0.8390	0.170 0.2023	0.144 0.2842	0.089 0.5079	-0.107 0.4252		-0.654 0.0033	-0.377 0.0035
aTPO	0.580 0.0116	-0.360 0.1428	-0.358 0.1452	0.158 0.5323	0.124 0.6235	0.192 0.4449	-0.079 0.7562	-0.654 0.0033		0.065 0.7982
FT4	0.215 0.1049	-0.069 0.6071	-0.146 0.2757	-0.180 0.1760	-0.243 0.0684	-0.150 0.2617	0.132 0.3228	-0.377 0.0035	0.065 0.7982	

There was a strong negative correlation and significant statistical difference between peak latency and conduction velocity; a statistically negative correlation and statistically significant difference among SNAP and conduction velocity and BMI; a distinct negative correlation of SNAP and BS with patients' age. A statistically significant difference and statistically negative correlation was registered between FT4 and TSH. Moreover, aTPO was in a negative significant correlation and statistically significant difference with TSH.

Table 6: Significance in difference and correlation coefficient of parameters of median sensory nerve conduction and the other analyzed parameters in hypothyroid patients

r p	sPL	sSNAP	sBS	BMI (kg/m2)	BMI/ WHO class.	Age	TSH	aTPO	FT4
sPL		-0.713 <0.0001	-0.694 <0.0001	0.611 <0.0001	0.619 <0.0001	0.287 0.0288	0.050 0.7094	-0.065 0.7973	-0.095 0.4763
sSNAP	-0.713 <0.0001		0.756 <0.0001	-0.688 <0.0001	-0.679 <0.0001	-0.578 <0.0001	-0.040 0.7651	-0.142 0.5729	-0.011 0.9364
sBS	-0.694 <0.0001	0.756 <0.0001		-0.633 <0.0001	-0.619 <0.0001	-0.380 0.0032	-0.085 0.5270	0.167 0.5083	0.083 0.5356
BMI (kg/ m2)	0.611 <0.0001	-0.688 <0.0001	-0.633 <0.0001		0.919 <0.0001	0.216 0.1062	0.144 0.2842	0.124 0.6235	-0.243 0.0684
BMI/ WHO class.	0.619 <0.0001	-0.679 <0.0001	-0.619 <0.0001	0.919 <0.0001		0.121 0.3639	0.089 0.5079	0.192 0.4449	-0.150 0.2617
Age	0.287 0.0288	-0.578 <0.0001	-0.380 0.0032	0.216 0.1062	0.121 0.3639		-0.107 0.4252	-0.079 0.7562	0.132 0.3228
TSH	0.050 0.7094	-0.040 0.7651	-0.085 0.5270	0.144 0.2842	0.089 0.5079	-0.107 0.4252		-0.654 0.0033	-0.377 0.0035
aTPO	-0.065 0.7973	-0.142 0.5729	0.167 0.5083	0.124 0.6235	0.192 0.4449	-0.079 0.7562	-0.654 0.0033		0.065 0.7982
FT4	-0.095 0.4763	-0.011 0.9364	0.083 0.5356	-0.243 0.0684	-0.150 0.2617	0.132 0.3228	-0.377 0.0035	0.065 0.7982	

A high statistical significance and a strong positive correlation was detected in peak latency, BMI and WHO classification for BMI. A strong positive correlation and significant statistical difference was registered between conduction velocity and SNAP.

Discussion

The association of pathological processes of the peripheral nervous system directly caused by hypothyroidism has raised many questions in scientific studies in terms of the mode of axonal damage and demyelination process with no clue which of these two mechanisms is primary or both happen at the same time without pathophysiological predilection.

In our study, the comparison of hypothyroid and euthyroid patients revealed a larger number of pathological findings regarding the sensory part of median nerve involving delayed peak latency, decreased conduction velocity and SNAP.

With regard to motor part of the nerve, a statistical significance was observed between conduction velocity and CMAP potential, which means that conduction velocity decreases with decreasing of SNAP, that is, CMAP. The possible etiopathogenesis of the damage of the motor part has been explained by ATP deficiency in hypothyroidism and reduced activity of ATPase that causes a decrease in the activity of Na+/K+ pump resulting in consequent alterations in the axonal transport [9]. These findings are in the context of understanding the preponderous axonal damage of axonal cylinders as a leading pathology and support the evidence of primary axonal genesis in the occurrence of median nerve injury in the carpal tunnel [10], [11].

Contrary to these findings, Garima et al. included newly diagnosed hypothyroid patients without therapeutic treatment and patients receiving substitutional therapy, but with not attained euthyroid state, yet. Their results showed a significant reduction in the conduction velocity of sensory part of median nerve and concluded that their patients had only one type of electrophysiological abnormality – demyelination [12]. These results are opposite to those about predominant motor involvement in the pathological process of hypothyroidism no matter whether it is focal or diffuse [13], [14], [15].

Concerning F latency values, a negative significant correlation with CAMP and motor conduction velocity was obtained in our study. The obtained values might point not only to a latent local, but also diffuse lesion of the peripheral nervous system. However, to investigate this condition a new methodological approach is necessary. In our study, BMI showed a high degree of significant difference and a positive significant correlation with conduction velocity of median nerve, especially to its sensory part. Moreover, BMI presented with a statistically significant negative correlation with SNAP.

In the study by Wiberg et al. (2022) comprising 400,000 subjects, BMI levels were increased in patients with carpal tunnel syndrome compared to control group of subjects, by an average of 2.0 kg/m^2, and this effect was consistent in both genders [16]. In our study, findings of median nerve distal lesion were present only in patients with pathological BMI, and in

most cases in the category obesity class I. It remains an open question why some obese patients are susceptible to peripheral nerve lesions and to other diseases in general. Having in mind that detection of asymptomatic carpal tunnel syndrome is a complex procedure, a retrospective study was conducted including patients with primary hypothyroidism. In a large percentage of analyzed patients, EMNG finding was in a physiological range, but on direct compression, applying the Phalen and Tinnel test, these patients manifested symptomatology in favor of carpal tunnel syndrome. Thus, EMNG examination is not a definitive and sufficient procedure in the evaluation of the latent form of carpal tunnel syndrome aimed at establishing a timely/early diagnosis and preventing irreversible disorders associated with this syndrome [17]. In return, these would require creating a multifactorial theory that would unite the system of scientific balance, and would reflect, both experimentally and clinically, the scientific knowledge of all crucial scientists.

In their review paper, Otelea et al. (2022) gave a critical review of the possible pathogenetic and pathophysiological mechanisms of median nerve damage in obese patients. Direct compression by lipid deposition in radiocarpal space and, on the other hand, insulin resistance that directly affects the peripheral nervous system and indirectly the blood vessels, tendons and muscles along with the oxidative stress, are all factors that participate with their own pathophysiological mechanisms in the pathogenesis of median nerve distal lesions [18].

These findings can be interpreted in the light of the explanation given by Karne et al. They reported that neurography values of the median nerve can be within the reference range at disease onset, and it may be due to the assumption that deposits of mucopoly-saccharides and mucinous substances have still not been expressed to a degree that can cause a decrease in the nerve conduction velocity, but due to mechanical stimuli they elicit clinical symptoms [19].

Our study results are in agreement with other studies that involved a larger number of EMNG pathological findings with increased BMI levels suggesting it to be an important risk factor for the development of carpal tunnel syndrome. A predominant lesion of sensory nerves that correlated with our results, especially regarding latency of sensory median nerve, was found in the study of Garg et al. They suggest that peripheral nerve damage is rather sensory than motor [20], whereas Somay et al. and Ajeena et al. confirm the finding of early distal median nerve dysfunction [21], [22].

Similar results about the correlation of TSH and pathological EMNG findings were presented in the study by Sinu et al. Their electrodiagnostic study of the median nerve in newly diagnosed hypothyroidism found that by the increase of TSH levels distal latency was prolonged (positive correlation), and at the same time CMAP and conduction velocity were decreased (negative correlation) [23]. A study using linear regression analysis found that TSH level was an independent predictor of neuropathy in patients with subclinical hypothyroidism [24].

Our results are also similar to those reported by Murugiah et al. (2018). These authors showed that median nerve with motor and sensory parts were damaged in majority of cases, and the most commonly affected electrophysiological features were conduction velocity, motor and sensory potential [25].

Conclusion

Having more evidence to change the classical doctrine of the neuron will be an intellectual and moral stimulus for the creation of new notions in line with the scientific paradigm standards, especially in the field of regenerative and reparative medicine. Discovery, definition and explanation of etiopathogenic nodes in peripheral nervous system diseases will require extensive and multidisciplinary strategies in the next decades. These complex conditions, in our opinion, will claim a steady approach to the problems, as well as consistency and symmetry in the design and methodology of the research procedures. Further studies should be designed and directed towards establishing more sensitive standards for diagnosing carpal tunnel syndrome in patients with hypothyroidism.

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