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Prediction of motor disorders in multiple sclerosis using muscle change structure assessment

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Abstract

Introduction: The neuropathogenesis of multiple sclerosis (MS) lesions has been explained by several mechanisms, which emphasize the unpredictable nature of these lesions. The aim of this study is to present the neuromuscular changes in MS at the patients without gait or motor disorders using a noninvasive method named tensiomyography (TMG). *Patients and Methods*: The studied group included a number of seven MS patients without clinically detected gait disorders, with mean age of 33.28 years (min. 22 years–max. 60 years), diagnosed with progressive multiple sclerosis with relapses – three patients and with relapsing-remitting multiple sclerosis (RRMS). They have been evaluated using clinical, functional scales for evaluation and neuromuscular assessment using TMG parameters (displacement Dm, contraction time – Tc, delay time – Td, supporting time – Ts, relaxation time – Tr), for rectus femoris (mRF). *Results*: The group with MS patients recorded functional asymmetries with higher values in the left lower limb. We determined Tc values lower than the minimum normally required, which meant that in the group with MS there was an increase in the percentage of type II fibers. Other TMG parameters show important difference between left and right side even if they do not have gait disorders. *Discussion and Conclusions*: These patients with MS underwent modifications in their muscle tone, muscle strength and other changes related to the presence or absence of muscle atrophy. The muscle tone could be affected by the muscle atrophy or hypertrophy. In conclusion, this type of assessment performs the non-invasive assessment of contractile properties of the muscles, without the integration of the tendon properties, joint mechanics or connective tissue in the mechanical response to muscle deformation produced by electrical stimulation.

Keywords: tensiomyography, multiple sclerosis, assessment, muscle tone.

Introduction

The neuropathogenesis of multiple sclerosis (MS) lesions has been explained by several mechanisms, which emphasize the unpredictable nature of these lesions. The presence of the old and new lesions illustrates the dynamic [1] nature of the disease. The lesions, called “active plaques”, are also characterized by inflammation, active myelin degradation and phagocytosis of the primary lesion, if the myelin or its host cell, the oligodendrocyte [2], is directly damaged.

The blocks in the nervous impulse conduct may be dependent on the impulse rate, the conduct occurs in the low frequency impulses. The blocks in the high frequency impulses can occur due to the hyperpolarization determined by the active electrogenic pump (Na^+/K^+-ATPase). It has also been suggested that an increase of the intracellular sodium concentration at the node level, associated with the accumulation of extracellular potassium into the demyelinated areas, could lead to the inactivation of the sodium channel and to the blocking of nervous impulse conduct. Hyperexcitability episodes also occur in the demyelinated axons [3].

The diagnosis of MS is based on a thorough medical history associated with clinical [4] and laboratory examination. Among the typical, frequently encountered symptoms of this disease there are the motor disorders (muscle spasticity) with severe damage of the autonomous muscles (urinary dysfunction, sexual dysfunction and bowel damage); the spinal cord damage: decreased physical force [5] in the upper and lower limbs, sometimes leading to paralysis (especially in the lower limbs); mono-, hemi- and paraparesis, myoclonus, exaggeration of the osteotendinous reflexes, presence of pathological reflexes – positive Babinski, lack of abdominal skin reflexes, hypertonic pyramid [6].

The aim of this study is to present the neuromuscular changes in MS at the patients without gait or motor disorders using a noninvasive method named tensiomyography (TMG).

Patients and Methods

The studied group included a number of seven MS patients without clinically detected gait disorders, with mean age of 33.28 years (min. 22 years–max. 60 years), diagnosed with progressive multiple sclerosis with relapses – three patients and with relapsing-remitting multiple sclerosis (RRMS) – four patients. The clinical data of MS patients were reported to a control group of 10 patients with a mean age of 35.2 years and anthropometric characteristics similar to those of the study group.

The MS patients were investigated from the clinical and functional point of view and there were reported paresthesia, balance disorder, narrowing of the visual field. Their functional evaluation was performed using

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ADL (activities of daily living) score that showed a value of 8 points, which corresponded to a normal functional status.

According to Kurze score, the group of the patients presented a score between 1 (not disabled – minimal signs of disability) and 3 (moderate disability).

Imaging investigation – magnetic resonance imaging (MRI) – showed band and nodular demyelination in the brain with multiple areas of subcortical and periventricular gliosis.

In the studied group, we realized a distribution of the subjects depending on the gait symmetry, the patients falling into three categories: patients with normal symmetrical gait, patients with symmetrical abnormal gait and patients with asymmetrical gait (Figure 1; Table 1).

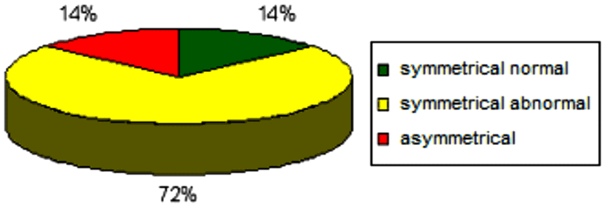

Figure 1 – *Graphic representation of the distribution of MS patients, depending on the symmetry of the lower limb. MS: Multiple sclerosis.*

Table 1 – *Distribution of MS patients, depending on the symmetry of the lower limb*

Type of symmetry	No. of subjects
Symmetrical normal gait	1
Symmetrical abnormal gait	5
Asymmetrical gait	1

MS: Multiple sclerosis.

Neuromuscular evaluation

Neuromuscular evaluation of the patients was performed through tensiomyography. TMG is a non-invasive method which determines the diagnosis of a certain muscular type (types of muscular fibers) and muscular status/condition (fatigue, stress influence on the body, etc.), the diagnosis of a functional muscular symmetry, either temporal or morphological, the evaluation of muscular synchronization, fast detection of an infra-clinical lesion of the muscle *in situ* (less than 5 minutes).

Tensiomyography is an evaluation method for the morphofunctional potential of the muscle, which allows the detection of the muscular reaction to electrical stimulation. Through this method, we could appreciate the ratio between type I muscular fibers (fatigue-resistant) and type II muscular fibers (white, fast-twitch, with low resistance to fatigue – this phenomenon appearing before the completion of the electrical stimulation process). In order to complete the data supplied by the clinical and paraclinic examination, we suggested the use of TMG as an evaluation method for muscular fatigue and skeletal muscle composition, taking place within MS and being necessary to establish the connection between the structure and morphofunctional properties of the muscle on the one hand, and its functional potential on the other hand. The evaluation of muscular fatigue could be made under intermittent electrical stimulation of the muscle. This stimulation was made with a TMG–S1 electrostimulator (Furlan & Co., Ltd.), using 5/5 cm platinum-type electrodes. The stimulation was performed under increasing electrical current intensities, between 10–65 mA, the length of the stimulation being one millisecond. An isometric contraction was produced because of electrical stimulation. The detection of the muscular response to the electrical stimulus was performed with a G40 (RLS Inc.) sensor, perpendicular to the muscle surface, in the area in which the muscular geography was well displayed (this could be more precisely determined if the subject was requested to perform an isotonic contraction, if a muscle strength higher than 2 was possible). The sensor was placed at this level; it exerted a 0.7 N/mm^2 pressure on the contact surface. This pressure is called pretension and its role is to increase the response to the applied electrical stimulus. Because of the electrical stimulation, a transversal movement of the muscular fibers occurred and the sensor recorded this. The amplitude of this transversal movement was proportional with the muscular force and the percentage of type I muscle fibers, which enabled us, together with the data from the other parameter, to evaluate muscle fatigue and transmission speed. The measurement of the muscular response and the data storage and analysis were made with a dedicated TMG software.

Signal recording

The TMG signals were received by a Matlab Compiler Toolbox on a 1 kHz frequency. Two supra-maximal responses were stored and then the mean was calculated (Figure 2).

Figure 2 – *The technical devices used to record TMG parameters. TMG: Tensiomyography.*

In the study, we recorded the muscular response to the stimulation in the right femoral muscle (mRF). From a technical standpoint, the collection of muscle response to stimulation was done by adopting certain segmentation positions as follows: for the right femoral (RF) – the patient was placed in dorsal decubitus, with his knees semi-flexed, resting on a prismatic support. From this position, by extending the knee, we could determine the maximum relief of the right femoral and this was the point where we placed the sensor, perpendicular, exerting a pressure of $1.5\times1–2$ N/mm^2. We applied the sensor in this position. The stimulation electrodes were placed symmetrically, proximal and distal from the pressure point (Figure 3).

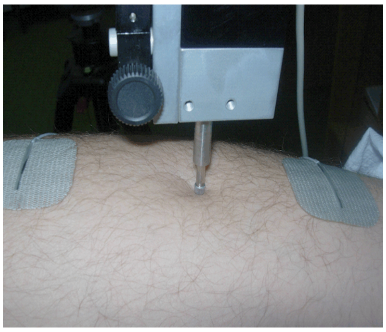

Figure 3 – ***Placing the stimulation electrodes and femoral stimulus for the right femoral.***

The parameters assessed by TMG were:

▪ delay time (Td) – the time elapsed since the stimulation moment till the muscle reached a contraction of 10% (ms).

▪ contraction time (Tc) – the time elapsed between a muscle contraction of 10% and 90% of maximum (ms). The value of the contraction time depended on the percentage of fast or slow muscle fibers of the studied muscle. Thus, the values decreased with the increasing percentage of type II fibers and increased when the percentage of type II fibers was low and that of type I fibers was higher.

▪ supporting time (Ts) – the time elapsed between the moment in which the muscular contraction was of 50% and the moment the muscle was relaxed 50% (ms).

▪ relaxation time (Tr) – the time elapsed between the moment the muscle was relaxed 50% and the moment it reached 90% relaxation (ms).

▪ the amplitude of muscle transversal displacement – Dm (mm) – a parameter that was also correlated with the values of Tc and depended on the elasticity of muscle tissue. Thus, Dm values grew with the development of explosive strength, which aimed to the increase of the motion amplitude and decreased when the muscle tone increased.

Results

The muscular displacement (Dm) had a normal average value of 8.17 mm and the values recorded in our study are shown in Tables 2 and 3.

Table 2 – ***The parameters assessed by TMG***

		Dm		Tc		Td		Tr		Ts	
		Right	***Left***	***Right***	***Left***	***Right***	***Left***	***Right***	***Left***	***Right***	***Left***
Control group	Mean	**6.59**	**6.79**	**27.94**	**27.47**	**26.14**	**26.23**	**46.12**	**27.39**	**98.28**	**118.13**
	Standard dev.	1.79	3.00	5.59	5.19	3.22	3.56	41.40	19.77	69.29	129.00
	Min.	4.10	2.00	19.60	19.00	21.50	22.40	9.80	9.30	36.90	32.00
	Max.	10.10	12.40	36.30	36.60	32.80	34.10	155.10	82.20	250.00	499.20
	No. val.	12.00	12.00	12.00	12.00	12.00	12.00	12.00	12.00	12.00	12.00
MS group with gait disorder	Mean	**3.17**	**2.80**	**21.26**	**22.21**	**37.46**	**25.56**	**20.57**	**35.64**	**75.20**	**69.71**
	Standard dev.	2.28	2.32	5.08	11.48	19.68	13.22	15.24	28.47	66.10	41.82
	Min.	0.00	-1.00	12.00	-1.00	24.70	-1.00	0.00	-1.00	2.00	-1.00
	Max.	5.60	5.50	26.10	34.00	81.00	43.00	48.90	80.30	205.20	124.00
	No. val.	7.00	7.00	7.00	7.00	7.00	7.00	7.00	7.00	7.00	7.00

TMG: Tensiomyography; MS: Multiple sclerosis; Dm: Displacement; Tc: Contraction time; Td: Delay time; Tr: Relaxation time; Ts: Supporting time.

Table 3 – ***P-values (Student's t-test) for the investigated parameters***

Dm	***Right***	0.000186	0.786852	0.001313	0.006351
	Left	0.002341	0.807669	0.006976	0.005364
Tc	***Right***	0.046139	0.505413	0.190886	0.018665
	Left	0.178855	0.769015	0.354041	0.28786
Td	***Right***	0.015665	0.777618	0.042142	0.180388
	Left	0.494397	0.697509	0.259275	0.898578
Tr	***Right***	0.996011	0.546818	0.536533	0.073054
	Left	0.059364	0.643553	0.069377	0.514445
Ts	***Right***	0.54123	0.399492	0.190932	0.483344
	Left	0.906064	0.434366	0.679963	0.250608

Dm: Displacement; Tc: Contraction time; Td: Delay time; Tr: Relaxation time; Ts: Supporting time; *p*: 0.05–0.01 – significant; 0.01–0.001 – highly significant; <0.001 – very highly significant.

In the rectus femoris (mRF), we noted significant differences between the control group, where the average values were of 6.59 mm in the right lower limb and of 6.79 mm in the left lower limb, and the group of the patients with MS, where the values were of 3.17 mm in the right lower limb and of 2.8 mm in the left lower limb. The group with MS patients recorded functional asymmetries with higher values in the left lower limb again, which was also found in the control group. The muscular displacement movement was highly significant for mRF, bilaterally in the control group compared to the group of MS patients, as noted in Table 3. In terms of the mean values, we noted that in the mRF, the mean values of MS group were much lower than those recorded in the control group; also, the maximum values were below normal, while the minimum values reached zero, which meant that there were cases where stimulation caused no response from the muscle. These changes were evident in the subgroup of the patients with MS without gait disorders. The low values of Dm indicated an increased muscle tone.

For mRF, the average Tc was 30.25±3.5 ms and in our study, the mean values recorded in the MS group were not significantly different in the lower limbs: 21.26 ms in the right lower limb and 22.21 ms in the left one; the data are shown in Table 2. We determined Tc values lower than the minimum normally required, which meant that in the group with MS there was an increase in the percentage of type II fibers. The conduct speed in mRF indicated values of 0.14 m/ms in the right limb and of 0.12 m/ms in the left limb; in the control group, there was recorded a value of 0.25 m/ms bilaterally.

Regarding Td values recorded in mRF, we got similar values for both legs in the control group, 26.14 ms (right) and 26.23 ms (left), while the values got in the group with MS patients were of 37.46 ms (right) and of 25.56 ms (left).

For mRF, Tr recorded values in the right lower limb were of 46.12 ms in the control group and of 20.57 ms in the MS group; Tr values in the left lower limb were of 27.39 ms in the control group and of 35.64 ms in the MS group.

For mRF, Ts recorded values in the left lower limb were of 98.28 ms in the control group and of 75.2 ms in the group with MS; Ts values in the left lower limb were of 118.13 ms in the control group and of 69.71 ms in the group with MS patients.

Discussion

The motor performance [7] of the lower limb muscles was affected by the properties of the muscle distribution [8] at this level [9]. Using TMG records, we obtained relevant information of the morphological and functional changes, [10] that occurred in the skeletal muscles [11] in patients with MS.

These patients with MS underwent modifications in their muscle tone, muscle strength [12] and other changes related to the presence or absence of muscle atrophy. The muscle tone could be affected by the muscle atrophy or hypertrophy.

Generally, the patients with MS often faced a more or less evident muscle atrophy, which caused the development of muscle imbalance [13]. So far, there have been no specialty studies to deal specifically with structural changes in the muscles of MS patients, most of them referring to the appearance of neuromuscular conduction and connection with the process of demyelination, which is quantified by investigations such as MRI, computed tomography (CT) and electromyography (EMG). This latest type of investigation is of great importance in assessing the electrical activity of the fatigued muscles, specific to MS patients, revealing the way in which certain additional motor units are recruited [14], which we have achieved using TMG parameters (Td).

Analyzing the anterior thigh in terms of the amplitude muscle displacement, we found low levels of Dm and a higher muscle tone in the mRF, which had a great impact on the control of the knee and, therefore, of the forces transmitted to the ankle.

Compensatory mechanisms that developed as a result of the damaged nerve conduction and, implicitly, as a result of balance disorders, were based on structural and functional muscle changes. This was clearly noticed in the distribution of the muscle tone in the lower limbs, as seen in the case of mRF, which had an increased muscle tone, arousing from the need to increase muscular intervention in knee stability [15].

In MS patients, the values of Td were higher than in the patients from the control group and, therefore, it was a shortage in recruitment the motor units on the one hand, and on the other hand, the correlation with decreasing Tc led to the development of type II fibers [16] in the detriment of type I fibers resistant to muscle fatigue.

Analyzing the evolution of Tr, we found a right–left asymmetry, with elevated values in the group with MS, which meant an increased muscle tone.

Ts had lower values in MS group compared to the values recorded in the control group, which indicated the impossibility to maintain isometric muscle contraction, hence a reduced resistance to muscle fatigue.

This research stands among the first ones in the field in terms of investigating MS patients; so far, the assessment of structural muscular modifications has been done only in patients with hemiplegia [17], on spastic muscles, knowing the fact that spasticity characterizes MS patients, too, with structural implications at muscular level. Thus, the studies [18] carried out in patients with hemiplegia have monitored the effects of the administration of botulinum toxin BTX-A using TMG and recording Tr, Ts, and Dm parameters. This study confirms the utility of an investigation like TMG, in assessing patients with MS.

Conclusions

We strongly believe that this method not only provides information related to the structural–adaptive changes in muscle but also allows monitoring certain therapeutic programs. In conclusion, this type of assessment performs the non-invasive assessment of contractile properties of the muscles, without the integration of the tendon properties, joint mechanics or connective tissue in the mechanical response to muscle deformation produced by electrical stimulation. Tc and Ts, as TMG parameters, record low values in the anterior thigh muscle group, which corresponds to latent muscle fatigue, clinically undetectable, shown in gait disturbance.

Conflict of interests

The authors declare that they have no conflict of interests.

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