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Importance of cutaneous silent period in fibromyalgia and its relationship with disease characteristics, psychological disorders and quality of life of patients

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ABSTRACT

Introduction: Cutaneous silent period (CSP) is an inhibitory spinal protective reflex and its afferents consist of A-delta nerve fibers. We aimed to evaluate patients with fibromyalgia (FM) and healthy controls to determine any differences between the groups in terms of CSP duration and latency, and if present, to determine whether there is any relationship with disease characteristics, psychological disorders and quality of life.

Materials and methods: Thirty-two patients with FM and 32 healthy volunteers were included in the study. The patient and control groups were compared in terms of CSP latency and duration in both upper and lower extremities. Disease characteristics, psychological disorders and quality of life of patients were assessed using the Fibromyalgia Impact Questionnaire (FIQ) and Short Form-36 (SF-36). Patients with CSP measurements equal to or lower than those of the control group were compared with those with higher values than controls in terms of disease characteristics, psychological status and quality of life.

Results: Significantly prolonged CSP latencies in both upper and lower extremities were determined in patients compared to controls. We found that prolongation of CSP latency in the lower extremity is associated with disease severity and functional disability.

Conclusions: CSP latencies in both upper and lower extremities in patients with FM are longer than in healthy volunteers. Moreover, prolongation of CSP latency in the lower extremity is associated with disease severity and physical functional disability.

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Importância do período de silêncio cutâneo na fibromialgia e sua relação com as características da doença, distúrbios psicológicos e qualidade de vida dos pacientes

Palavras-chave:
Fibromialgia
Período de silêncio cutâneo
Deficiência

RESUMO

Introdução: O período de silêncio cutâneo (PSC) é um reflexo protetor inibitório da coluna vertebral e seus aferentes consistem em fibras nervosas A-delta. Nosso objetivo foi avaliar pacientes com fibromialgia (FM) e controles saudáveis para determinar as diferenças entre os grupos em relação à duração e latência do PSC, e quando presente, determinar se há alguma relação com as características da doença, distúrbios psicológicos e qualidade de vida.
Materiais e métodos: Trinta e dois pacientes com FM e 32 voluntários saudáveis foram incluídos no estudo. Os dois grupos foram comparados em relação à latência e duração do PSC em ambos os membros superiores e inferiores. Características da doença, distúrbios psicológicos e qualidade de vida dos pacientes foram avaliados utilizando o *Fibromyalgia Impact Questionnaire* (FIQ), e o *Short Form-36* (SF-36). Os pacientes com medida de PSC igual ou inferior às do grupo controle foram comparados com aqueles com valores mais elevados do que os controles em termos de características da doença, estado psicológicos e qualidade de vida.
Resultados: Latências significativamente prolongadas de PSC nos membros superiores e inferiores foram determinadas em pacientes comparados com os controles. Observou-se que a prolongamento da latência do PSC no membro inferior estava associado com a gravidade da doença e incapacidade funcional.
Conclusões: Latências do PCS nos membros superiores e inferiores em pacientes com FM são mais longas do que em voluntários saudáveis. Além disso, o prolongamento da latência do PSC no membro inferior está associado com a gravidade da doença e incapacidade funcional física.

Introduction

Fibromyalgia (FM) is a chronic pain syndrome characterized by widespread pain and tender points at specific anatomic areas that cannot be understood regarding its etiology, despite all the new developments.[1] Some symptoms and signs, including chronic fatigue, headache, sleep disturbance, psychological disorders, irritable bowel and bladder syndromes, dysmenorrhea, sensory disorders such as paraesthesia and dysesthesia without neuropathy, and Raynaud's phenomenon, are common in FM.[1,2]

Although the etiopathogenesis is not yet fully elucidated, studies have reported that various factors might be effective, such as neuroendocrine and autoimmune dysfunction and genetic predisposition.[3] Further, studies have shown that hyperexcitability of spinal and supraspinal neurons in FM play an important role in the development and maintenance of chronic pain.[4,5]

Studies that used the nociceptive flexion reflex (NFR) to show the excitability of dorsal horn neurons of the spinal cord, which formed with peripheral C fibers (a nociceptive afferent), have reported that this excitability in patients with FM causes central sensitization and chronic pain.[6,7]

The assessment method of the A-delta fiber (the other nociceptive afferent) is the cutaneous silent period (CSP).[8] The NFR and CSP are the excitatory and inhibitory parts of the same spinal protective reflex, respectively.[9] Although the CSP has been measured in various muscles using different methods, there is only one study[10] in the literature, and only the upper extremity was evaluated in that study. To our knowledge, no study in the literature has evaluated the relationship between CSP and disease duration, pain level, numbers of total symptoms and tender points, severity of FM, psychological disorders, and quality of life.

Therefore, we aimed to compare patients with FM and healthy controls to determine any difference in CSP duration and latency in the upper and lower extremities, and if present, to determine whether there is any relationship between CSP and disease characteristics, psychological disorders and quality of life.

Materials and methods

Study population

Thirty-two patients who were admitted to the Physical Medicine and Rehabilitation Clinic and were diagnosed with FM according to the American College of Rheumatology (ACR) 1990 classification criteria were included in the study.[1] Thirty-two healthy volunteers consisting of hospital staff and relatives of patients were included in the study as controls.

Exclusion criteria for patients and volunteers were as follows: presence of any central and/or peripheral neurologic disease such as peripheral neuropathy, radiculopathy or multiple sclerosis, muscle disease such as inflammatory myopathy or myositis, any inflammatory, endocrine, cardiac, or psychiatric disease, osteoarthritis, trauma of the hand or foot, tenosynovitis, or a history of surgery. Those who were

Abbreviations

FM:	fibromyalgia
NFR:	nociceptive flexion reflex
CSP:	cutaneous silent period
EMG:	electromyogram
DML:	Distal motor latency
MCV:	motor conduction velocity
SCV:	sensory conduction velocity
APB:	abductor pollicis brevis
TA:	tibialis anterior
MUAP:	motor unit action potential
VAS:	Visual Analogue Scale
FIQ:	Fibromyalgia Impact Questionnaire
BDI:	Beck Depression Inventory
BAI:	Beck Anxiety Inventory
SF-36:	Short Form-36
SPSS:	Statistical Package for the Social Sciences
OR:	odds ratio
HPA:	hypothalamic-pituitary-adrenal
NMDA:	N-methyl-D-aspartic acid
CNS:	central nervous system

pregnant or lactating or who had used any psychotropic and/or antihistamine drugs in the last month were also excluded from the study.

Patients and volunteers with normal musculoskeletal and neurologic examinations including range of motion, muscle strength, superficial sensation, and deep tendon reflex, and who had normal laboratory parameters including complete blood count, complete urinalysis, erythrocyte sedimentation rate, vitamin B12, thyroid function tests, and biochemical tests including electrolytes and enzymes of liver, kidney and muscle were included in the study.

Patients and volunteers were informed about the study and their written consents were obtained at the start of the study. The study was approved by the local Ethical Board and was performed in accordance with the principles of the Declaration of Helsinki.

Electrophysiologic tests

Electrophysiologic evaluations were performed in the electrophysiology laboratory of Gülhane Military Medical Academy Department of Neurology using a 2+8 channel electromyogram (EMG) device (MEDELEC Synergy-Oxford, U.K.) and according to the protocol described by Oh.[11] The room temperature was 24 ± 1°C, and the skin temperature of patients and volunteers was over 32°C. While measurements of the upper extremity were applied in the sitting position, measurements of the lower extremity were applied in the supine position.

Nerve conduction tests

Sensory nerve conduction tests were evaluated from the right median, left ulnar and right sural nerves. Motor nerve conduction tests were evaluated from the right median, left ulnar, right peroneal, and left tibial nerves. Distal motor latency (DML) (ms) and motor conduction velocity (MCV) in motor nerves and sensory conduction velocity (SCV) (m/s) in sensory nerves were recorded.

CSP investigations

Sensory nerves were stimulated in the lower extremity using bar electrode and in the upper extremity using ring electrode. First, the sensory threshold was found. For this purpose, an electrical current of 0.5 ms duration starting from an intensity of 0.6 mA was performed laterally to the lateral malleolus in the lower extremity and to the second finger of the upper extremity. The lowest intensity, which was determined by gradually increasing the intensity until it was felt by the individual, was recorded as the sensory intensity threshold. CSP measurements were performed in the right upper and lower extremities using the abductor pollicis brevis (APB) and tibialis anterior (TA) muscles, respectively. The second finger in the right upper extremity was stimulated, and recordings were obtained from the APB muscle. Before the recording, the patient was asked to perform thumb abduction with maximal effort, and the maximal motor unit action potential (MUAP) amplitude was measured on the screen. Subjects were asked to perform thumb abduction with MUAP amplitudes of at least 25% of the maximal MUAP amplitude. While the patient was constantly performing this abduction, the median nerve was stimulated at an intensity of 15 times the sensory threshold. Five recordings were obtained at 30-second intervals. The CSP latency and duration were measured by assessing the average of 5 traces. The endpoint at which an observable clear-cut inhibition in muscle activity started was considered as the CSP latency (ms). The CSP duration (ms) was determined by measuring the time between the point of inhibition of muscle activity and the point at which it started to return to baseline muscle activity. The sural nerve was stimulated superficially laterally to the lateral malleolus in the right lower extremity, and recordings were obtained from the TA muscle by using the same method described above.

Clinical tests

Disease characteristics including disease duration, symptoms associated with FM and pain level were questioned. The numbers of tender points and symptoms were recorded. Total numbers of symptoms were calculated and recorded. The general pain level felt in the last 48 hours was assessed by visual analogue scale (VAS) with 0-10 cm.

To assess severity of disease, functional disability and specific quality of life, the Fibromyalgia Impact Questionnaire (FIQ)[12] was used, according to which the total score was evaluated between 0-100, with a higher score showing a greater impact of the syndrome on the person.

To assess possible depression symptoms of the patients, the Beck Depression Inventory (BDI)[13] was used, and to assess anxiety symptoms, the Beck Anxiety Inventory (BAI)[14] was used. Twenty-one Likert-type questions were asked with these scales, and each question was evaluated between 0-3.

The general quality of life of patients was evaluated with Short Form-36 (SF-36).[15] Accordingly, two sub-group scores were created as physical health and mental health. The total score was evaluated between 0-100.

Comparisons

The patient and control groups were compared in terms of CSP latency and duration in the upper and lower extremities. Sub-groups were formed according to the CSP latency and duration levels that were determined to be significantly different between groups on the basis of the CSP mean of the control group. Patients with CSP measurements equal to or below values of the control group (group 1) were compared to patients with CSP measurements above the values of the control group (group 2) in terms of disease duration, number of total symptoms and tender points, pain level evaluated by VAS, FIQ score, levels of depression and anxiety, and quality of life.

Statistical analysis

Data analyses were made using the Statistical Package for the Social Sciences (SPSS Inc., USA) 11.5 for Windows. Descriptive statistics were shown as mean ± standard deviation and median for continuous variables and observation number (%) for nominal variables using chi-square tests. Statistically significant differences between groups in terms of continuous variables were studied with Mann-Whitney U test (according to Kolmogorov-Smirnov test, continuous variables were not the distribution normal) and nominal variables with Pearson chi-square test. Significance of the difference in variables between groups 1 and 2 was analyzed using Pearson chi-square test. Regression analysis was used for significant correlations by using group 1 values as the dependent variable. Values of $P < 0.05$ were considered as statistically significant.

Results

The median age of the 64 participants included in the study (46 [71.9%] females, 18 [28.1%] males) was 41.00 (38.53 ± 8.02) years. The distribution and comparison of demographic characteristics and motor and sensory nerve conduction values of patients (n = 32) and volunteers (n = 32) according to groups are presented in Table 1. There was no significant difference between groups in terms of age, gender and motor and sensory conduction values ($P > 0.05$).

The distribution and comparison of CSP latency and duration measured from the APB and TA muscles of patients and controls according to groups are shown in Table 2.

While the mean CSP latencies in the upper and lower extremities of patients were 87.25 and 107.75 ms and CSP durations were 46.25 and 51.15 ms, respectively, these values in controls were 80.75 and 101.62 ms (latencies) and 48.75 and 54.50 ms (durations), respectively.

Significantly prolonged CSP latencies in both upper and lower extremities were determined in patients compared to the control group ($P < 0.05$).

The distribution of disease duration, numbers of total symptoms and tender points, VAS level, FIQ score, levels of depression and anxiety, and quality of life of patients are presented in Table 3.

With respect to sub-groups formed according to mean CSP latency of the control group (patients with equal/lower values versus higher values compared to controls), it was found that while the number of patients with normal CSP latency in the upper extremity (group 1 for upper extremity) was 4 (12.5%), the number of patients with normal latency in the lower extremity (group 1 for lower extremity) was 12 (37.5%).

The comparisons between group 1 and group 2 for upper and lower extremities in terms of disease duration, numbers of total symptoms and tender points, pain level evaluated by VAS, FIQ score, levels of depression and anxiety, and quality of life are shown in Tables 4 and 5.

Table 1 – Distribution and comparison of demographic characteristics and motor and sensory nerve conduction values of patients and volunteers according to groups.

	Patient group (n = 32) n(%), mean ± SD	Control group (n = 32) n(%), mean ± SD	P
Age (year)	39.59 ± 7.03	37.47 ± 8.89	0.293
Gender			
Female	26 (81.3)	20 (62.5)	0.098
Male	6 (18.7)	12 (37.5)	
Right median nerve DML (ms)	2.57 ± 0.18	2.43 ± 0.37	0.069
Right median nerve MCV (m/s)	59.32 ± 3.23	59.48 ± 4.36	0.871
Left ulnar nerve DML (ms)	2.21 ± 0.18	2.14 ± 0.33	0.982
Left ulnar nerve MCV (m/s)	68.30 ± 10.59	64.75 ± 9.60	0.165
Right peroneal nerve DML (ms)	3.45 ± 0.72	3.67 ± 0.81	0.262
Right peroneal nerve MCV (m/s)	54.56 ± 5.14	53.63 ± 6.37	0.524
Left tibial nerve DML (ms)	4.06 ± 0.77	3.83 ± 0.80	0.240
Left tibial nerve MCV (m/s)	46.26 ± 3.75	47.38 ± 5.32	0.335
Right median nerve SCV (m/s)	54.93 ± 2.21	55.62 ± 3.06	0.300
Left ulnar nerve SCV (m/s)	58.21 ± 4.21	57.45 ± 4.09	0.469
Right sural nerve SCV (m/s)	51.77 ± 7.46	51.45 ± 6.83	0.859

SD, standard deviation; DML, distal motor latency; MCV, motor conduction velocity; SCV, sensory conduction velocity.

Table 2 – Distribution and comparison of CSP latency and duration measured from APB and TA muscles of patients and controls according to groups.

CSP (ms)	Patient group (n = 32) Mean ± SD	Control group (n = 32) Mean ± SD	P
Upper extremity			
Latency	87.60 ± 7.49	79.77 ± 8.15	0.001
Duration	47.17 ± 7.33	49.92 ± 9.74	0.151
Lower extremity			
Latency	108.85 ± 10.03	103.42 ± 10.37	0.037
Duration	52.91 ± 13.20	55.93 ± 9.11	0.692

APB, Abductor pollicis brevis; TA, tibialis anterior; SD, standard deviation; CSP, cutaneous silent period.

Table 3 – Distribution of disease duration, numbers of total symptoms and tender points, VAS level, FIQ score, levels of depression and anxiety, and quality of life of patients.

Parameters	Patient group (n = 32) Mean ± SD
Disease duration (year)	5.40 ± 2.97
Number of total symptoms (0-37)	25.53 ± 8.88
Number of tender points (0-18)	15.56 ± 2.15
Pain level (VAS: 0-10 cm)	8.03 ± 0.98
FIQ score (0-100)	66.71 ± 9.48
Beck Depression Inventory level (0-63)	20.93 ± 11.15
Beck Anxiety Inventory level (0-63)	22.78 ± 11.85
Quality of life	
Physical health level (0-100)	26.79 ± 2.30
Mental health level (0-100)	19.75 ± 1.49

SD, standard deviation; VAS, visual analogue scale; FIQ, Fibromyalgia Impact Questionnaire.

Table 4 – Comparisons between group 1 and group 2 for upper extremities in terms of disease duration, number of total symptoms and tender points, pain level evaluated by VAS, FIQ score, levels of depression and anxiety, and quality of life.

Parameters	Group 1 Normal CSP latency (n = 4) Mean ± SD	Group 2 Prolonged CSP latency (n = 28) Mean ± SD	P
Disease duration (year)	5.25 ± 2.06	5.42 ± 3.10	0.913
Number of total symptoms (0-37)	24.92 ± 9.02	29.75 ± 7.50	0.318
Number of tender points (0-18)	15.50 ± 2.25	16.03 ± 1.41	0.671
Pain level (VAS: 0-10 cm)	8.08 ± 0.45	8.11 ± 1.05	1.000
FIQ score (0-100)	66.12 ± 9.74	70.81 ± 6.98	0.364
Beck Depression Inventory level (0-63)	15.10 ± 12.72	21.78 ± 10.90	0.262
Beck Anxiety Inventory level (0-63)	18.50 ± 11.09	23.39 ± 12.01	0.069
Quality of life			
Physical health level (0-100)	27.06 ± 2.08	24.92 ± 3.26	0.062
Mental health level (0-100)	20.52 ± 1.24	19.64 ± 1.51	0.278

CSP, cutaneous silent period; SD, standard deviation; VAS, visual analogue scale; FIQ, Fibromyalgia Impact Questionnaire.

As a result of the comparisons, while there was no relationship between prolongation of CSP latency in the upper extremity and the evaluation parameters, we detected a relationship between prolongation of CSP latency in the lower extremity and numbers of total symptoms, FIQ score and physical health level. Accordingly, there was a positive correlation between prolongation of CSP latency and number of total symptoms and FIQ score and a negative correlation between prolongation of CSP latency and physical health level.

Table 5 – Comparisons between group 1 and group 2 for lower extremities in terms of disease duration, number of total symptoms and tender points, pain level evaluated by VAS, FIQ score, levels of depression and anxiety, and quality of life.

Parameters	Group 1 Normal CSP latency (n = 12) Mean ± SD	Group 2 Prolonged CSP latency (n = 20) Mean ± SD	P
Disease duration (year)	5.25 ± 2.95	5.66 ± 3.11	0.708
Number of total symptoms (0-37)	21.50 ± 8.45	27.95 ± 8.42	0.045
Number of tender points (0-18)	15.33 ± 2.30	15.70 ± 2.10	0.649
Pain level (VAS: 0-10 cm)	7.83 ± 1.11	8.10 ± 0.91	0.467
FIQ score (0-100)	61.50 ± 10.82	69.78 ± 7.23	0.015
Beck Depression Inventory level (0-63)	20.40 ± 11.56	21.83 ± 10.87	0.731
Beck Anxiety Inventory level (0-63)	21.83 ± 13.02	23.35 ± 11.40	0.732
Quality of life			
Physical health level (0-100)	27.85 ± 0.27	26.16 ± 2.74	0.043
Mental health level (0-100)	19.81 ± 1.54	19.65 ± 1.48	0.769

CSP, cutaneous silent period; SD, standard deviation; VAS, visual analogue scale; FIQ, Fibromyalgia Impact Questionnaire.

A regression analysis done for significant correlations by using group 1 values as the dependent variable demonstrated that prolongation of CSP latency in the lower extremity was associated with disease severity and functional disability measured with FIQ (odds ratio [OR]: 0.467, P = 0.002) and physical health level measured with the physical health subscale of SF-36 (OR: –0.231, P = 0.024).

Discussion

Fibromyalgia (FM) is not directly associated with organ dysfunction. Various gene polymorphisms, alterations of the hypothalamic-pituitary-adrenal (HPA) axis, abnormal concentration of neuropeptides and biogenic amines such as serotonin, norepinephrine, cortisol, and substance P, and alterations of activation of receptors such as N-methyl-D-aspartic acid (NMDA) and glutamate have been described in its etiopathogenesis.[16]

A reduction in inhibitory mediators such as serotonin and an increase in excitatory mediators such as substance P induced by various factors of stress, trauma or infectious agents in genetically predisposed individuals may explain the symptoms, including psychological and sleep disorders and

muscle weakness.[17] Inadequate levels of cortisol, growth hormone and insulin-like growth factor-1 due to dysfunction of the HPA may cause symptoms such as fatigue and exercise intolerance.[18]

However, these theories are not sufficient to explain the chronic and widespread pain in FM. The pain threshold decrease in FM and pain are not limited to tender point sites, and there is increased sensitivity to nonspecific stimuli such as mechanical pressure and cold/warm sensations in areas outside tender point sites or in areas without spontaneous pain. Moreover, there is an aberration of the central pain mechanisms.[7,19]

Studies in the literature have reported that hyperexcitability of spinal and supraspinal neuron plays an important role in the development and maintenance of chronic pain.[4,5]

Indirect evidences such as regional increase in cerebral blood flow of some brain areas, alterations of the nociceptive modulating system, central sensitization, increase in temporal summation, late evoked potentials, sensitivity of C fibers, and alteration in levels of substance P, which are known to play an effective role in the transmission of pain in patients with FM, have been reported in the literature.[20,21]

Peripheral nociceptors can be stimulated with tissue trauma and/or up-regulation of nociceptor expression. Impulses from peripheral nociceptors are transmitted to the spinal cord by myelinated A delta and unmyelinated C fibers. First pain is mediated by A delta fiber, and chronic pain occurs by C fibers with following continued stimulus[22]. Although studies evaluating C fibers by NFR are found in the literature,[22,23] only one study has evaluated A delta fibers using the CSP measurement.[10]

Therefore, we aimed to compare patients with FM with healthy controls in order to evaluate any differences in CSP latency and duration in the upper and lower extremities, and if present, to determine whether any relationship exists between CSP and disease characteristics, psychological disorders and quality of life.

Based on the results of our study, while significantly prolonged CSP latencies in both upper and lower extremities were found in patients compared to the control group, there was no significant difference between groups in terms of CSP duration. In addition, we found that prolongation of CSP latency in the lower extremity was correlated with disease severity and physical functional disability of patients.

The CSP is a protective reflex that causes a pause in voluntary muscle contraction in the presence of painful stimuli of a cutaneous nerve. The afferent impulses that generate the CSP are carried by A delta fibers, but the central mechanism of CSP is not known.[24] The CSP is useful to evaluate the components and segments of A delta fibers (not evaluated by modern electrodiagnostic methods) and to understand the central nervous system (CNS) diseases with motor and sensory disorders.[25] Some studies have used CSP to evaluate the nociceptive pathway function at spinal and supraspinal levels in patients with neuropathic pain.[26]

Studies in the literature have shown that CSP was recorded in various sensory neuropathies including Friedreich's ataxia, abetalipoproteinemia and Fabry disease, entrapment neuropathies such as carpal and ulnar tunnel syndromes, spinal cord lesions including myelopathy, radiculopathy, syringomyelia, and root avulsion, and disorders of the CNS including Parkinson's disease and dystonia.[25,27-31] In addition, studies have reported that CSP measurements can be done with various muscles and with different methods. A study similar to our study in the literature, by Sahin et al.,[10] showed that CSP latency recorded from the APB muscle with stimulation of the 5th finger of patients with FM (n = 28) was longer than in the control group (n = 18), but there was no significant difference between groups in terms of CSP duration. Further, only the upper extremity was evaluated in their study.

In the present study, although we used different methods of stimulation from those in the literature, a significant prolongation in CSP latencies (measured in APB and TA muscles) in both upper and lower extremities was found in patients compared to controls. Moreover, there was no difference in terms of CSP duration. This result is compatible with that reported by Sahin et al.[10]

Studies have reported that CSP latency occurs at three times: peripheral conduction time conducted by A delta fibers, the time required for inhibition in the spinal cord, and the time from the spinal cord to muscle motor fibers.[32] Our results are compatible with theories that cite changes in the pain pathway. Studies in the literature have reported that CSP duration is shortened and latency increased in peripheral neuron disorders such as neuropathy and loss of A delta fibers. Furthermore, both CSP latency and duration are extended in Parkinson's disease and dystonia. None of our patients had evidence suggesting neuropathy in conduction velocity studies or evidence of loss of A delta fibers such as myelopathy, radiculopathy or root avulsion. Studies in Parkinson's disease have explained that prolonged CSP duration is related to longer-lasting activity in inhibitory circuits in the spinal cord.

According to our results, while there was a slight shortening in CSP duration in patients when compared to the control group, the difference was not statistically significant. Although our patients had no major disorder suggesting the loss of A delta fibers, Onal et al.,[33] in their study performed in patients with no large fiber neuropathy with early stage diabetes mellitus, and Oz et al.[34] in their study performed in patients with restless legs syndrome, reported that prolonged CSP latency is related to small fiber neuropathy. Moreover, Ulas et al.[35] evaluated the presence of dysautonomia in FM and showed that latency of sympathetic skin response is longer than in the control group, and they also reported that this result may be an indicator of small fiber neuropathy in patients with FM.

In light of this information, we think that our patients may have had a small fiber neuropathy. However, except for the above-mentioned possibilities, the reason for normal CSP duration may be related to technical problems during the measurements.

In the literature, it has been reported that pain has two emotional components. Accordingly, the primary pain effect is the unpleasantness of the sensation, while the secondary pain effect is the occurrence of negative feelings like depression, anger and fear.[36] FM affects the psychological and functional emotional health as well as the quality of life of patients due to the chronicity of the pain. Studies about the pathogenesis of FM have shown that depression and anxiety are affected by similar neuroendocrine mechanisms.[37] As a result of our study, although there was no relationship between CSP latency and levels of anxiety and depression, our levels

of anxiety and depression were above normal values. As reported in the literature, these psychological disorders may be risk factors for the development of FM, and it is theorized that these disorders are present from the onset of the disease.[38]

Quality of life assessment instruments can be generic or specific. We used SF-36 for the generic assessment and FIQ for specific assessment. Studies in the literature have reported that quality of life levels assessed by FIQ and SF-36 in patients with FM were significantly higher than in healthy volunteers.[39,40] Our results could not be compared, since there is no study in the literature that investigated CSP latency in patients with FM.

Pagano et al.[41] evaluated the quality of life in patients with FM using FIQ and SF-36, and reported that FIQ is better for assessing the quality of life than SF-36. This study also showed a limitation in physical functioning in patients with FM, reduced by 10-fold compared with the control group.

Our results, showing that prolongation of CSP latency is associated with the scores of FIQ and the physical health subscale of SF-36, demonstrate that the abnormality in pain pathways is reflected in the physical function of the patients. Further, this result may be related to a potential small fiber neuropathy. Considering the results discussed above, the presence of a potential small fiber neuropathy in these patients may explain the lack of difference in the mental health according to the SF-36 subscale and the levels of anxiety and depression. Although large-scale studies are needed, we think that the evaluation of CSP latency in patients with FM may shed light on the functional disability of patients.

The association of CSP latency in the lower extremity with disease severity and limitation of physical function may be explained by measurements in the upper extremity that were carried out in the sitting position, while measurements in the lower extremity were carried out in the supine position, which is more comfortable. Therefore, the maintenance of the voluntary muscle contraction may be easier in the supine position than in the sitting position. Studies have reported that muscle distance may be effective on latency and duration of CSP.[28,42] The effect of this reflex increases from the proximal to the distal muscles. The upper extremity has a shorter reflex pathway compared to the lower extremity in terms of limb length; therefore, functional disability may be associated with the prolongation of CSP latency in the lower extremity.

Study limitations

This study is subject to several limitations. Clinical assessment scales were not implemented in the control group; thus, adequate comparisons could not be made. Further, no test such as skin biopsy or study of the autonomic nervous system was done to confirm the diagnosis of small fiber neuropathy in our study, thereby precluding the statement of any definitive result.

Conclusion

CSP latencies in both upper and lower extremities in patients with FM are longer than in healthy volunteers. We think that this result supports the theory of abnormalities in the pain pathway at peripheral and spinal levels in the pathogenesis of FM. These abnormalities may be due to the changes in the posterior horn of the spinal cord as well as to a small fiber neuropathy due to a direct loss of A delta fibers. To determine the exact cause, studies evaluating the A delta fiber and utilizing several tests simultaneously are needed. As a secondary outcome, it was found that the prolongation of the CSP latency in the lower extremity is associated with disease severity and physical functional disability. Accordingly, we think that CSP latency may be used as an assessment method for evaluating the disease severity and physical disability in FM. However, prior to its use as a standard measurement method, large-scale studies should be done and normal values created.

Conflicts of interest

The authors declare no conflicts of interest.

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