Serum level of brain-derived neurotrophic factor in fibromyalgia

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Introduction
Fibromyalgia syndrome (FMS) is a complex clinical syndrome that primarily affects middle-aged women. Fibromyalgia (FM) is characterized by pain associated with sleep disturbances (nonrefreshing sleep, hypersomnolence), the presence of specific painful sites (tender points), and is often accompanied by fatigue and depression. It is believed to arise from the abnormal central sensory processing of pain signals, involving the interaction between neurotransmitters, external stressors, behavioral constructs, hormones, and the sympathetic nervous system. Brain-derived neurotrophic factor (BDNF), a member of neurotrophines, is the most prevalent growth factor in the central nervous system. It is essential for the development of the central nervous system and for neuronal plasticity. Because BDNF plays a crucial role in the development and plasticity of the brain, it is widely implicated in psychiatric diseases.

Aim of the work
This study aimed to evaluate serum level of BDNF in FM patients and its relation with depression.

Patients and methods
Thirty patients with primary fibromyalgia syndrome were enrolled into this study. These patients were subjected to clinical examination and assessment of depression using the Hamilton Rating Scale for depression. Serum BDNF levels were determined using an enzyme-linked-immunosorbent assay. Twenty age-matched and sex-matched healthy volunteers were included as controls.

Results
The mean serum BDNF level was age-dependent in healthy controls. FMS patients had higher level of serum BDNF compared with healthy controls. In addition, serum level of BDNF showed correlation with depression, but not with other disease manifestations. The mean serum level of BDNF increased with higher values of depression score in FM patients.

Conclusion
BDNF is involved in the pathophysiology of FMS. Moreover, it seems to be correlated with the intensity of depression symptoms in FMS patients.

Keywords:
brain-derived neurotrophic factor, depression, fibromyalgia syndrome, Hamilton Rating Scale for depression, pain

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Introduction

Fibromyalgia syndrome (FMS) is a chronic, painful, nonarticular, widespread, musculoskeletal disorder characterized by widespread pain, pressure hyperalgesia, morning stiffness, sleep problems, fatigue, headache, anxiety, bowel and bladder abnormalities, tingling and numbness, and increased incidence of depression symptoms and cognitive dysfunction [1]. It has been estimated to affect 2–8% of the population. Predominantly, it affects women between 20 and 50 years of age; however, it has also been observed in men, children, adolescents, and older individuals, with a female-to-male incidence ratio that is between 7: 1 and 9: 1 [2].

Fibromyalgia (FM) or depression can be precipitated by events ranging from injury to psychosocial stressors [3], including physical trauma, illness, infections such as HIV, surgery, autoimmune disease, and motor vehicle accidents [4]. Depression worsens FM symptoms and vice versa, and antidepressants represent a cornerstone of FM therapy [5]. Converging evidence suggests that a polymorphism in the serotonin transporter (5-HTT) gene, implicated in major depressive disorder, may also be implicated in FM. Psychiatric disorders most commonly described in FM are mood disorders. Current major depression has been detected in 20–80% of patients with FM [6].

Brain-derived neurotrophic factor, or BDNF, is a member of the neurotrophin family of growth factors

that induce the survival, development, and function of neurons [7]. It supports the survival of existing neurons and encourages the growth and differentiation of new neurons and synapses through axonal and dendritic sprouting. In the brain, it is active in the hippocampus, cortex, cerebellum, and basal forebrain: the areas vital for learning, memory, and higher thinking [8].

Despite its name, BDNF is actually found in various tissues and not just the brain; it can be seen in the retina, the central nervous system, motor neurons, the kidneys, and the prostate [9]. It is also secreted by Th1 and Th2 lymphocytes and macrophages [10] and is mainly stored in platelets/thrombocytes; thus, it takes part in the regulation of homeostasis and later release with increased demand [11].

BDNF is synthesized as a precursor protein known as prepro-BDNF that is cleaved into pro-BDNF, and further cleaved into mature BDNF, which is released from the postsynaptic membrane and binds to receptors on the surface of cells, TrkB (pronounced 'Track B') [12]. It plays a role in variety of neuroplasticity processes, including pain modulation and mental symptoms, such as depression [13], schizophrenia [14], and Alzheimer's disease [15].

The pathophysiology of both stress-induced depression and FM has been described [6]. Some reported a link between overactive stress system and BDNF expression in the brain. Chronic stress or prolonged exposure to glucocorticoids results in reduction of BDNF levels and impair hippocampal function. Repeated stress can lead to neuronal atrophy including the hippocampus and it reduces the BDNF mRNA expression [16].

Depression is a state of low mood and aversion to activity, which can affect an individual's thoughts, behavior, feelings, and sense of well-being. Careful evaluation of FM patients' history suggests that FM patients often suffer from one or more depressive episodes. The relationship between depression and pain in FM can be attributed to the fact that FMS is characterized by the obligatory presence of diffuse and chronic pain and suffering from any type of pain or just having a medical condition can lead to appropriate reactive depression [6].

As BDNF itself plays a major role in depressive disorder patients and depression symptom is frequent in FMS, it is still elusive whether serum level of BDNF is involved in depression symptom of FMS [13].

The aim of this study was to evaluate serum level of BDNF in FM patients and its relationship with depression.

Patients and methods

Study approval: The study was approved by the Ethical Committee of Benha University. All participants gave written informed consent before participation in the study.

Patients

Thirty patients with primary FMS who fulfilled the recent preliminary diagnostic criteria for diagnosis of FMS [17] were enrolled in the study together with 20 age-matched and sex-matched apparently healthy volunteers as controls.

These patients were selected randomly from the inpatient and the outpatient clinic of the Rheumatology & Rehabilitation Department of Benha University Hospitals.

Criteria for exclusion of fibromyalgia patients

Exclusion criteria were as follows: history of psychological disorders before diagnosis of FM; family history of psychological disorders; presence of autoimmune disease; severe chronic disabling conditions such as severe complicated diabetes mellitus or hypertension, and known malignancy.

All patients included in this study were subjected to full history taking and general and local examination. Pain was assessed using the visual analogue scale (VAS) [18]. The VAS comprised a 10-cm-long straight line with no marks or numbers on it, with the left end of the line representing 'absence of pain' (corresponding to 0 cm) and the right end of the scale representing 'unbearable pain' (corresponding to 10 cm). Disability and current health status were assessed using the Fibromyalgia Impact Questionnaire (FIQ). The FIQ is composed of 10 items. The first item contains 11 questions related to physical functioning [19]. The FIQ is scored in such a way that a higher score indicates a greater impact of the syndrome on the individual. Each of the 10 items has a maximum possible score of 10. Thus, the maximum possible score is 100. An average FM patient scores about 50, and severely afflicted patients usually score more than 70.

Scale	Item #	Recode	Score range	Normalization
Physical impairment	1	No	0–3	S × 3.33
Feel good	2	Yes	0–7	S × 143
Work missed	3	No	0–7	S × 143
Do work	4	No	0–10	None
Pain	5	No	0–10	None
Fatigue	6	No	0–10	None
Rested	7	No	0–10	None
Stiffness	8	No	0–10	None
Anxiety	9	No	0–10	None
Depression	10	No	0–10	None

To maintain a maximum possible score of 100, it is necessary to use an 'equalization calculation' if a patient does not answer all 10 items. If one or more items are missed, the final summative score needs to be multiplied by 10/× [e.g. if one question is missed, multiply by 10/9 (i.e. 1.111); if two questions are missed multiply by 10/8 (i.e. 1.25)].

Hamilton Rating Scale for depression

The original version contains 17 items on symptoms of depression experienced over the past week. Eight items were scored on a five-point scale, ranging from 0, representing not present, to 4, representing severe, and nine were scored from 0 to 2. Scores 0–7 indicate normal; 8–13 indicate mild depression; 14–18 indicate moderate depression; 19–22 indicate severe depression; and scores 23 or greater indicate very severe depression [20].

Laboratory investigations

Laboratory investigations included the following: complete blood count, erythrocyte sedimentation rate, C-reactive protein, serum creatinine. blood urea, creatinine clearance, serum glutamate-pyruvate transaminase (SGPT), serum glutamic oxaloacetic transaminase (SGOT), serum albumin, serum bilirubin, prothrombine time, fasting blood sugar and 2 h postprandial, and hepatitis C virus antibody. Antinuclear antibodies were evaluated using indirect immunofluorescence technique; rheumatoid factor was evaluated using latex agglutination test; and serum BDNF was evaluated using BioVision's Human BDNF (human) (enzyme-linked immunosorbent assay) ELISA Kit catalog#K4788-100 (BioVision Inc., California, USA), which is an in-vitro enzyme-linked immunosorbent assay for the quantitative measurement of human BDNF.

Statistical analysis

Statistical analysis was performed using the Statistical Package for Social Sciences, version 21.0 (SPSS for Windows 21.0; SPSS Inc., Chicago, Illinois, USA).

A *P*-value greater than 0.05 was considered nonsignificant; *P*-value less than 0.05 was considered significant; and *P*-value less than 0.001 was considered highly significant.

Results

Group 1 included 30 patients with primary fibromyalgia syndrome (PFM), of whom 27 (90%) were female and three (10%) were male. Their ages ranged between 19 and 53 years, with a mean of 34.71 ± 1.29 years. The disease duration ranged between 1 and 18 years (4.88 ± 4.19 years).

Group 2 included 20 healthy controls (HC), of whom 16 (80%) were female and four (20%) were male. Their ages ranged between 20 and 46 years, with a mean of 32.94 ± 1.34 years.

There was no statistical difference as regards mean age and sex distribution between PFM patients and the HC group ($P > 0.05$) (Tables 1 and 2).

Significantly higher frequencies were observed among PFM patients compared with HCs as regards the above-mentioned symptoms, with statistically significant difference ($P < 0.05$) for mental confusion and high statistically significant difference ($P < 0.001$) for all except for Raynaud's phenomenon, morning stiffness, and joint swelling (Table 3).

There was statistically significant difference ($P < 0.05$) between PFM and HCs as regards the Hg level and C-reactive protein and high statistically significant difference ($P < 0.001$) as regards erythrocyte sedimentation rate first hour (Table 4).

No statistically significant difference was found between the two groups ($P > 0.05$) as regards red blood cell count, white blood cell count, platelet count, serum urea and serum creatinine, rheumatoid factor, and antinuclear antibodies, although higher positive frequencies were observed among PFM patients compared with HCs.

Table 5 presents serum BDNF level and age in HCs and FMS patients.

The mean serum BDNF level was statistically significantly elevated in PFM patients with depression

Table 1 Demographic characteristics in primary fibromyalgia syndrome patients and controls enrolled to the study

Parameters	Group			
	PFM (*n* = 30)	HCs (*n* = 20)	$\chi^2_{calc.}$	*P*-value
Male [*n* (%)]	3 (10)	4 (20)	0.339	0.561
Female [*n* (%)]	27 (90)	16 (80)		
Ratio (M/F)	3: 27	4: 16		

HC, healthy control; PFM, primary fibromyalgia syndrome.

Table 2 Age distribution in primary fibromyalgia syndrome patients and controls enrolled to study

Age (years)	PFM (*n* = 30)	HC (*n* = 20)	*t*-Value	*P*-value
Mean	34.71 ± 1.29	32.94 ± 1.34	0.1196	0.9053
Minimum	19	20		
Maximum	53	46		

HC, healthy control; PFM, primary fibromyalgia syndrome.

Table 3 Prevalence of symptoms in the primary fibromyalgia syndrome and healthy control groups

Variables	PFM (n = 30) [n (%)]	HCs (n = 20) [N (%)]	$\chi^2_{calc.}$	P-value
Fatigue	26 (86.67)	3 (15)	34.94	<0.000**
Diffuse pain	30 (100.00)	0 (0)	50.00	<0.000**
Joint pain	28 (93.33)	0 (0)	42.424	<0.000**
Postexertional pain	30 (100.00)	0 (0)	50.00	<0.000**
Joint swelling	3 (10.00)	0 (0)	2.128	0.265 (NS)
Soft tissue swelling	16 (53.33)	1 (5)	12.493	0.001**
Weight loss	14 (46.67)	0 (0)	12.963	<0.000**
Loss of appetite	18 (60.00)	3 (15)	9.975	0.003**
Irritable bowel syndrome	10 (33.33)	3 (15)	8.389	0.005**
Raynaud's phenomenon	5 (16.67)	3 (15)	0.025	1.000 (NS)
Sicca-like symptoms	9 (30.00)	0 (0)	7.317	0.007**
Morning stiffness	5 (16.67)	3 (15)	0.025	1.000 (NS)
Paresthesia	21 (70.00)	3 (15)	14.543	<0.000**
Sleep disturbance	19 (63.33)	1 (5)	17.014	<0.000**
Migraine headache	17 (56.67)	1 (5)	13.903	<0.000**
Depression	27 (90.00)	3 (15)	28.125	<0.000**
Anxiety	23 (76.67)	3 (15)	18.283	<0.000**
Confusion	8 (26.67)	0 (0)	6.349	0.015*
Memory disorders	15 (50.00)	0 (0)	14.286	<0.000**

HC, healthy control; PFM, primary fibromyalgia syndrome; *Significant difference if $P < 0.05$; **Highly significant difference if $P < 0.001$.

Table 4 Hematological parameters in the primary fibromyalgia syndrome group

Parameters	Group			
	PFM	HC	t-Value	P-value
HB (g/dl)	9.93 ± 0.31	12.05 ± 0.43	2.16	0.0356*
RBCs (in millions)	4.19 ± 0.10	4.51 ± 0.19	1.654	0.1046 (NS)
WBCs (in thousands)	7.90 ± 0.27	8.77 ± 0.39	3.348	0.065 (NS)
PL (in thousands)	290.05 ± 8.80	298.25 ± 12.70	0.549	0.5857 (NS)
ESR 1st hour (mm/h)	24.05 ± 1.26	11.6 ± 0.91	7.26	<0.000**
Serum urea (mg/dl)	35.4 ± 15.83	33.3 ± 9.74	1.78	0.0812 (NS)
Serum creatinine (mg/dl)	1.36 ± 0.04	1.14 ± 0.06	1.65	0.1042 (NS)
	N (%)	N (%)	$\chi^2_{calc.}$	P-value
CRP	10 (33.33)	1 (5)	4.688	0.037*
ANA	4 (13.3)	0 (0)	2.899	0.140 (NS)
RF	3 (10.0)	0 (0)	2.128	0.265 (NS)

ANA, antinuclear antibody; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; HC, healthy control; PFM, primary fibromyalgia syndrome; RBC, red blood cell; RF, rheumatoid factor; WBC, white blood cell; PL, platelet; *Significant difference if $P < 0.05$; **Highly significant difference if $P< 0.001$.

Table 5 Serum brain-derived neurotrophic factor and age in healthy controls and fibromyalgia syndrome patients

	Age
BDNF	
PFM	0.052
HC	–0.873**

BDNF, brain-derived neurotrophic factor; HC, healthy control; PFM, primary fibromyalgia syndrome; *Correlation is significant at the 0.05 level (two-tailed); **Correlation is significant at the 0.01 level (two-tailed).

($P < 0.000$), whereas there was no increase in BDNF mean serum level with other clinical manifestations ($P > 0.05$) (Table 6).

As regards the mean serum BDNF level, there was a statistically highly significant difference between PFM patients and HCs, being statistically significantly elevated in PFM patients with depression than in PFM patients without depression and HCs (Table 7).

Depression affected 27 cases of PFM. Twenty patients suffered from mild depression, six from moderate depression, and one patient suffered from severe depression. The mean serum BDNF level was elevated with increasing grade of depression (Table 8).

Higher values of VAS of pain were observed in PFM patients compared with HCs (Table 9).

There was a highly statistically significant difference ($P < 0.001$) between PFM patients and HCs with respect to FIQ total scores for all dimensions. The highest mean FIQ subscale scores were observed for fatigue and depression (Table 10).

Table 6 Relation of brain-derived neurotrophic factor and clinical manifestations of primary fibromyalgia syndrome patients

Fibromyalgia symptoms	*N*	Mean ± SE (ng/ml)	*t*-value	*P*-value
Fatigue				
Present	26	25 294.46 ± 821	0.898	0.377
Absent	4	23 322.29 ± 1598		
Diffuse pain				
Present	30	25 031.50 ± 744.14	—	—
Absent	0	—		
Joint pain				
Present	28	25 026.79 ± 790	−0.023	0.982
Absent	2	25 097.51 ± 2187		
Postexertional pain				
Present	30	25 031.50 ± 744.14	—	—
Absent	0	—		
Joint swelling				
Present	3	24 599.66 ± 1357	0.19	0.851
Absent	27	25 079.49 ± 818		
Soft tissue swelling				
Present	16	25 792.1 ± 1063	1.096	0.282
Absent	14	24 162.25 ± 1023		
Weight loss				
Present	14	25 453.19 ± 1131	0.523	0.605
Absent	16	24 662.53 ± 1008		
Loss of appetite				
Present	18	25 815.16 ± 1033	1.305	0.202
Absent	12	23 856.01 ± 983		
IBS				
Present	10	25 772.04 ± 1306	0.697	0.491
Absent	20	24 661.24 ± 918		
Raynaud's phenomenon				
Present	5	26 574.19 ± 2244	0.925	0.363
Absent	25	24 722.97 ± 782		
Sicca-like symptoms				
Present	9	25 767.38 ± 1460	0.641	0.527
Absent	21	24 716.13 ± 875		
Morning stiffness				
Present	5	23 267.87 ± 1411	−1.062	0.297
Absent	25	25 384.23 ± 840		
Paresthesia				
Present	21	2 5191.32 ± 947	0.323	0.749
Absent	9	24 658.59 ± 1197		
Sleep disturbance				
Present	19	25 626.4 ± 995	1.053	0.302
Absent	11	24 003.96 ± 1064		
Migraine headache				
Present	17	25 495.04 ± 1042	0.706	0.486
Absent	13	24 425.35 ± 1068		
Depression				
Present	27	25 606.89 ± 747	−7.389	<0.000**
Absent	3	19 853.03 ± 219		
Anxiety				
Present	23	25 489.67 ± 911	1.121	0.272
Absent	7	23 526.12 ± 987		
Confusion				
Present	8	26 244.3 ± 1565	0.982	0.334
Absent	22	24 590.49 ± 843		
Memory disorders				
Present	15	25 972.37 ± 1192	1.372	0.181
Absent	15	23 956.23 ± 778		

IBS, irritable bowel syndrome; **In depression there is highly significant difference: $P < 0.001$.

Table 7 Comparison brain-derived neurotrophic factor serum levels in different groups

Parameters	Group			
	PFM with depression	PFM without depression	HCs	*P*-value
BDNF (ng/ml)	25 606.89 ± 747	19 853.03 ± 219	13 526.13 ± 759	<0.000**

BDNF, brain-derived neurotrophic factor; HC, healthy control; PFM, primary fibromyalgia syndrome.

Table 8 Prevalence and grades of depression in fibromyalgia according to the HDR-scale and its relation with brain-derived neurotrophic factor

HDR-S	PFM (*n* = 30) [*N* (%)]	BDNF (ng/ml)
No depression (0–7)	3 (10.00)	19 853.03 ± 219
Mild (8–13)	20 (66.67)	20 934.45 ± 791
Moderate (14–18)	6 (20.00)	22 102.55 ± 751
Severe (19–22)	1 (3.33)	25 112.01 ± 766

BDNF, brain-derived neurotrophic factor; PFM, primary fibromyalgia syndrome.

Table 9 Comparison of clinical profile (visual analogue scale) of fibromyalgia syndrome and healthy controls

Tables	PFM	HCs	*t*-Value	*P*-value
VAS of pain (cm)	6.33 ± 0.11	0.90 ± 0.15	29.84	<0.000

HC, healthy control; PFM, primary fibromyalgia syndrome; VAS, visual analogue scale.

Table 10 Fibromyalgia Impact Questionnaire in primary fibromyalgia syndrome and healthy control group

Scale	PFM (*n* = 30)	HCs (*n* = 20)	*t*-Value	*P*-value
Physical impairment	4.7 ± 2.7	00 ± 0	—	—
Feel good	5.15 ± 0.71	—	—	—
Work missed	4.79 ± 0.66	00 ± 0	—	—
Interfere with Do job	5.65 ± 0.72	00 ± 0	—	—
Pain	6.65 ± 0.38	00 ± 0	—	—
Fatigue	7.35 ± 0.23	00 ± 0	—	—
Morning tiredness	6.35 ± 0.15	0.5 ± 0.02	31.61	<0.000
Stiffness	5.25 ± 2.17	00 ± 0	—	—
Anxiety	6.25 ± 1.71	0.2 + 0.01	2.878	0.006
Depression	7.1 ± 2.14	0.2 + 0.01	2.623	0.0116
Total FIQ score	59.03 ± 5.5	1.901 ± 0.05	8.45	<0.000

FIQ, Fibromyalgia Impact Questionnaire; HC, healthy control; PFM, primary fibromyalgia syndrome.

There was an inverse correlation between the mean serum level of BDNF and age in HCs, whereas there was a nonsignificant correlation between BDNF level and age in PFM patients.

Discussion

FM is a syndrome that is believed to arise from the abnormal central sensory processing of pain signals. BDNF belongs to neurotrophin family and plays a role in variety of neuroplasticity processes, including pain modulation and mental symptom, such as depression [21]. As FMS patients have pain and mood-related symptoms, several studies have been performed and have shown an alteration of BDNF in FMS patients.

In our study, there was a negative correlation between the mean serum level of BDNF and age of HCs. These results were similar to those reported by Nugraha *et al.* [22]. However, this result is in disagreement with the study by Lang *et al.* [23], which showed a positive correlation of serum BDNF and age in HCs. Factors that can alter BDNF in healthy individuals could be body weight [24], physical activity, personal characteristics (e.g. depression), but not sex [23,24].

In this study, we found that 90% of FM patients suffered from depression. The results of Nugraha *et al.* [22] confirmed the prevalence of FMS in patients who had depression and anxiety (21 and 46%, respectively). Our results supported the results of Güven *et al.* [25], who evaluated depression in FM patients and found that, according to (Beck depression inventory) the BDI score, 90% of FM patients were classified as depressed, of whom 50% had mild, 38% had moderate, and 2% had severe depression.

Serum levels of BDNF were significantly higher in PFM patients than in HCs and the mean serum BDNF level was statistically significantly elevated in PFM patients with depression. This is in agreement with the findings of Haas *et al.* [26] and Uçeyler *et al.* [27].

Laske *et al.* [28] studied the mean serum level of BDNF in FM patients compared with HCs, which were significantly increased in FM patients (19.6 ng/ml; SD = 3.1) than in HCs (16.8 ng/ml; SD = 2.7; $P < 0.0001$). In addition, BDNF serum concentrations in FM patients were independent of age, sex, illness duration, pre-existing recurrent major depression, and antidepression medication in low doses. Authors interpreted this finding as being reasonable to assume that platelets are also activated in FM. This could explain their results that showed a significant increase in the serum concentration of BDNF in patients with FM.

Higher levels of BDNF in FMS patients may be caused by several reasons. The most leading hypotheses is that BDNF plays a role as a pain modulator [13].

Taskin *et al.* [29] reported that the level of BDNF was not significantly different in the migraine, FM,

and control groups (depressed patients and healthy individuals), and there was no significant correlation of serum BDNF levels with age and sex.

To assess the severity of depression, the HDR-scale was applied. The results of our study revealed that only 10% of FM patients reported no depression and that depression affects 90% of PFM patients, with 66.67% patients suffering from mild depression, 20% from moderate depression, and 3.33% suffering from severe depression. The mean serum BDNF level was elevated with increasing grade of depression. This is in agreement with the findings of Nugraha *et al*. [22]. This result reflected the correlation of BDNF and depression score. In contrast, Haas *et al*. [26] reported no correlation of plasma BDNF levels with age, disease duration, pain score, number of pain points, and HAM-D score.

Two meta-analysis studies demonstrated that BDNF levels were lower in depressed patients than in HCs, which significantly increased after antidepressant treatment. There was a significant correlation between changes in BDNF level and depression score changes, thus supporting the notion that depression improvement with treatment is associated with neuroplastic changes [13].

Dwivedi [30] reported that suicidal behavior may be associated with a decrease in BDNF level. Another study reported that the BDNF mRNA expression was reduced in peripheral blood mononuclear cells (PBMCs) of patients with major depression compared with HCs [31].

Major depressive disorder patients showed lower level of serum BDNF, which were correlated with high depression rating scores [32].

In this study, we measured affection of our patients with FMS as reflected by their total FIQ score. The highest mean FIQ subscale scores were observed in fatigue and depression. Schaefer *et al*. [33] found that the highest mean FIQ subscale scores were observed for fatigue and stiffness, whereas in a study conducted by Linares *et al*. [34] the average FIQ total score was 63.6 in depressed patients and the most affected were activities of daily living.

Conclusion

BDNF is involved in the pathophysiology of FMS. Moreover, it seems to be correlated with the intensity of depression symptoms in FMS.

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Conflicts of interest

There are no conflicts of interest.

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