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Pain catastrophizing, depression, and anxiety in fibromyalgia patients

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Abstract

Psychiatric findings may be seen in Fibromyalgia (FM) patients. We aimed to evaluate the relationship between anxiety, depression, and pain catastrophizing in FM patients and normal individuals. The study group consisted of FM patients and a healthy control group. Socio-demographic data form, Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), Visual Analogue Scale (VAS), Fibromyalgia Impact Questionnaire (FIQ), and Pain Catastrophizing Scale (PCS) were administered to the participants. It was evaluated whether there was a statistical difference between the groups in terms of BDI, BAI, PCS, VAS, and FIQ. Of the 178 patients in our study, 85 were FM patients and 93 were control groups. The BDI, BAI, PCS, PCSH (PCS Helplessness), PCSM (PCS Magnification), and PCSR (PCS Rumination) were found to be higher in FM patients compared to the control group. The FM patients were found to have moderate depression according to the BDI score (18.7±10.6) and moderate anxiety according to the BAI score (16.5±9.9). There was a positive correlation between BDI and BAI, FIQ and VAS, PCS and BDI, BAI and FIQ, and BAI and FIQ. It was found that the FM patients had "moderate" depression and anxiety, and their level of pain catastrophizing increased with the increase in depression and anxiety severity.

Keywords: fibromyalgia, depression, anxiety, pain catastrophizing

1. Introduction

Fibromyalgia (FM) is a chronic pain condition characterized by symptoms such as widespread musculoskeletal pain, the presence of tender points, fatigue, anxiety, sleep disturbances, and cognitive and mood disorders (1). According to the criteria of the American College of Rheumatology (ACR), FM patients should have tenderness in at least 11 of 18 specific tender point sites in addition to widespread pain (2). The etiology and pathogenesis of fibromyalgia have not been fully understood yet (3).

Since FM causes widespread chronic pain, it can seriously affect the quality of life (4). FM may be associated with some psychiatric disorders. FM patients' depression status can be evaluated by Beck Depression Inventory (BDI) and their anxiety status by Beck Anxiety Inventory (BAI) (5). Depression symptoms, which are quite common in the chronic course of pain, make it difficult for the patient to comply with the treatment (6).

Catastrophizing is the tendency to evaluate one's situation or physical complaint, fearing that it will worsen each time (7). As a result of the catastrophizing, individuals have difficulty suppressing thoughts about their pain (rumination), exaggerate

the pain, and worry about the negative consequences of the pain (magnification), and believe that there is nothing they can do to relieve the pain (helplessness). This situation is evaluated by the Pain Catastrophizing Scale (PCS) (8). Catastrophizing pain has been associated with various diseases, chronic pain, deterioration of quality of life, increased disability, and more healthcare use (9). In individuals with FM, pain catastrophizing has been associated with poor response to treatment (10).

In this study, we aimed to compare the levels of anxiety, depression, and pain catastrophizing between FM patients and normal individuals.

2. Materials and methods

A total of 178 people were included in our study. Eighty-five people included in the study were FM patients who had previously been diagnosed with FM according to the ACR criteria (2). As the control group, 93 people without FM diagnosis and with similar socio-demographic characteristics were included. The data was collected using the socio-demographic data form, Fibromyalgia Impact Questionnaire (FIQ), Visual Analogue Scale (VAS), BDI, BAI, and PCS. Statistical differences between groups and the relationships

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between VAS, BDI, BAI, FIQ, and PCS were evaluated. A correlation analysis was carried out between BDI, BAI, PCS, FIQ, and VAS scores in the FM group.

The socio-demographic data form includes the following information: age, gender, marital status, history of chronic illness, and duration of illness.

Fibromyalgia Impact Questionnaire (FIQ) evaluates the following ten characteristics in FM patients: physical function, not going to work, feeling unwell, pain, difficulty at work, stiffness, fatigue, morning fatigue, anxiety, and depression. The maximum score for each subtitle is 10 points, so the total maximum score is 100. (11) In VAS, the pain level is scored between 0 (no pain) and 10 (unbearable pain) (11).

Beck Depression Inventory (BDI) is used to assess depression levels. In BDI, the scores within the range of 0-9 refer to "no depression", 10-16 to "mild depression", 17-23 to "moderate depression", and 24 or more to "severe depression" (12, 13).

Beck Anxiety Inventory (BAI) is used to assess anxiety levels. In BAI, 0-7 points refer to minimal anxiety symptoms, 8-15 points to mild, 16-25 points to moderate, and 26-63 points to severe (7).

Pain Catastrophizing Scale (PCS) is a self-administered questionnaire and includes the subscales of rumination, magnification, and helplessness. PCS is used to assess the patient's feelings and thoughts about pain. PCS score ranges between 0 and 52 points (8). The subscales "helplessness" (inability to cope with pain effectively), "magnification" (discontent created by focusing excessively on the negative consequences of pain), and "rumination" (inability to inhibit thoughts about pain) reflects the cognitive content of anxiety and depression accompanying headache (14).

Inclusion criteria: Participants (FM patients and control group) over 18 years of age, whose cognitive functions were sufficient to answer the questions, who did not have a history of psychiatric illness and who did not use psychiatric medication were included in our study. Exclusion criteria: Those with cognitive impairment that prevented them from

answering the questions, those who did not fully answer the questionnaire, and those with missing socio-demographic data were excluded (Fig. 1).

Statistical data were analyzed using the IBM SPSS software package (v.22.0). To compare groups, a one-way ANOVA test was used for normally distributed values in non-categorical data based on the data distribution. Mann-Whitney U test was used for non-parametric data. Categorical data were compared with the Chi-square test. The Pearson Correlation test was used to analyze the relationship between scale scores. The values with p<0.05 were evaluated as statistically significant.

Ethical approval was taken from the local University Clinical Research Ethics Committee for this study (Approval letter number: 2020/327, Date of approval: 27/08/2020).

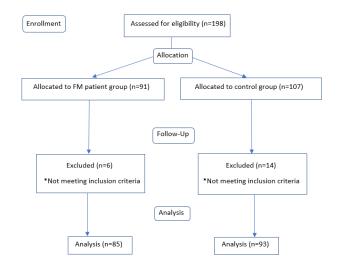


Fig. 1. Flow diagram of the study

3. Results

Of the 178 individuals participating in the study, 85 were FM patients and 93 were healthy controls. The mean age of the FM patients was 43.0 ± 7.4 years. The mean duration of FM disease was 7.3 ± 3.3 years (Table 1).

Table 1. Sociodemographic and clinical characteristics of FM patients and control groups

Variables	All participants (n=178)	FM patients (n=85)	Control groups (n=93)	p
Age (year), (mean \pm sd)	42.0±7.3	43.0±7.4	41.1±8.5	0.121
Gender, n (%) Female Male	153 (85.9) 25 (14.1)	78 (91.8) 7 (8.2)	75 (80.6) 18 (19.4)	0.081
Marriage status, n (%) Single Married	24 (13.5) 154 (86.5)	15 (17.6) 70 (82.4)	9 (9.7) 84 (90.3)	0.120
Chronic disease history, n (%) Yes No	27 (15.2) 151 (84.8)	7 (8.2) 78 (91.8)	20 (21.5) 73 (78.5)	0.051
Duration of FM disease (year), (mean \pm sd)	-	7.3±3.3	-	-

p, chi square test; n, number; sd, standard deviation

A statistically significant difference was observed between FM patients and the control group in terms of BDI, BAI, PCS Total (PCST), PCS Helplessness (PCSH), PCS Magnification (PCSM), and PCS Rumination (PCSR) (p<0.001, all). The BDI, BAI, PCST, PCSH, PCSM, and PCSR were higher in FM

patients. FM patients were found to have "moderate" depression according to the BDI score (18.7 ± 10.6) and "moderate" anxiety according to the BAI score (16.5 ± 9.9) (Table 2).

Table 2. BDI, BAI, PCS, FIQ and VAS scores of FM patients and control groups

Scales	FM Patients (mean±sd)	Control Groups (mean±sd)	Mean Difference	95% CI	p
BAI	16.5±9.9	3.8±1.8	12.658	10.580, 14.737	< 0.001
BDI	18.7 ± 10.6	5.1±4.1	13.638	11.295, 15.981	< 0.001
PCST	23.2±12.5	10.7 ± 12.8	12.493	8.727, 16.260	< 0.001
PCSH	9.6±6.4	3.8 ± 5.4	5.754	3.989, 7.519	< 0.001
PCSM	5.9±2.9	3.4 ± 3.3	2.523	1.586, 3.459	< 0.001
PCSR	7.6 ± 3.8	3.7±4.4	3.963	2.730, 5.195	< 0.001
FIQ	63.1±6.5	-	-	-	N/A
VAS	6.7 ± 2.0	-	-	-	N/A

p, independent sample T-test; sd, standard deviation; CI, Confidence Interval; N/A, Not applicable; BDI, Beck Depression Inventory; BAI, Beck Anxiety Inventory; PCST, Pain Catastrophizing Scale Total; PCSH, PCS Helplessness; PCSM, PCS Magnification; PCSR, PCS Rumination; FIQ, Fibromyalgia Impact Questionnaire; VAS, Visual Analogue Scale

The PCS subscale scores of the FM patients with and without depression were evaluated in terms of their total BDI scores, and those of the patients with and without anxiety in terms of their BAI total scores. The PCS total score (p<0.001) and the scores for the PCS subscales of "helplessness", "magnification", and "rumination" were found to be

significantly higher in the FM patients with depression than in those without. Likewise, the PCS total score (p<0.001) and the scores for the PCS subscales of "helplessness", "magnification", and "rumination" were found to be higher in the FM patients with anxiety compared to those without (Table 3).

Table 3. PCS subscale scores according to the presence of depression or anxiety in FM patients

PCS Subscales	No Depression (BDI) (mean±sd)	Depression (BDI) (mean±sd)	Mean Difference	95% CI	p
Helplessness	7.5±6.4	13.4 ± 4.6	-5.921	-8.565, -3.277	< 0.001
Magnification	5.3±3.0	7.0 ± 2.3	-1.721	-2.989, -0.454	0.008
Rumination	6.8±3.9	9.2 ± 3.0	-2.430	-4.096, -0.765	0.005
Total	19.6±12.8	29.8 ± 8.8	-10.145	-15.396, -4.895	< 0.001
	No Anxiety (BAI) (mean±sd)	Anxiety (BAI) (mean±sd)	Mean Difference	95% CI	p
Helplessness	7.4 ± 6.0	13.8±4.9	-6.416	-9.031, -3.801	< 0.001
Magnification	5.2±2.8	7.3 ± 2.4	-2.113	-3.363, -0.862	0.001
Rumination	6.6 ± 3.6	9.7±3.4	-3.134	-4.757, -1.510	< 0.001
Total	19.2±11.9	30.9±9.8	-11.733	-16.875, -6.873	< 0.001

p, independent sample T-test; sd, standard deviation; BDI, Beck Depression Inventory; BAI, Beck Anxiety Inventory; PCS, Pain Catastrophizing Scale

There was a statistically significant correlation between the PCS total scores and "severe depression" (p=0.006) from the BDI subscales and "severe anxiety" (p<0.001) from the BAI subscales. As the severity of BDI and BAI increased, the PCS total scores also increased statistically significantly (Table 4).

A correlation analysis was carried out between BDI, BAI,

PCS, FIQ, and VAS scores and the duration of disease in FM patients. There was a positive correlation between the scores for BAI and BDI, PCS and BDI, FIQ and BDI, VAS and BDI, PCS and BAI, FIQ and BAI, and PCS and FIQ in FM patients. There was no correlation between the disease duration and the scales (Table 5).

Table 4. PCS Total Scores by BDI and BAI Subscale Scores in FM patients

Scales		PCS Total Score (mean±sd)	Mean Difference	95% CI	p
	Normal	22.7±15.3	-	-	-
BDI	Mild Depression	17.2±10.2	5.492	-1.437, 12.421	0.118
	Moderate Depression	22.2±7.0	0.550	-9.823, 10.932	0.915
	Severe Depression	33.6±7.0	-10.850	-18.362, -3.338	0.006
BAI	Normal	18.0±10.6	-	-	-
	Mild Anxiety	19.8±12.6	-1.785	-8.592, 5.022	0.601
	Moderate Anxiety	25.0±9.7	-6.947	-14.698, 0.803	0.077
	Severe Anxiety	35.1±7.8	-17.124	-23.498, -10.749	< 0.001

p, independent sample T-test; sd, standard deviation; BDI, Beck Depression Inventory; BAI, Beck Anxiety Inventory; PCS, Pain Catastrophizing Scale

Table 5. Correlation analysis between BDI, BAI, PCS, FIQ, VAS scores and duration of illness in FM patients

Variables		BDI	BAI	PCS	FIQ	VAS
BDI	r	-	0.803	0.424	0.385	-0.247
	95% CI	-	0.685, 0.894	0.224, 0.627	0.200, 0.544	-0.436, -0.070
	p	-	< 0.001	< 0.001	< 0.001	0.022
BAI	r	0.803	-	0.507	0.528	-0.107
	95% CI	0.685, 0.894	-	0.323, 0.662	0.374, 0.656	-0.321, 0.081
	p	< 0.001	-	< 0.001	< 0.001	0.329
	r	0.424	0.507	-	0.351	0.025
PCS	95% CI	0.224, 0.627	0.323, 0.662	-	0.163, 0.520	-0.192, 0.247
	p	< 0.001	< 0.001	-	0.001	0.823
	r	0.385	0.528	0.351	-	0.058
FIQ	95% CI	0.200, 0.544	0.374, 0.656	0.163, 0.520	-	-0.166, 0.269
	p	< 0.001	< 0.001	0.001	-	0.595
VAS	r	0.247	-0.107	0.025	0.058	-
	95% CI	-0.436, -0.070	-0.321, 0.081	-0.192, 0.247	-0.166, 0.269	-
	p	0.022	0.329	0.823	0.595	-
Duration of illness	r	0.071	-0.078	0.131	0.032	-0.026
	95% CI	-0.140, 0.260	-0.241, 0.086	-0.084, 0.334	-0.131, 0.181	-0.216, 0.153
	p	0.521	0.478	0.231	0.768	0.815

p value, Pearson Partial Correlation Test; r, Correlation Coefficient; CI, Confidence Interval; BDI, Beck Depression Inventory; BAI, Beck Anxiety Inventory; PCS, Pain Catastrophizing Scale; FIQ, Fibromyalgia Impact Questionnaire; VAS, Visual Analogue Scale

4. Discussion

There is a strong relationship between chronic pain and depression, and both can aggravate each other (15). Chronic pain can occur as part of a pain syndrome such as fibromyalgia (16). A study published in 2014 showed a higher prevalence of anxiety and depression in FM patients (17). Our FM patients perceived higher intensity of pain due to increased levels of anxiety and depression. Similar to the studies in the literature, BDI and BAI levels were higher in FM patients compared to the control group in our study (18).

A study reported that, according to BDI, 10% of the FM patients had no depression, 50% had mild depression, 38% had moderate depression, 2% had severe depression, and the average BDI score was 15 (19). In our study, the FM patients were found to have "moderate" depression according to the BDI score and "moderate" anxiety according to the BAI score. It can be considered that FM patients are depressed due to having a chronic disease for a long time and have anxiety due to pain and other effects of the disease.

Our study observed a positive correlation between BDI and BAI, FIQ and VAS, and BAI and FIQ in FM patients. In a previous study, FM patients were reported to have fatigue, sleep disorders, and anxiety, and a significant correlation was found between their scores for FIQ and BDI (r=0.430, p=0.008) (20). One study reported that anxiety and depression correlated independently with pain and fatigue in FM patients (21). It has been reported that FM can be a symptom of psychiatric disorders or psychophysiological abnormalities since depression and anxiety often accompany chronic painful conditions (22). One recent study measured pain intensity. The results showed that the higher the pain score, the higher the mood disorder (23). Incompatible responses to pain can worsen the pain experience and further impair function. Excessive rumination about pain is associated with a magnification of distress and extreme helplessness, poorer response to pain

treatments, and greater disability (24). One study reported that FM responds to anti-depressant drugs and is one of the medical, neurological, and psychological disorders that show high comorbidity with depression, known as "Affective Spectrum Disorder" and other affective spectrum disorders (25). Anti-depressants have the most evidence for treating chronic pain with accompanying anxiety or depression. Chronic pain has been shown to significantly impair dopamine activity in the limbic midbrain region (26). Depression can occur when monoamine neurotransmitters such as NE and 5-HT are decreased in the nervous system (27). The SNRIs have been shown to reduce FM and neuropathic pain with and without depression (28).

Pain catastrophizing is the tendency to feel increased pain, whether real or imaginary. This inability to distract the focus of attention from pain causes an increase in pain perception and sensitivity (29). In our study, according to the control list, a higher cognition was found in the PCS total score and the scores for the PCS subscales "helplessness", "magnification", and "rumination", which shows emotional and cognitive attitudes towards pain. In a study, catastrophizing was reported to be associated with pain activation, as it appeared to increase the perception of pain, according to brain MRI findings from FM patients (30). The same areas of the central nervous system are responsible for the sensation of pain and depression (15).

Our study found that anxiety and depression were associated with pain catastrophizing and increased helplessness, rumination, and magnification. The subscales "helplessness", "magnification", and "rumination" reflects the cognitive content of anxiety and depression accompanying headache (14). In our study, it was observed that the PCS total score of the FM patients increased in cases of "severe depression" from the BDI subscales and "severe anxiety" from the BAI subscales. This shows that the level of depression and anxiety increases the level of pain catastrophizing. Our study

observed A positive correlation between PCS and BDI, BAI and FIQ. This shows that pain catastrophizing increases with the effect of depression, anxiety, and illness.

As a result, given that catastrophe is associated with increased disease activity, depression, and anxiety in patients with fibromyalgia, the improvement and implementation of cognitive, psychosocial and medical interventions designed to reduce disaster in patients with fibromyalgia would potentially represent a significant improvement in disease management.

In most of the previous studies, anxiety, depression, pain level and quality of life were evaluated in patients with fibromyalgia, generally using one or both of the scales such as BDI, BAI, VAS, FIQ and PCS (10, 19-21). Similar to the study of Gürbüz at all (31) and Jesus at all (32), our study is one of the few studies in which this relationship can be explained by using scales such as BDI, BAI, VAS, and FIQ for pain status in patients with fibromyalgia.

Our study is limited in that it is single-centered. Future studies should be carried out in multi-centers with more participants. The strength of our study lies in that it is a prospective study and compares FM patients and normal individuals in terms of the symptom levels of anxiety, depression, and pain catastrophizing.

In conclusion, our study observed that the levels of depressive symptoms, anxiety, and pain catastrophic were significantly higher in the FM patients. It was found that the FM patients generally had "moderate" depression and anxiety. It was also found that as the severity of depression and anxiety increased in FM patients, their levels of pain catastrophizing, helplessness, magnification, and rumination also increased. In FM patients, in addition to medical treatments, psychiatric approaches should be incorporated into the treatment for patients who are indicated after psychosocial evaluations.

Ethical Statement

Ethical approval was taken from the local University Clinical Research Ethics Committee for this study (Approval letter number: 2020/327, Date of approval: 27/08/2020).

Conflict of interest

The authors declare no conflicts of interest.

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None to declare.

Authors' contributions

Concept: H.İ., F.İ., Design: H.İ., F.İ., Data Collection or Processing: H.İ., F.İ., Analysis or Interpretation: H.İ., F.İ., Literature Search: H.İ., F.İ., Writing: H.İ., F.İ.

References

 Mist SD, Jones KD. Randomized Controlled Trial of Acupuncture for Women with Fibromyalgia: Group Acupuncture with

- Traditional Chinese Medicine Diagnosis-Based Point Selection. Pain Med. 2018 Sep 1;19(9):1862-1871.
- Galvez-Sánchez CM, Reyes Del Paso GA. Diagnostic Criteria for Fibromyalgia: Critical Review and Future Perspectives. J Clin Med. 2020 Apr 23;9(4):1219..
- **3.** Ribeiro VGC, Mendonça VA, Souza ALC, Fonseca SF, Camargos ACR, Lage VKS, et al. Inflammatory biomarkers responses after acute whole body vibration in fibromyalgia. Braz J Med Biol Res. 2018 Mar 1;51(4):e6775.
- Karatay S, Okur SC, Uzkeser H, Yildirim K, Akcay F. Effects of Acupuncture Treatment on Fibromyalgia Symptoms, Serotonin, and Substance P Levels: A Randomized Sham and Placebo-Controlled Clinical Trial. Pain Med. 2018 Mar 1;19(3):615-628.
- Croft PR, Papageorgiou AC, Ferry S, Thomas E, Jayson MI, Silman AJ. Psychologic distress and low back pain. Evidence from a prospective study in the general population. Spine (Phila Pa 1976). 1995 Dec 15;20(24):2731-7.
- Demyttenaere K, Bonnewyn A, Bruffaerts R, Brugha T, De Graaf R, Alonso J. Comorbid painful physical symptoms and depression: prevalence, work loss, and help seeking. J Affect Disord. 2006 Jun;92(2-3):185-93.
- 7. Buenaver LF, Edwards RR, Smith MT, Gramling SE, Haythornthwaite JA. Catastrophizing and pain-coping in young adults: associations with depressive symptoms and headache pain. J Pain. 2008 Apr;9(4):311-9.
- 8. Sullivan MJ, Bishop SR, Pivik J. The pain catastrophizing scale: development and validation. Psychological assessment. 1995;7(4):524.
- 9. de Boer MJ, Struys MM, Versteegen GJ. Pain-related catastrophizing in pain patients and people with pain in the general population. Eur J Pain. 2012 Aug;16(7):1044-52.
- 10. Gracely RH, Geisser ME, Giesecke T, Grant MA, Petzke F, Williams DA, et al. Pain catastrophizing and neural responses to pain among persons with fibromyalgia. Brain. 2004 Apr;127(Pt 4):835-43.
- 11. Alev A, Mihriban A, Bilge E, Ayça E, Merve K, Şeyma C, et al. Effects of whole body vibration therapy in pain, function and depression of the patients with fibromyalgia. Complement Ther Clin Pract. 2017 Aug;28:200-203.
- **12.** Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch Gen Psychiatry. 1961 Jun;4:561-71.
- 13. Hisli NJJP. Beck depresyon envanterinin universite ogrencileri icin gecerliligi, guvenilirligi. (A reliability and validity study of Beck Depression Inventory in a university student sample). J Psychol, 1989;7:3-13.
- 14. Yavuz KF, Yavuz N, Ulusoy S, Alniak I, Günes HNG. Gerilim ve Migren Tipi Bas Agrilarina Eslik Eden Islevsel Olmayan Bilissel Içerikler ve Tutumlar/Maladaptive cognitive content and attitudes accompanying tension type headache and migraine. Dusunen Adam. 2013;26(1):12.
- **15.** Szkutnik-Fiedler D, Grzeskowiak E. Coexistence of chronic pain and depression: A short review with a focus on the anti-depressant effect of tramadol and buprenorphine. Neuropsychiatry. 2018;8(1):80-8.
- 16. Holmes A, Christelis N, Arnold C. Depression and chronic pain. Med J Aust. 2013 Sep 16;199(S6):S17-20.
- 17. Borg C, Padovan C, Thomas-Antérion C, Chanial C, Sanchez A, Godot M, et al. Pain-related mood influences pain perception differently in fibromyalgia and multiple sclerosis. J Pain Res. 2014 Jan 22;7:81-7.

- 18. Thieme K, Turk DC, Flor H. Comorbid depression and anxiety in fibromyalgia syndrome: relationship to somatic and psychosocial variables. Psychosom Med. 2004 Nov-Dec;66(6):837-44.
- 19. Güven AZ, Kul Panza E, Gündüz OH. Depression and psychosocial factors in Turkish women with fibromyalgia syndrome. Eura Medicophys. 2005 Dec;41(4):309-13.
- 20. Turkyilmaz AK, Kurt EE, Karkucak M, Capkin E. Sociodemographic characteristics, clinical signs and quality of life in patients with fibromyalgia. Eurasian J Med. 2012 Aug;44(2):88-93.
- 21. Kurtze N, Gundersen KT, Svebak S. The role of anxiety and depression in fatigue and patterns of pain among subgroups of fibromyalgia patients. Br J Med Psychol. 1998 Jun;71 (Pt 2):185-94.
- 22. 2Grothe DR, Scheckner B, Albano D. Treatment of pain syndromes with venlafaxine. Pharmacotherapy. 2004 May;24(5):621-9.
- 23. Salazar A, Dueñas M, Mico JA, Ojeda B, Agüera-Ortiz L, Cervilla JA, et al. Undiagnosed mood disorders and sleep disturbances in primary care patients with chronic musculoskeletal pain. Pain Med. 2013 Sep;14(9):1416-25.
- 24. Burns JW, Johnson BJ, Mahoney N, Devine J, Pawl R. Cognitive and physical capacity process variables predict long-term outcome after treatment of chronic pain. J Consult Clin Psychol. 1998 Apr;66(2):434-9.
- **25.** Hudson JI, Mangweth B, Pope HG Jr, De Col C, Hausmann A, Gutweniger S, et al. Family study of affective spectrum disorder. Arch Gen Psychiatry. 2003 Feb;60(2):170-7.

- 26. Taylor AMW, Becker S, Schweinhardt P, Cahill C. Mesolimbic dopamine signaling in acute and chronic pain: implications for motivation, analgesia, and addiction. Pain. 2016 Jun;157(6):1194-1198.
- **27.** Haase J, Brown E. Integrating the monoamine, neurotrophin and cytokine hypotheses of depression--a central role for the serotonin transporter? Pharmacol Ther. 2015 Mar;147:1-11.
- **28.** Häuser W, Urrútia G, Tort S, Uçeyler N, Walitt B. Serotonin and noradrenaline reuptake inhibitors (SNRIs) for fibromyalgia syndrome. Cochrane Database Syst Rev. 2013 Jan 31;(1):CD010292.
- **29.** Hubbard CS, Khan SA, Keaser ML, Mathur VA, Goyal M, Seminowicz DA. Altered Brain Structure and Function Correlate with Disease Severity and Pain Catastrophizing in Migraine Patients. eNeuro. 2014 Dec 30;1(1):e20.14.
- 30. Sheng J, Liu S, Wang Y, Cui R, Zhang X. The Link between Depression and Chronic Pain: Neural Mechanisms in the Brain. Neural Plast. 2017;2017:9724371.
- **31.** Jesus DXGd, Pacheco CdR, Rezende RM. The use of Pilates for pain control in patients with fibromyalgia. Fisioterapia em Movimento. 2022;35.
- **32.** Gürbüz C, Yilmaz H, Odabaşi FÖ, Göksu H, Akkurt HE. Type and Frequency of Primary Headache in Female Patients with Fibromyalgia Syndrome. Journal of Physical Medicine & Rehabilitation Sciences/Fiziksel Tıp ve Rehabilitasyon Bilimleri Dergisi. 2021;24(2).