

ORIGINAL ARTICLE

Evaluation of affective temperament and anxiety-depression levels in fibromyalgia patients: a pilot study

Selen Işık-Ulusoy 

Başkent University School of Medicine, Psychiatry Department, Konya, Turkey.

Objective: Fibromyalgia (FM) patients have higher rates of depression and anxiety disorders than healthy controls. Affective temperament features are subclinical manifestations of mood disorders. Our aim was to evaluate the affective temperaments of FM patients and investigate their association with depression and anxiety levels and clinical findings.

Methods: This cross-sectional study included FM patients and healthy controls. The Hospital Anxiety and Depression Scale (HADS) was used to determine patient anxiety and depression levels, and the Temperament Scale of Memphis, Pisa and San Diego, self-administered version was applied to assess affective temperaments in all subjects. Disease severity was assessed in FM patients with the Fibromyalgia Criteria and Severity Scales and the Fibromyalgia Impact Questionnaire (FIQ). Differences between groups were evaluated using Student's *t*-tests. Correlations among parameters were performed.

Results: This study involved 38 patients with FM (30 female) and 30 healthy controls (25 female). Depressive, anxious and cyclothymic temperaments were significantly higher in FM patients than healthy controls. Statistically significant positive correlations were found between HADS depression score and all temperaments except hyperthymic, as well as between HADS anxiety score and cyclothymic and anxious temperaments. HADS depression and anxiety scores were correlated with symptom severity. We found a higher risk of depression and anxiety among FM patients with higher FIQ scores.

Conclusion: This study is the first to evaluate affective temperament features of FM patients. Evaluating temperamental traits in FM patients may help clinicians determine which patients are at risk for depression and anxiety disorders.

Keywords: Fibromyalgia; anxiety; depression; affective temperament

Introduction

Fibromyalgia (FM) is a rheumatologic disorder characterized by chronic, diffuse, widespread musculoskeletal pain and fatigue, sleep disturbance, cognitive dysfunction, depression and anxiety.¹ Approximately 3% of the population is affected by FM in developed countries.² Women are more likely than men to have FM. Using the 1990, 2010 and modified 2010 American College of Rheumatology (ACR) criteria, a Scottish study found that the ratio of females to males was 13.7:1, 4.8:1 and 2.3:1.³ FM is also more prevalent in people over 50 years old with low education levels, low socioeconomic status and rural residence.⁴

The pathophysiology of fibromyalgia involves a number of factors, including abnormalities in the neuroendocrine and autonomic nervous systems, genetic factors, psychosocial variables and environmental stressors.⁵ Widespread chronic pain could be explained by “central sensitivity” or “central sensitization” that amplifies the central nervous system's response to peripheral input.⁶ Regarding its affective

component, the central sensitization mechanism in FM is conceptualized as an emotional dysregulation that results in a dysregulation of pain perception.⁷

FM patients often complain about several psychiatric disorders. Mental disorders, especially mood disorders, have been associated with a negative impact on pain, sleep, fatigue, physical functioning and quality of life in FM.⁸⁻¹⁰ Anxiety disorders and depression are the most common psychiatric disorders in FM, with prevalence rates of 18-36% for depression and 11.6-32.2% for anxiety disorders.¹¹⁻¹³

A number of factors, including genetic or neurobiological mechanisms, play an important role in the etiology of psychiatric disorders, and recent studies have confirmed that affective temperaments may help predict manifestations of specific psychopathologies in different conditions.¹⁴⁻¹⁶ Akiskal et al. defined affective temperament as a highly heritable phenomenon that describes a personality's underlying biological and genetic tendency and establishes an individual's activity level, rhythms, mood and related cognitions.^{14,15,17}

Correspondence: Selen Işık Ulusoy, Başkent Üniversitesi Tıp Fakültesi, Konya Araştırma Hastanesi, Psikiyatri Anabilim Dalı, 42000 Konya, Türkiye.
E-mail: drselen82@gmail.com
Submitted Feb 15 2018, accepted Aug 10 2018, Epub Apr 15 2019.

How to cite this article: Işık-Ulusoy S. Evaluation of affective temperament and anxiety-depression levels in fibromyalgia patients: a pilot study. Braz J Psychiatry. 2019;41:428-432. <http://dx.doi.org/10.1590/1516-4446-2018-0057>

Affective temperament features are psychiatric indicators that may help predict vulnerability to mood disorders.¹⁸ We aimed to evaluate affective temperament in FM patients and its association with depression and anxiety levels and clinical findings compared to healthy controls.

Material and methods

Subjects

In this cross-sectional study, 38 patients diagnosed with FM according to 2010 ACR criteria and 30 healthy controls were enrolled. We selected patients who had been admitted to the outpatient rheumatology unit of Başkent University Hospital in Konya, Turkey between June 2017 and September 2017. Each participant signed an informed consent form in accordance with the Declaration of Helsinki. Because of the retrospective nature of the study, the local research ethics committee waived ethical approval.

Exclusion criteria for patients and controls included age under 18 years, inability or unwillingness to cooperate, having taken drugs that affect the central nervous system in the last month, having used medication for a chronic medical illness, having taken nonsteroidal anti-inflammatory drugs or opioids in the last week, having used psychotropic drugs, such as antidepressants or anxiolytic drugs, in the last 3 months for any reason. Thirty age-, sex- and education-matched healthy control subjects were chosen randomly from among hospital staff and patient companions. All patients were interviewed with the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I).

Measures

Fibromyalgia Criteria and Severity Scales (FCSS)

Both FM diagnosis and disease severity were determined using the FCSS, which have been used to diagnose FM in epidemiological and clinical studies and are based on the 2010 ACR criteria.^{19,20} This questionnaire includes two scales: the widespread pain index (WPI) and the symptom severity scale (SSS). The results of these two scales are used to establish a diagnosis of FM and evaluate its severity.^{19,20}

Fibromyalgia Impact Questionnaire (FIQ)

The FIQ, a ten-item self-administered questionnaire, was used to determine the physical functioning and health status of FM patients. Since each item has a maximum score of 10, the highest possible score is 100. Higher scores indicate greater impairment in daily activities. The FM patients were subdivided into 2 groups based on FIQ scores: group 1 was less symptomatic (FIQ < 50), while group 2 was more symptomatic (FIQ ≥ 50). The validity and reliability of the Turkish version of the FIQ have been evaluated.²¹

Hospital Anxiety and Depression Scale (HADS)

This scale was used to determine patient anxiety and depression levels. It includes of 14 items related to anxiety

(7 items) and depression (7 items). Scores for each item were between 0 and 3, with a total score between 0 and 21. The cutoff point is 8/21 for anxiety and depression.²²

Temperament Scale of Memphis, Pisa and San Diego, self-administered version (TEMPS-A)

Akiskal et al. developed the TEMPS-A scale to assess affective temperament.¹⁵ The validity and reliability of the Turkish version of the scale were confirmed by Vahip et al.²³

Although the original scale consists of 109 items for men and 110 for women, the Turkish version consists of 99 items. The Turkish version contains 18 items for depressive, 19 items for cyclothymic, 20 items for hyperthymic, 18 items for irritable and 24 items for anxious temperamental characteristics, with cutoff points for dominant temperaments of 13, 18, 20, 13, and 18, respectively.

Statistical analysis

Statistical data were analyzed using SPSS version 21.0, with values expressed as mean ± standard deviation. Data normality was analyzed with the Kolmogorov-Smirnov test. Student's *t*-test was used according to the Kolmogorov-Smirnov results. Differences were considered significant at $p < 0.05$. Correlations between the WPI, SSS and FIQ and HADS scores and TEMPS-A subscales were investigated based on Pearson's or Spearman's correlation coefficient.

Results

Comparison of sociodemographic features

The present study included 38 FM patients (30 female [78.9%]; mean age 40.4±10 years) and 30 healthy controls (25 female/5 male; mean age 39.9±10 years). No statistically significant differences were found between the FM and control groups regarding age, gender or education level (Table 1). The mean FIQ score was 58.11±19.48 (range 26.2-96.6) and the mean duration of FM was 39.21±48.04 months (range 3-160). The mean WPI and SSS scores were 10.2±2.92 (range 5-17) and 8.85±1.64 (range 7-12), respectively (Table 1).

Comparison of temperament and anxiety depression scores

When the mean TEMPS-A scores were compared, we found that depressive, cyclothymic, and anxious temperaments were significantly higher among FM patients than controls (Table 2). FM patients had higher depression (47.4% n=18) and anxiety (42.1% n=16) cut-off scores for HADS than controls (16.6% n=5, 10.0% n=3) ($p = 0.036$, $p = 0.027$ respectively).

Correlations between TEMPS-A subscales, clinical findings and HADS scores

We performed a correlation analysis between temperament, HADS score, symptom severity and WPI. HADS

Table 1 Demographic and clinical findings for patient and control groups (proportions and means with standard deviation)

Variables	Patients (n=38)	Controls (n=30)	p-value
Age (years)	40.4±10	39.9±10	0.94
Years of education	7.06±3.22	7.85±3.51	0.095
Female/male, n (%)	30 (78.94)/8 (21.05)	25 (83.33)/5 (16.66)	0.62
Widespread pain index	10.2±2.92	-	
Symptom severity scale	8.85±1.64	-	
Fibromyalgia Impact Questionnaire	58.11±19.48	-	
Duration of fibromyalgia (months)	39.21±48.04	-	

Data presented as mean ± standard, unless otherwise specified.

Table 2 Comparison of TEMPS-A and HADS scores between patient and control groups

Variables	Patients (n=38)	Controls (n=30)	p-value
TEMPS-depressive	9.15±3.40	5.42±1.80	< 0.001
TEMPS-cyclothymic	10.84±4.28	7.47±2.61	0.006
TEMPS-hyperthymic	8.31±3.74	7.47±2.56	0.42
TEMPS-irritable	5.57±2.85	4.26±1.93	0.1
TEMPS-anxious	12.57±5.55	8.15±2.14	0.003
HADS-anxiety	10.0±3.71	5.47±1.98	< 0.001
HADS-depression	8.26±4.27	4.05±1.92	< 0.001

Data presented as mean ± standard deviation.

HADS = Hospital Anxiety and Depression Scale; TEMPS-A = Temperament Scale of Memphis, Pisa and San Diego, self-administered version.

Bold font indicates statistical significance.

Table 3 Correlations between TEMPS-A subscales, clinical findings and HADS scores

TEMPS-A subscales	HADS anxiety scores		HADS depression scores		Symptom severity scale		Widespread pain index	
	r	p-value	r	p-value	r	p-value	r	p-value
TEMPS-depressive	0.403	0.087	0.696	0.001	0.092	0.708	0.09	0.97
TEMPS-cyclothymic	0.487	0.035	0.801	< 0.001	0.167	0.495	0.173	0.480
TEMPS-hyperthymic	0.156	0.523	-0.311	0.194	-0.148	0.546	-0.06	0.807
TEMPS-irritable	0.270	0.263	0.479	0.038	-0.218	0.371	-0.154	0.528
TEMPS-anxious	0.777	< 0.001	0.796	< 0.001	0.493	0.032	-0.035	0.887

HADS = Hospital Anxiety and Depression Scale; TEMPS-A = Temperament Scale of Memphis, Pisa and San Diego, self-administered version.

Bold font indicates statistical significance.

depression scores were positively correlated with TEMPS-A depressive, cyclothymic, irritable and anxious scores. There was a positive correlation between HADS anxiety scores and TEMPS-A cyclothymic and anxious scores (Table 3). Only anxious temperament was found to be positively correlated with symptom severity ($p = 0.032$; $r = 0.493$). There was no correlation between TEMPS-A subscales and WPI (Table 3). Additionally, HADS depression and anxiety scores were correlated with symptom severity ($p = 0.008$, $r = 0.589$; $p = 0.037$, $r = 0.482$ respectively).

When patients were subgrouped according to FIQ score (group 1 < 50; group 2 ≥ 50); group 2 had a higher risk of anxiety and depression ($p = 0.003$ and $p = 0.006$, respectively) Moreover, TEMPS-A depressive, cyclothymic and anxious temperament scores were higher in group 2 than group 1 ($p = 0.002$; $p = 0.002$; $p < 0.05$ respectively).

Discussion

In the present study we compared clinical findings, affective temperament, depression and anxiety scores between FM

patients and healthy controls. To the best of our knowledge, this is the first study to investigate affective temperament in FM patients using the TEMPS-A scale. The most widely used tools to evaluate temperament and character in previous studies have been the Temperament and Character Inventory and the Minnesota Multiphasic Personality Inventory. Most of the studies using the Minnesota Multiphasic Personality Inventory have found that FM patients had higher hypochondriasis, hysteria and depression scale scores than healthy controls.²⁴ Previous studies using the Temperament and Character Inventory have found higher harm avoidance scores and lower self-directedness scores.^{25,26}

Depression and anxiety disorders are the most common psychiatric disorders among FM patients, with depression ranging from 20 to 80% and anxiety ranging from 13 to 63%.²⁷ The higher HADS anxiety and depression scores in our study are consistent with the findings of previous studies. From a pathophysiological perspective, low serum serotonin levels, low cerebrospinal fluid levels of serotonin metabolites, norepinephrine and dopamine, and higher plasma cortisol levels were found as evidence of abnormal pain processing in

FM patients, being similar to levels found in psychiatric disorders.²⁸⁻³⁰

Affective temperament features are subclinical manifestations of classical mood disorders.^{14,16,18} In our investigation of affective temperaments in FM patients, depressive, anxious and cyclothymic temperaments were significantly higher in FM patients than healthy controls. FM patients with higher FIQ scores also had higher depressive, anxious and cyclothymic temperament scores. The depressive and anxious temperament domains appear to cluster across mood disorders.³¹ In addition to the pathophysiological similarities, depressive and anxious temperaments are higher in both FM and mood disorders.

In this study, the TEMPS-A cyclothymic subscale was one of the highest in FM patients. High TEMPS-A cyclothymic scores have been reported as temperamental feature of bipolar disorder, subclinical bipolar psychopathology, major depressive disorder and borderline-like symptoms.³² Recent clinical reviews summarized that 17.9-21.7% of FM patients also manifest bipolar disorder and proposed a close relationship between FM patients and Cluster B personality disorders, mainly borderline or histrionic.^{9,33,34} According to these studies, cyclothymia may be a sign of bipolarity and borderline personality traits in FM patients. Circadian and social rhythm instability have long been implicated in bipolar spectrum disorders.^{35,36} Since abnormalities in the circadian rhythm of hormonal profiles and cytokines have been observed in FM, circadian and social rhythms may be an important factor in the pathophysiology of FM.³⁷ Further research is needed on the mutual relations between circadian and social rhythm dysregulation and FM. Cyclothymic temperament may play a role in this relationship in FM patients.

Solmi et al. found higher cyclothymic, depressive, irritable and anxious TEMP-S scores in a major depressive disorder group than healthy controls.³⁸ The positive correlation we found between HADS depression score and TEMPS-A cyclothymic, depression, irritable and anxious subscales may also support these results in FM patients. Solmi et al. also found that depressive and anxious temperaments were associated with mood and anxiety disorders.³⁸ The other positive correlation found in the present study was between HADS anxiety scores and TEMPS-A cyclothymic and anxious subscales. Both the cyclothymic and anxious temperaments may be subclinical manifestations of anxiety disorders in FM patients.

The American College of Rheumatology has developed the WPI and SSS as diagnostic criteria and severity scales for characteristic FM symptoms.²⁰ FIQ scores have been used to evaluate FM disease activity as well as severity.³⁸ We found a higher risk of depression and anxiety in the group with higher FIQ scores, as well as a positive correlation between HADS depression and anxiety scores and symptom severity. A study by Davis et al. on the effects of mood and psychosocial stressors on reported pain found that FM patients affected by negative mood reported greater increases in clinical pain.³⁹ This finding is also consistent with our findings, as are frequent reports of a bidirectional relationship between mood and chronic pain.⁴⁰

Our study has some limitations that should be addressed in future research. First, the sample was limited to participants from the rheumatology unit of a single hospital in Turkey. Thus, our findings may not be generalizable to other more racially and ethnically diverse patient populations. Second, the sample size could be considered relatively small, although it is reassuring that the differences found in such comparisons were statistically robust. Third, instead of scales applied by a psychiatrist, self-rating scales were used to evaluate depression and anxiety levels. Thus, we used self-rating scales for depression and anxiety to evaluate the link between temperament subscales, which were screened using the TEMPS-A. Fourth, since this is a cross-sectional study, the relationship between FM symptoms and depression or anxiety scores may not be clear.

In conclusion, FM patients are more likely to have a higher frequency of depression and anxiety disorders than healthy controls. Considering these higher rates, predicting clinical psychiatric conditions becomes more important. Our study is the first to evaluate affective temperament in FM patients, and we found that FM patients have different temperaments than healthy controls. This study supports the idea that the affective temperament properties of FM patients may predispose them to depression and anxiety disorders. Consequently, by evaluating temperament traits in FM patients, it may be possible to identify those at risk of depression and anxiety disorders, who may require more psychiatric support.

Disclosure

The authors report no conflicts of interest.

References

- Mease PJ. Further strategies for treating fibromyalgia: the role of serotonin and norepinephrine reuptake inhibitors. *Am J Med.* 2009;122:S44-55.
- Helmick CG, Felson DT, Lawrence RC, Gabriel S, Hirsch R, Kwoh CK, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part I. *Arthritis Rheum.* 2008;58:15-25.
- Jones GT, Atzeni F, Beasley M, Fließ E, Sarzi-Puttini P, Macfarlane GJ. The prevalence of fibromyalgia in the general population: a comparison of the American College of Rheumatology 1990, 2010, and modified 2010 classification criteria. *Arthritis Rheumatol.* 2015;67:568-75.
- Queiroz LP. Worldwide epidemiology of fibromyalgia. *Curr Pain Headache Rep.* 2013;17:356.
- Bradley LA. Pathophysiology of fibromyalgia. *Am J Med.* 2009;122:S22-30.
- Yunus MB. Editorial review: an update on central sensitivity syndromes and the issues of nosology and psychobiology. *Curr Rheumatol Rev.* 2015;11:70-85.
- Ablin J, Neumann L, Buskila D. Pathogenesis of fibromyalgia - a review. *Joint Bone Spine.* 2008;75:273-9.
- Consoli G, Marazziti D, Ciapparelli A, Bazzichi L, Massimetti G, Giacomelli C, et al. The impact of mood, anxiety, and sleep disorders on fibromyalgia. *Compr Psychiatry.* 2012;53:962-7.
- Kudlow PA, Rosenblat JD, Weissman CR, Cha DS, Kakar R, McIntyre RS, et al. Prevalence of fibromyalgia and co-morbid bipolar disorder: a systematic review and meta-analysis. *J Affect Disord.* 2015;188:134-42.
- Plazier M, Ost J, Stassijns G, De Ridder D, Vanneste S. Pain characteristics in fibromyalgia: understanding the multiple dimensions of pain. *Clin Rheumatol.* 2015;34:775-83.

- 11 Thieme K, Turk DC, Flor H. Comorbid depression and anxiety in fibromyalgia syndrome: relationship to somatic and psychosocial variables. *Psychosom Med.* 2004;66:837-44.
- 12 Epstein SA, Kay G, Clauw D, Heaton R, Klein D, Krupp L, et al. Psychiatric disorders in patients with fibromyalgia. A multicenter investigation. *Psychosomatics.* 1999;40:57-63.
- 13 Wolfe F, Ross K, Anderson J, Russell IJ, Hebert L. The prevalence and characteristics of fibromyalgia in the general population. *Arthritis Rheum.* 1995;38:19-28.
- 14 Akiskal HS, Akiskal KK, Haykal RF, Manning JS, Connor PD. TEMPS-A: progress towards validation of a self-rated clinical version of the Temperament Evaluation of the Memphis, Pisa, Paris, and San Diego Autoquestionnaire. *J Affect Disord.* 2005;85:3-16.
- 15 Rihmer Z, Akiskal KK, Rihmer A, Akiskal HS. Current research on affective temperaments. *Curr Opin Psychiatry.* 2010;23:12-8.
- 16 Kesebir S, Gündoğar D, Küçüksubaşı Y, Tatlıdil Yaylacı E. The relation between affective temperament and resilience in depression: a controlled study. *J Affect Disord.* 2013;148:352-6.
- 17 Park CI, An SK, Kim HW, Koh MJ, Namkoong K, Kang JI, et al. Relationships between chronotypes and affective temperaments in healthy young adults. *J Affect Disord.* 2015;175:256-9.
- 18 Rihmer Z, Gonda X, Torzsa P, Kalabay L, Akiskal HS, Eory A. Affective temperament, history of suicide attempt and family history of suicide in general practice patients. *J Affect Disord.* 2013;149:350-4.
- 19 Wolfe F, Clauw DJ, Fitzcharles MA, Goldenberg DL, Häuser W, Katz RS, et al. Fibromyalgia criteria and severity scales for clinical and epidemiological studies: a modification of the ACR preliminary diagnostic criteria for fibromyalgia. *J Rheumatol.* 2011;38:1113-22.
- 20 Wolfe F, Clauw DJ, Fitzcharles MA, Goldenberg DL, Katz RS, Mease P, et al. The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. *Arthritis Care Res (Hoboken).* 2010;62:600-10.
- 21 Sarmer S, Ergin S, Yavuzer G. The validity and reliability of the Turkish version of the Fibromyalgia Impact Questionnaire. *Rheumatol Int.* 2000;20:9-12.
- 22 Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand.* 1983;67:361-70.
- 23 Vahip S, Kesebir S, Alkan M, Yazici O, Akiskal KK, Akiskal HS. Affective temperaments in clinically-well subjects in Turkey: initial psychometric data on the TEMPS-A. *J Affect Disord.* 2005;85:113-25.
- 24 Johnson AL, Storzbach D, Binder LM, Barkhuizen A, Kent Anger W, Salinsky MC, et al. MMPI-2 profiles: fibromyalgia patients compared to epileptic and non-epileptic seizure patients. *Clin Neuropsychol.* 2010;24:220-34.
- 25 Mazza M, Mazza O, Pomponi M, Di Nicola M, Padua L, Vicini M, et al. What is the effect of selective serotonin reuptake inhibitors on temperament and character in patients with fibromyalgia? *Compr Psychiatry.* 2009;50:240-4.
- 26 Gencay-Can A, Can SS. Temperament and character profile of patients with fibromyalgia. *Rheumatol Int.* 2012;32:3957-61.
- 27 Fiotta P, Fiotta P, Manganelli P. Fibromyalgia and psychiatric disorders. *Acta Biomed.* 2007;78:88-95.
- 28 Russell IJ, Michalek JE, Vipraio GA, Fletcher EM, Javors MA, Bowden CA. Platelet 3H-imipramine uptake receptor density and serum serotonin levels in patients with fibromyalgia/fibrositis syndrome. *J Rheumatol.* 1992;19:104-9.
- 29 Russell IJ, Vaeroy H, Javors M, Nyberg F. Cerebrospinal fluid biogenic amine metabolites in fibromyalgia/fibrositis syndrome and rheumatoid arthritis. *Arthritis Rheum.* 1992;35:550-6.
- 30 McCain GA, Tilbe KS. Diurnal hormone variation in fibromyalgia syndrome: a comparison with rheumatoid arthritis. *J Rheumatol Suppl.* 1989;19:154-7.
- 31 Solmi M, Zaninotto L, Toffanin T, Veronese N, Lin K, Stubbs B, et al. A comparative meta-analysis of TEMPS scores across mood disorder patients, their first-degree relatives, healthy controls, and other psychiatric disorders. *J Affect Disord.* 2016;196:32-46.
- 32 Takeshima M, Oka T. Comparative analysis of affective temperament in patients with difficult-to-treat and easy-to-treat major depression and bipolar disorder: possible application in clinical settings. *Compr Psychiatry.* 2016;66:71-8.
- 33 Sancassiani F, Machado S, Ruggiero V, Cacace E, Carmassi C, Gesi C, et al. The management of fibromyalgia from a psychosomatic perspective: an overview. *Int Rev Psychiatry.* 2017;29:473-88.
- 34 Stubbs B. A random effects meta-analysis investigating the prevalence of bipolar disorder in people with fibromyalgia: an updated analysis. *J Affect Disord.* 2016;191:308-9.
- 35 Banks FD, Lobban F, Fanshawe TR, Jones SH. Associations between circadian rhythm instability, appraisal style and mood in bipolar disorder. *J Affect Disord.* 2016;203:166-75.
- 36 Sylvia LG, Alloy LB, Hafner JA, Gauger MC, Verdon K, Abramson LY. Life events and social rhythms in bipolar spectrum disorders: a prospective study. *Behav Ther.* 2009;40:131-41.
- 37 Mahdi AA, Fatima G, Das SK, Verma NS. Abnormality of circadian rhythm of serum melatonin and other biochemical parameters in fibromyalgia syndrome. *Indian J Biochem Biophys.* 2011;48:82-7.
- 38 Schaefer C, Chandran A, Hufstader M, Baik R, McNett M, Goldenberg D, et al. The comparative burden of mild, moderate and severe fibromyalgia: results from a cross-sectional survey in the United States. *Health Qual Life Outcomes.* 2011;9:71.
- 39 Davis MC, Zautra AJ, Reich JW. Vulnerability to stress among women in chronic pain from fibromyalgia and osteoarthritis. *Ann Behav Med.* 2001;23:215-26.
- 40 Adams LM, Turk DC. Psychosocial factors and central sensitivity syndromes. *Curr Rheumatol Rev.* 2015;11:96-108.