Affective temperaments and emotional traits are associated with a positive screening for premenstrual dysphoric disorder

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Abstract

Objectives: Preliminary evidence indicates that premenstrual dysphoric disorder (PMDD) may be frequently co-morbid with bipolar spectrum disorders. In addition, the manifestations of PMDD seem similar to a subthreshold depressive mixed state. Nevertheless, the associations between PMDD and affective temperaments and emotional traits have not been previously investigated.

Methods: A consecutive sample of 514 drug-free Brazilian women (mean age: 22.8; SD = 5.4 years) took part in this cross-sectional study. Screening for PMDD was obtained with the validated Brazilian Portuguese version of the Premenstrual Symptoms Screening Tool (PSST). Affective temperaments and emotional dimensions were evaluated with the Affective and Emotional Composite Temperament Scale (AFECTS). In addition, socio-demographic and data on menstrual cycle were collected.

Results: According to the PSST, 83 (16.1%) women screened positive for PMDD, while 216 (42.0%) women had no/mild premenstrual symptoms. The cyclothymic temperament was independently associated with PMDD (OR = 4.57; 95% CI: 2.11–9.90), while the euthymic temperament had an independent association with a lower likelihood of a positive screening for PMDD (OR = 0.28; 95% CI: 0.12–0.64). In addition, anger and sensitivity emerged as emotional dimensions significantly associated with PMDD.

Conclusions: A positive screening for PMDD was associated with a predominant cyclothymic temperament, while an euthymic temperament was associated with a lower likelihood for a positive screening for PMDD. These data deserve replication in prospective studies.
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1. Introduction

Female reproductive life events are often associated with physical and psychological complaints [1]. Two to five percent of women may present with premenstrual dysphoric disorder (PMDD), the most severe manifestation of the premenstrual syndrome [2]. PMDD has been consistently associated with a detrimental impact on quality of life and functioning [3]. Notwithstanding relationships between PMDD and bipolarity have been suggested, relatively limited evidence is available. For example, a significant proportion of women with bipolar disorder (BD) experience an aggravation of affective symptomatology in the premenstrual phase [4,5]. In addition, a cross-sectional study provided preliminary evidences that PMDD is frequently co-morbid with bipolar spectrum disorders, notably type II bipolar disorder (BD) and cyclothymia [6], and women with PMDD frequently experience marked lability of affect, irritability, anger, and inner tension, which frequently co-occur with depressive symptoms, thus resembling a subthreshold mixed affective state. Finally, the differential diagnosis of severe PMDD and BD is often challenging [7].

Affective temperaments may be an inherited part of personality [8], which appear to be relatively stable throughout the lifespan [9]. Several lines of evidence indicate that affective temperaments are possible intermediate phenotypes for mood disorders [10] and that certain types of predominant affective temperaments (e.g., the cyclothymic and hyperthymic temperaments) may either be a harbinger of bipolarity in patients presenting with a major depressive episode or portend a higher risk for bipolar spectrum disorders [11–13].

To our knowledge no previous study has investigated the possible relationships between affective temperaments in women with PMDD. We hypothesized that affective temperaments (e.g. cyclothymic temperament) related to bipolarity could be associated with PMDD. To test this hypothesis we investigated the independent associations between affective temperaments and a positive screen for PMDD in a cross-sectional study of Brazilian women.

2. Methods

2.1. Participants

We selected a consecutive sample of 514 women from Fortaleza, CE, Brazil, who were either staff from the Walter Cantídio University Hospital (HUWC) or who were students enrolled at medicine, psychology or nursing courses at three universities: Federal University of Ceará (UFC), University of Fortaleza (UNIFOR) and Christus University (UniChristus). Participants were ≥18 years old. Exclusion criteria were: (1) refusal to participate in the study; (2) use of psychotropic medication in the past two months; and (3) no menstrual periods (i.e., pregnancy or menopause). Data were collected from July 2013 to December 2014.

2.2. Measures and procedures

The Premenstrual Symptoms Screening Tool (PSST) [14] was used to screen for PMDD. The PSST consists of 19 items subdivided into two domains: the first domain comprises the 14 DSM-IV physical and psychological manifestations of PMDD, while the second domain is composed of 5 items assessing the functional impact of premenstrual symptoms. We developed and validated a Brazilian Portuguese version of this instrument using a standard "forward-backward" translation procedure. In the current sample, the translated version had content validity, as well as internal consistency and test–retest reliability (Cronbach's alpha = 0.91; intraclass correlation coefficient = 0.867; content validity index = 0.94). According to the developers of the PSST [14], a positive screen for PMDD requires: (1) the presence of at least five symptoms from the first domain, rated as moderate to severe; (2) presence of at least one of the first four symptoms (anger/irritability, anxiety/tension, tearful or depressed mood/hopelessness), rated as severe; and (3) presence of at least one symptom from the second domain, rated as severe. Moderate to severe PMS requires the same criteria of PMDD, but the severity of criteria 2 and 3 must be rated moderate to severe instead of severe. All other cases are considered as no/mild PMS.

Affective temperaments were assessed with the affective section of the validated Brazilian Portuguese version of the Affective and Emotional Composite Temperament Scale (AFECTS) instrument [15]. Briefly, twelve short descriptions of each temperament are presented and the participants select which one most accurately describes their predominant temperament. The AFECTS consider 12 affective temperaments namely euthymic, depressive, anxious, apathetic, obsessive, cyclothymic, dysphoric, irritable, volatile, disinhibited, hyperthymic and euphoric temperaments. In accordance to this model, each type of affective temperament derives from emotional dimensions, which are assessed by the emotional section of the AFECTS. This section is a 7-point bipolar scale with 48 items, divided in 6 dimensions of 8 questions (volition, anger, inhibition, sensitivity, coping and control), and the desire dimension with 4 additional questions [15]. The total score of each dimension is the sum of scores from 1 to 7 for each question, therefore the dimension scores range from 8 to 56.

The ethics committee of the HUWC approved the study under protocol number 321.019. Participants signed a written informed consent and then answered a paper form containing a sociodemographic questionnaire (that also included questions about the menstrual cycle, such as menstrual status, hormonal contraception and age of first period), as well as the PSST and AFECTS. However, to specifically test the association of temperaments with PMDD, only women that met the screening criteria for either PMDD or no/mild PMS according to the PSST were considered in the analyses. The assessments were made at any time of the menstrual cycle (the PSST is a valid screening measure at any time of the menstrual cycle).

2.3. Statistical analysis

All analyses were carried out using SPSS for Windows version 22.0 (IBM Software). The significance level was set as $P < 0.05$ in all analyses. The frequency of each of the twelve affective temperaments was compared as a function of a positive screen for PDMM; for these analyses a Bonferroni correction was applied to correct for multiple comparisons. Continuous variables are presented as mean ± SD and/or median (interquartile range). The Kolmogorov–Smirnov test was used to assess a normal distribution of the data. Normally distributed continuous variables were compared using Student's t test, and non-normally distributed continuous or ordinal variables were compared using the Mann–Whitney U test. Categorical variables are presented as frequencies (%), and were compared using Pearson's chi-square (χ^2) or Fisher's exact test as appropriate.

The independent associations of affective temperaments and a positive screen for PMDD were investigated in multiple logistic regression models. Hormonal contraceptive use and other demographic variables that were possibly associated with PSST scores in univariate analyses ($P < 0.2$: marital status and education) were included in these models. The temperament classifications were entered as categorical variables, and twelve separate models were built to assess the association of each temperament with respect to all the others. To assess the independent association of the emotional dimensions with PSST scores, a logistic regression model was built with the continuous emotional dimension scores as independent variables.

3. Results

3.1. Sample characteristics

The PSST identified 216 (42.0%) women with no or mild PMS symptoms (no/mild PMS group), and 83 (16.1%) women that met the screening criteria of PMDD (PMDD group). Two women with a positive screen for PMDD did not provide complete responses for the AFECTS instrument, and thus were excluded from analysis. Therefore, the final sample to study the associations between PMDD and affective temperaments and emotional dimensions comprised 297 women (i.e., 216 women with no or mild PMS symptoms and 81 women with a positive screen for PMDD). The mean ± SD age of the participants was 22.8 ± 5.5 years and the mean ± SD age of the first period was 12.0 ± 1.3 years. Menstrual cycle was regular in 232 participants (78.1%), and 142 (47.8%) participants used hormonal contraceptives. Age, number of children, education, race, marital status, religion, monthly gross income, hormonal contraceptive use or age of the first period were not associated with a positive screen for PMDD (Table 1).

3.2. Association of affective temperaments and PMS severity

A predominantly cyclothymic temperament was associated with a positive screening for PMDD (OR = 4.64,

$P < 0.01$), while women with an euthymic temperament had a lower likelihood of screening positive for PMDD (OR = 0.26, $P < 0.01$). No other statistically significant associations were found for other variables or temperaments. Significant and independent associations between the cyclothymic and euthymic temperaments and a positive screen for PMDD remained after adjustment for education or hormonal contraceptive use (OR = 4.57 for cyclothymic and OR = 0.28 for euthymic) (Table 2A). No significant differences emerged in the frequency of affective temperaments as a function of hormonal contraceptive use (data not shown).

3.3. Association of emotional dimensions and PMDD

Table 2B presents the associations between emotional dimensions of the AFECTS and a positive screen for PMDD. Anger (OR = 1.05) and sensitivity (OR = 1.08) were associated with PMDD, with a higher score associated with an increased likelihood for a positive screen for PMDD. These associations persisted following multivariable adjustment for potential confounders. Scores of emotional dimensions of the AFECTS did not significantly differ as a function of hormonal contraceptive use (data available upon request).

4. Discussion

The main findings of this study were the independent associations between the cyclothymic temperament and a positive screen for PMDD, while the euthymic temperament was independently associated with a lower likelihood for a positive screen for PMDD. In addition, the emotional dimensions anger and sensitivity were closely associated with a positive screen for PMDD.

The cyclothymic temperament is characterized not only by affective instability, but also by impulsiveness, mood reactivity, and anxiety [16]. The cyclothymic temperament may increase the risk for several mental disorders, including but not limited to mood, anxiety, personality, eating, impulse control disorders, and behavioral addictions [17]. In addition, it is particularly well demonstrated that a cyclothymic temperament predisposes an individual to the development of bipolar spectrum disorders [10]. Notwithstanding the associations between PMDD and affective temperaments have not been previously investigated, PMDD has been associated with neuroticism, a personality trait consistently related to affective instability [18]. Finally, PMDD has been related to impulsiveness, which is another characteristic dimension of the cyclothymic temperament [19].

Frequent mood changes of both polarities and the tendency to over-react to internal or external stimuli represent the constitutional basis of cyclothymic temperament [16]. In this perspective, the cyclothymic disposition might influence the intense response to the hormonal fluctuations associated with PMDD. Indeed, it has been

Table 1
Sociodemographic characteristics of the sample.

	Valid N (Total = 297)	No/Mild PMS (N = 216)	PMDD (N = 81)	P-value
Age (mean ± SD/median)	291	22.5 ± 4.8/21.0	23.3 ± 6.7/21.0	0.799[a]
Number of children (N, %)				
None		192 (95.0)	71 (91.0)	
1 to 2	280	8 (4.0)	5 (6.4)	0.341[b]
3 or more		2 (1.0)	2 (2.6)	
Years of education (N, %)				
10 to 12 years	292	17 (8.1)	13 (16.0)	0.072[b]
13 or more		194 (91.9)	68 (84.0)	
Race (N, %)				
Caucasian		82 (39.2)	28 (35.0)	
African American	289	7 (3.3)	2 (2.5)	0.666[b]
Mulatto(a)		112 (53.6)	49 (61.3)	
Asian		8 (3.8)	1 (1.3)	
Marital status (N, %)				
Single		195 (90.7)	70 (86.4)	
Married/stable union	296	18 (8.4)	7 (8.6)	0.104[b]
Divorced		2 (0.9)	4 (4.9)	
Religion (N, %)				
Catholic		154 (72.0)	50 (63.3)	
Evangelical (Protestant)		25 (11.7)	13 (16.5)	
Spiritist	293	6 (2.8)	4 (5.1)	0.365[b]
Other		3 (1.4)	2 (2.5)	
Without religion		26 (12.1)	10 (12.7)	
Gross monthly income (N, %)				
Less than US$ 319.00		44 (21.5)	15 (20.3)	
Between US$ 319.00 and US$ 638.00		37 (18.0)	16 (21.6)	
Between US$ 638.00 and US$ 1276.00	279	49 (23.9)	12 (16.2)	0.629[c]
Between US$ 1276.00 and US$ 2552.00		32 (15.6)	14 (18.9)	
More than US$ 2552.00		43 (21.0)	17 (23.0)	
Menstrual status (N, %)				
Regular		171 (79.2)	61 (75.3)	
Irregular	297	45 (20.8)	20 (24.7)	0.648[c]
Hormonal contraception				
Yes	297	106 (49.1)	36 (44.428)	0.570[c]
No		110 (50.9)	45 (55.6)	
Age of first period (mean ± SD)	291	12.0 ± 1.3	12.0 ± 1.3	0.688[d]

Abbreviations: PMS = premenstrual syndrome; PMDD = premenstrual dysphoric disorder.
  [a] Mann–Whitney U test;
  [b] Fisher's exact test;
  [c] Pearson's chi-square test;
  [d] Student's t test;

hypothesized that PMDD may occur due to a differential sensitivity to mood perturbing effects of gonadal steroid fluctuations [20,21]. In other words, mood reactivity and instability related to a cyclothymic temperament may represent a predisposing factor for PMDD. Conversely, the euthymic temperament, which is by definition characterized by marked affective stability was associated with a lower likelihood of a positive screening for PMDD in our sample. Although our findings support such hypothesis, it is not possible to draw definitive conclusions from this cross-sectional study.

A positive screen for PMDD was also independently and significantly associated in our sample to the emotional dimensions of anger and sensitivity. Our findings are in agreement with findings from Ko and colleagues, who found that women with PMDD had a higher sensitivity to aversive stimuli (i.e., behavior inhibition) compared to healthy women [22]. In addition, previous report indicates that anger is a burdensome manifestation of PMDD [23]. Consistently, sensitivity and anger are higher in individuals with a predominant cyclothymic temperament according to the AFECTS model [15].

Abnormalities in serotoninergic (5-HT) neurotransmission may provide a biological explanation for the association between the cyclothymic temperament and PMDD. For example, a higher frequency of the short (s) allele of the serotonin transporter gene has been reported in individuals with a predominant cyclothymic temperament [8,24] and in women with PMDD [25]. In addition, preliminary findings indicate that least a group of patients could be satisfactorily treated with a combination of selective serotonin reuptake inhibitors and mood stabilizing medications [26,27].

Table 2
Association of temperament and emotional dimension with PMDD.

A. AFECTS temperaments

Temperament	N in PMDD (%)		Unadjusted		Adjusted[a]	
	Yes	No	OR[b] (95% CI)	*P*-value[d]	OR[b] (95% CI)	*P*-value[d]
Depressive	1 (1.2)	80 (98.8)	1.30 (0.12–14.54)	0.831	1.51 (0.13–17.05)	0.737
Anxious	6 (7.4)	75 (92.6)	1.12 (0.42–3.02)	0.823	1.30 (0.48–3.55)	0.606
Apathetic	0 (0.0)	81 (100.0)	0.98 (0.96–1.00)	0.999	0.00 (0.00–0.00)	0.999
Cyclothymic	19 (23.5)	62 (76.5)	**4.64 (2.17–9.94)**	**<0.001**	**4.57 (2.11–9.90)**	**<0.001**
Dysphoric	5 (6.2)	76 (93.8)	3.39 (0.89–12.95)	0.074	3.37 (0.86–13.13)	0.080
Volatile	1 (1.2)	80 (98.8)	0.32 (0.04–2.56)	0.281	0.28 (0.03–2.34)	0.239
Obsessive	15 (18.5)	66 (81.5)	1.06 (0.55–2.06)	0.858	0.99 (0.50–1.98)	0.986
Euthymic	7 (8.6)	74 (91.4)	**0.26 (0.11–0.60)**	**0.002**	**0.28 (0.12–0.64)**	**0.003**
Hyperthymic	4 (4.9)	77 (95.1)	0.28 (0.10–0.81)	0.019	0.28 (0.09–0.82)	0.020
Irritable	9 (11.1)	72 (88.9)	1.52 (0.64–3.58)	0.343	1.47 (0.61–3.53)	0.387
Disinhibited	6 (7.4)	75 (92.6)	1.21 (0.44–3.31)	0.707	1.28 (0.46–3.51)	0.637
Euphoric	8 (9.9)	73 (90.1)	2.45 (0.91–6.58)	0.076	2.24 (0.80–6.27)	0.126

B. AFECTS emotional dimensions

Emotional dimension	Mean ± SD		Unadjusted		Adjusted[a]	
	No/Mild PMS	PMDD	OR[c] (95% CI)	*P*-value	OR[c] (95% CI)	*P*-value
Volition	42.7 ± 7.2	39.2 ± 7.7	0.98 (0.93–1.02)	0.332	0.98 (0.94–1.03)	0.537
Desire	16.2 ± 4.3	18.5 ± 4.9	1.06 (0.98–1.15)	0.138	1.06 (0.98–1.16)	0.132
Anger	27.1 ± 9.5	33.9 ± 9.8	**1.05 (1.01–1.08)**	**0.007**	**1.05 (1.01–1.09)**	**0.007**
Inhibition	37.8 ± 6.7	37.3 ± 7.2	1.00 (0.96–1.04)	0.885	1.01 (0.96–1.06)	0.776
Sensitivity	33.4 ± 7.9	40.1 ± 8.4	**1.08 (1.03–1.13)**	**0.001**	**1.09 (1.04–1.14)**	**<0.001**
Coping	42.6 ± 7.8	38.6 ± 9.2	0.99 (0.95–1.03)	0.655	0.98 (0.94–1.03)	0.395
Control	42.6 ± 8.2	37.7 ± 9.4	0.97 (0.93–1.01)	0.175	0.98 (0.94–1.03)	0.456

Abbreviations: OR = odds ratio; PMS = premenstrual syndrome; PMDD = premenstrual dysphoric disorder.
Statistically significant results are in bold.
[a] Adjusted for marital status, education and hormonal contraceptive use.
[b] Relative to participants with any other temperament.
[c] Per unity increase in dimension score.
[d] Bold values are significant at 5% level after Bonferroni correction for multiple comparisons.

However, this assumption deserves further investigation. Finally, the cyclothymic temperament has been related to a diagnosis of borderline personality disorder [16]. Nevertheless, the relationships of PMDD and borderline personality disorder remain unknown.

Some limitations should be considered when interpreting the findings of this study. First, a positive screen for PMDD does not substantiate the diagnosis of this mental disorder. Second, the cross-sectional design of the present study is not adequate to establish causal inferences, future prospective studies are necessary to confirm our preliminary findings. Third, co-morbid psychiatric disorders were not assessed in this study. Finally, this study also found a relatively high prevalence of PMDD in a university sample (16.1%). The PSST is not a diagnostic tool, thus it may have inflated the prevalence rates reported herein (i.e., several false-positive cases could screen positive with the PSST). Fourth, a biased pattern of responses to the AFECTS instrument could be generated by participants at different phases of the menstrual cycle. Despite these limitations, this study raises important clinical questions. For example, notwithstanding PMDD may represent a heterogeneous phenotype it is possible that

at least a subgroup of patients may have a bipolarity diathesis.

4.1. Conclusions

Our findings provide preliminary evidence for a possible association of affective temperaments and emotional dimensions with PMDD defined by the PSST screening tool. However, the high prevalence of a positive screening for PMDD in this study limits the interpretation of these data. Therefore, prospective studies are necessary to confirm whether cyclothymic and euthymic temperaments as well as anger and sensitivity emotional traits are risk factors for PMDD diagnosed by standard DSM criteria.

References

[1] Yonkers KA, O'Brien PM, Eriksson E. Premenstrual syndrome. Lancet 2008;371:1200-10.

[2] Epperson CN, Steiner M, Hartlage SA, Eriksson E, Schmidt PJ, Jones I, et al. Premenstrual dysphoric disorder: evidence for a new category for DSM-5. Psychiatry 2012;169:465-75.

[3] Rapkin AJ, Winer SA. Premenstrual syndrome and premenstrual dysphoric disorder: quality of life and burden of illness. Expert Rev Pharmacoecon Outcomes Res 2009;9:157-70.

[4] Dias RS, Lafer B, Russo C, Del Debbio A, Nierenberg AA, Sachs GS, et al. Longitudinal follow-up of bipolar disorder in women with premenstrual exacerbation: findings from STEP-BD. Psychiatry 2011;168:386-94.

[5] Teatero ML, Mazmanian D, Sharma V. Effects of the menstrual cycle on bipolar disorder. Bipolar Disord 2014;16:22-36.

[6] Fornaro M, Perugi G. The impact of premenstrual dysphoric disorder among 92 bipolar patients. Eur Psychiatry 2010;25:450-4.

[7] Studd J. Severe premenstrual syndrome and bipolar disorder: a tragic confusion. Menopause Int 2012;18:82-6.

[8] Gonda X, Rihmer Z, Zsombok T, Bagdy G, Akiskal KK, Akiskal HS. The 5HTTLPR polymorphism of the serotonin transporter gene is associated with affective temperaments as measured by TEMPS-A. J Affect Disord 2006;91:125-31.

[9] Kawamura Y, Akiyama T, Shimada T, Minato T, Umekage T, Noda Y, et al. Six-year stability of affective temperaments as measured by TEMPS-A. Psychopathology 2010;43:240-7.

[10] Fountoulakis KN, Gonda X, Koufaki I, Hyphantis T, Cloninger CR. The role of temperament in the etiopathogenesis of bipolar spectrum illness. Harv Rev Psychiatry 2016;24:36-52.

[11] Akiskal HS, Pinto O. The evolving bipolar spectrum. Prototypes I, II, III, and IV. Psychiatr Clin North Am 1999;22:517-34 [vii].

[12] Angst J. Bipolar disorder – methodological problems and future perspectives. Dialogues Clin Neurosci 2008;10:129-39.

[13] Goto S, Terao T, Hoaki N, Wang Y. Cyclothymic and hyperthymic temperaments may predict bipolarity in major depressive disorder: a supportive evidence for bipolar II1/2 and IV. J Affect Disord 2011;129:34-8.

[14] Steiner M, Macdougall M, Brown E. The premenstrual symptoms screening tool (PSST) for clinicians. Arch Womens Ment Health 2003;6:203-9.

[15] Lara DR, Bisol LW, Brunstein MG, Reppold CT, de Carvalho HW, Ottoni GL. The Affective and Emotional Composite Temperament (AFECT) model and scale: a system-based integrative approach. J Affect Disord 2012;140:14-37.

[16] Perugi G, Hantouche E, Vannucchi G, Pinto O. Cyclothymia reloaded: a reappraisal of the most misconceived affective disorder. J Affect Disord 2015;183:119-33.

[17] Perugi G, Akiskal HS. The soft bipolar spectrum redefined: focus on the cyclothymic, anxious-sensitive, impulse-dyscontrol, and binge-eating connection in bipolar II and related conditions. Psychiatr Clin North Am 2002;25:713-37.

[18] Gingnell M, Comasco E, Oreland L, Fredrikson M, Sundstrom-Poromaa I. Neuroticism-related personality traits are related to symptom severity in patients with premenstrual dysphoric disorder and to the serotonin transporter gene-linked polymorphism 5-HTTPLPR. Arch Womens Ment Health 2010;13:417-23.

[19] Hsu SC, Liu CY, Hsiao MC. A comparison of the tridimensional personality questionnaire in premenstrual dysphoric disorder and major depressive disorder. Compr Psychiatry 2007;48:366-70.

[20] Schmidt PJ, Nieman LK, Danaceau MA, Adams LF, Rubinow DR. Differential behavioral effects of gonadal steroids in women with and in those without premenstrual syndrome. Med 1998;338:209-16.

[21] Schneider T, Popik P. An animal model of premenstrual dysphoric disorder sensitive to antidepressants. Curr Protoc Neurosci 2009;9.31.1-9.31.10 [Chapter 9; Unit 9.31].

[22] Ko CH, Long CY, Yen CF, Chen CS, Wang PW, Yen JY. Gonadotrophic hormone and reinforcement sensitivity systems in women with premenstrual dysphoric disorder. Psychiatry Clin Neurosci 2014;68:785-94.

[23] Soyda Akyol E, Karakaya Arisoy EO, Caykoylu A. Anger in women with premenstrual dysphoric disorder: its relations with premenstrual dysphoric disorder and sociodemographic and clinical variables. Compr Psychiatry 2013;54:850-5.

[24] Borkowska A, Bielinski M, Szczesny W, Szwed K, Tomaszewska M, Kalwa A, et al. Effect of the 5-HTTLPR polymorphism on affective temperament, depression and body mass index in obesity. J Affect Disord 2015;184:193-7.

[25] Praschak-Rieder N, Willeit M, Winkler D, Neumeister A, Hilger E, Zill P, et al. Role of family history and 5-HTTLPR polymorphism in female seasonal affective disorder patients with and without premenstrual dysphoric disorder. Eur Neuropsychopharmacol 2002;12:129-34.

[26] Blumer D, Herzog AG, Himmelhoch J, Salgueiro CA, Ling FW. To what extent do premenstrual and interictal dysphoric disorder overlap? Significance for therapy. J Affect Disord 1998;48:215-25.

[27] Akiskal HS, Benazzi F. Toward a clinical delineation of dysphoric hypomania – operational and conceptual dilemmas. Bipolar Disord 2005;7:456-64.