Seasonality of Symptoms in Women With Late Luteal Phase Dysphoric Disorder

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Objective: Both late luteal phase dysphoric disorder (LLPDD) and seasonal affective disorder are cyclical disorders often manifested by "atypical" depressive features. The goal of this study was to determine whether patients with LLPDD demonstrate substantial seasonal variation in symptoms. Method: Consecutive female patients attending a subspecialty clinic in a university teaching hospital were assessed by means of DSM-III-R criteria. All subjects completed the Seasonal Pattern Assessment Questionnaire, modified to include items on the seasonality of premenstrual symptoms. The results were compared with those of a group of female nonclinical subjects (N=50). Results: One hundred patients met the DSM-III-R criteria for LLPDD. Compared to the nonclinical group, the LLPDD patients had a significantly higher mean global seasonality score (an index of seasonality of mood and vegetative symptoms) and a significantly higher rate of seasonal affective disorder (38% versus 8%) as determined by Seasonal Pattern Assessment Questionnaire criteria. Twenty-five percent of the LLPDD group rated their seasonal variation in premenstrual symptoms as marked or severe, while 30% considered seasonal changes in overall symptoms to be a marked or severe problem. Conclusions: These results suggest that patients with LLPDD have substantial seasonal patterns in mood and premenstrual symptoms. These seasonal patterns have implications for the clinical assessment and treatment of LLPDD. For example, light therapy may be beneficial for women with seasonal worsening of LLPDD.

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Late luteal phase dysphoric disorder (LLPDD) is a cyclical disorder in women in which symptoms are synchronous with the menstrual cycle (DSM-III-R). Specifically, symptoms are present during the last week of the luteal phase and remit within a few days after the onset of the follicular phase. Similarly, seasonal affective disorder is a diagnostic entity in which characteristic symptoms recur and remit in a rhythmic pattern. In this disorder, depressive symptoms cycle in response to the time of year, the most usual pattern being symptom onset in the fall or winter and remission in the spring (1). In DSM-IV, LLPDD has been renamed premenstrual dysphoric disorder, with minor wording changes and the addition of one new symptom in the set of criteria, and is included as a research category in Appendix B (Criteria Sets and Axes Provided for Further Study). Seasonal affective disorder is presented as the longitudinal course specifier "with seasonal pattern" for recurrent major depressive episodes.

The characteristic symptoms that cyclically recur and remit in LLPDD and seasonal affective disorder are strikingly similar. Both disorders include depressed mood, poor concentration, loss of interest in usual activities, and the more specific "atypical" features of depression: hypersomnia, hyperphagia, carbohydrate craving, and anergy (1, 2).

The overlap in these two disorders may also extend to the epidemiologic and treatment aspects. In a community survey of premenstrual syndrome (PMS) (3), it was noted that approximately 70% of women with this disorder reported fewer symptoms during the summer. One of us (R.W.L., unpublished data) has observed that 51% of 200 consecutive female patients with seasonal affective disorder complained of sub-

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stantial premenstrual mood changes, while 18% also noted marked winter worsening of their premenstrual symptoms. Light therapy, an effective treatment modality for seasonal affective disorder (1, 4–6), has shown potential efficacy in LLPDD (7–9).

The objective of this study was to examine the seasonal mood and the premenstrual symptom patterns in patients with LLPDD.

TABLE 1. Scores on Seasonal Variation Items From the Seasonal Pattern Assessment Questionnaire of Patients With Late Luteal Phase Dysphoric Disorder (LLPDD) and Nonclinical Comparison Subjects

	Score of Patients With LLPDD (N=100)[a]			Score of Nonclinical Subjects (N=50)[a]			
Item	Mean	SD	Median	Mean	SD	Median	Significance (p)[b]
Length of sleep	1.6	1.1	2	1.2	0.9	1	<0.03 (n.s.)
Social activity	2.0	1.1	2	1.5	1.1	2	<0.01
Mood	2.2	1.1	2	1.3	1.0	1	<0.001
Weight	1.4	1.1	1	0.9	0.8	1	<0.02 (n.s.)
Appetite	1.5	1.2	2	0.9	0.9	1	<0.002
Energy level	2.2	1.1	2	1.2	1.0	1	<0.001
Global seasonality score[c]	10.9	4.6	12.0	7.0	4.5	6.5	<0.001[d]

[a]Higher scores indicate greater seasonal variation in symptoms.
[b]Mann-Whitney U test with Bonferroni correction.
[c]The sum of the six Seasonal Pattern Assessment Questionnaire item scores.
[d]Student's t test, df=148.

METHOD

One hundred fifty-four consecutive patients referred by physicians to an outpatient PMS clinic at British Columbia Women's Hospital and Health Sciences Centre in Vancouver, Canada, were recruited for this study; all resided within the greater Vancouver area (latitude 49° N). The clinic patients were assessed with use of an unstructured clinical interview by one of two psychiatrists (S.M. and D.C.) with clinical and research expertise in premenstrual disorders. The diagnosis of LLPDD was made according to the DSM-III-R criteria on the basis of all available medical information and, when available, review of a prospective, patient-completed daily symptom diary (10). The likelihood of the LLPDD diagnosis was stratified as low, moderate, or high on the basis of the clinical judgment of the interviewers. The descriptor "high likelihood" was used for diagnoses that could be confirmed by a prospective symptom diary, while the term "moderate likelihood" was applied if the retrospective history strongly suggested a diagnosis of LLPDD but no prospective measures were available. For the purposes of the study, patients assessed as having a moderate or high probability of the LLPDD diagnosis (N=100) were included for further study, while the remainder (N=54) were excluded. The patients with LLPDD were compared with a nonclinical group composed of female hospital staff members and medical students (N=50) recruited by advertisement. The nonclinical group was not screened for LLPDD or other psychiatric illness. These subjects gave written informed consent for the study; the patients' assessments were part of their clinical workup. The study was approved by the Human Ethics Committee at the University of British Columbia.

As part of a larger assessment package, all subjects completed the Seasonal Pattern Assessment Questionnaire (11), which was modified to include questions about seasonality of PMS symptoms as described below. The Seasonal Pattern Assessment Questionnaire is a retrospective self-report that has been demonstrated to have reasonable reliability and validity in assessing seasonal changes in mood and vegetative symptoms (12, 13). Many studies have used the Seasonal Pattern Assessment Questionnaire to investigate seasonal mood changes in the general population (13–17) and in persons with psychiatric disorders such as nonseasonal depression (12), panic disorder (18), obsessive-compulsive disorder (19), and eating disorders (20–26). In addition to demographic data, the Seasonal Pattern Assessment Questionnaire includes items about seasonal changes in mood, sleep, appetite, weight, energy level, and social activity. These items are scored on a 5-point Likert scale (0=no change, 4=severe change), and the sum of these six scores is called the global seasonality score. The range of global seasonality scores is from 0 to 24, with higher scores indicating greater seasonality of symptoms. The Seasonal Pattern Assessment Questionnaire also asks whether the seasonal changes are a problem, with possible answers of none, mild, moderate, severe, and disabling. Similar items and responses were added to include seasonality of PMS symptoms. Other questions on the Seasonal Pattern Assessment Questionnaire relate to seasonal fluctuation in weight and daily hours of sleep in each season.

Criteria based on Seasonal Pattern Assessment Questionnaire data have been proposed to establish "caseness" for a diagnosis of seasonal affective disorder. Specifically, Kasper et al. (13) suggested that a global seasonality score of 11 or more, in conjunction with a seasonal problem rating of moderate to disabling, can be used for this purpose. Epidemiologic studies using these Seasonal Pattern Assessment Questionnaire criteria have reported a prevalence of seasonal affective disorder in the general population ranging from 1.4% in Florida (14) to 9.7% in New Hampshire (14) and Alaska (16). The criteria of Kasper et al. were adopted in the present study to define a diagnosis of seasonal affective disorder.

Subjects were also asked to indicate the month or months of the calendar year, if any, in which they felt best, felt worst, had PMS the most, and had PMS the least. To establish a diagnosis of winter seasonal affective disorder, subjects had to indicate that they felt worst in one or more of the four months of November to February and not during either of the summer months of July and August.

Parametric variables were compared by means of the two-tailed Student's t test or analysis of variance (ANOVA). Post hoc pairwise comparisons following the ANOVA were done with Student-Newman-Keuls tests to control for multiple comparisons. Ordinal data were analyzed with Mann-Whitney U tests and a Bonferroni correction for multiple comparisons. Chi-square tests were used to analyze categorical data. All analyses were done with the SPSS for Windows 3.0 statistical software package (27).

RESULTS

Data were analyzed for the 100 patients with LLPDD and the 50 nonclinical comparison subjects. The mean age of the LLPDD group (36.3 years, SD=5.4) was significantly greater than that of the nonclinical group (28.6 years, SD=4.9) (t=8.53, df=148, p<0.001). Despite this age difference, the LLPDD group and the nonclinical group had resided in the current climatic area for similar periods of time (mean=21.3 years, SD=12.9, and mean=20.2 years, SD=14.5, respectively; t=0.19, df=148, p>0.65). The mean current weight of the LLPDD group (140 lb, SD=24) was significantly higher than that of the nonclinical group (126 lb, SD=17) (t=3.74, df=141, p<0.001).

The mean and median scores on the six Seasonal Pattern Assessment Questionnaire items used to generate the global seasonality score for the LLPDD and nonclinical groups are presented in table 1. The LLPDD

TABLE 2. Seasonal Weight and Sleep Patterns of Patients With Seasonal and Nonseasonal Late Luteal Phase Dysphoric Disorder (LLPDD) and Nonclinical Comparison Subjects

	(A) Patients With Seasonal LLPDD (N=34)[a]		(B) Patients With Nonseasonal LLPDD (N=66)[b]		(C) Nonclinical Subjects (N=50)		
Item	Mean	SD	Mean	SD	Mean	SD	Significance[c]
Current weight (lb)	148	23	136	25	126	17	A>B>C
Seasonal weight change[d]	2.7	1.0	2.2	1.2	1.7	0.8	A>B>C
Sleep hours							
Spring	7.9	1.1	7.6	0.9	7.5	1.1	n.s.
Summer	7.5	1.0	7.4	1.0	7.4	1.0	n.s.
Fall	8.4	1.5	7.9	1.1	7.9	1.2	n.s.
Winter	9.0	1.9	8.3	1.4	8.2	1.2	A>B,C

[a]LLPDD subjects also meeting the Seasonal Pattern Assessment Questionnaire criteria for winter seasonal affective disorder.
[b]LLPDD subjects not meeting the Seasonal Pattern Assessment Questionnaire criteria for winter seasonal affective disorder.
[c]ANOVA followed by post hoc Student-Newman-Keuls tests, $p<0.05$.
[d]The weight change value is based on a Likert scale with the following anchor points: 1=0–3 lb, 2=4–7 lb, 3=8–11 lb, 4=12–15 lb, 5=16–20 lb, and 6=over 20 lb.

group had significantly higher scores on items relating to mood, energy, appetite, and social activity but not on length of sleep or weight. The global seasonality score was also significantly higher for the LLPDD patients than for the nonclinical subjects ($t=4.86$, $df=148$, $p<0.001$). Applying the Seasonal Pattern Assessment Questionnaire criteria of Kasper et al. (13), we found that 38 (38%) of the patients with LLPDD met the criteria for seasonal affective disorder, compared to four (8%) of the nonclinical group ($\chi^2=14.90$, $df=1$, $p<0.001$). Of the 38 LLPDD patients "diagnosed" with seasonal affective disorder, 34 had a winter pattern, two had a summer pattern, and two could not be classified as having a distinct seasonal pattern.

In response to the global problem question, "If you experience changes with the seasons, do you feel that these are a problem for you?," only 33 LLPDD patients (33%) answered no. Of the rest, 14 patients identified mild problems, 22 had moderate difficulties, 25 had severe problems, and five endorsed disabling problems. One patient did not respond.

One question addressed the PMS symptoms directly by asking, "To what degree do PMS symptoms change with the seasons?" The responses were no change (N=34), slight change (N=14), moderate (N=20), marked (N=19), and severe (N=6). Seven patients did not respond. Thus, 59 (59%) of the LLPDD patients acknowledged some seasonal change in PMS symptoms, and 25 (25%) considered these changes to be marked or severe.

The group of patients with LLPDD who met the Seasonal Pattern Assessment Questionnaire criteria for winter seasonal affective disorder ("seasonal" LLPDD, N=34) were segregated from the remaining LLPDD subjects who did not ("nonseasonal" LLPDD, N=66). Seasonal variations in the vegetative symptoms of weight and daily sleep time for these two patient groups and the nonclinical group are shown in table 2. The mean current weights and seasonal weight fluctuations for the three diagnostic groups were significantly different (current weight: $F=9.68$, $df=2, 140$, $p<0.001$; weight fluctuation: $F=8.40$, $df=2, 147$, $p<0.001$). Post hoc comparisons revealed that the current weights and seasonal weight changes of the seasonal and nonseasonal LLPDD groups were higher than those of the nonclinical group. Furthermore, the seasonal LLPDD group scored significantly higher than the nonseasonal LLPDD group on both measures. The seasonal LLPDD group reported significantly more daily sleep hours during the winter months than either of the other two groups ($F=3.63$, $df=2, 145$, $p=0.03$). However, despite more sleep hours in the seasonal LLPDD group across the other three seasons, none of the differences between groups was significant.

DISCUSSION

This study presents preliminary evidence for substantial seasonality of symptoms in LLPDD. Compared with a nonclinical group of female subjects, patients with LLPDD reported greater seasonal variation in both mood and neurovegetative symptoms. LLPDD subjects also described marked changes in PMS symptoms with the seasons. These fluctuations in mood and PMS symptoms over the seasons were experienced as a considerable problem by 25%–30% of the patients with LLPDD.

Furthermore, 38% of the LLPDD patients met previously validated Seasonal Pattern Assessment Questionnaire criteria for seasonal affective disorder, in sharp contrast to 8% of the nonclinical subjects and the 1%–10% prevalence rate of seasonal affective disorder commonly cited in the literature. Those LLPDD patients "diagnosed" as having winter seasonal affective disorder also had winter hypersomnia and seasonal weight gain similar to the clinical features found in patients with seasonal affective disorder (1, 2).

There are some limitations to this study. The Seasonal Pattern Assessment Questionnaire is a retrospective, self-report instrument and thus may be subject to various sources of bias. In addition, although the questionnaire identifies seasonal variation in some depressive symptoms, it does not measure seasonality of all of the DSM-IV depressive symptoms and fails to identify whether these symptoms meet the full criteria for a major depressive episode (as opposed to "subsyndromal" major depression).

The nonclinical group and the LLPDD group differed in two important ways. First, the nonclinical group,

consisting of female hospital staff members and medical students, may have been more functional than the general population. The higher seasonality reported in the LLPDD group might therefore be attributable to the nonclinical group's having less seasonality than the general population, rather than the LLPDD group's having more. Evidence against this hypothesis, however, includes the findings that the mean global seasonality score (7.0) and prevalence of seasonal affective disorder (8%) in the nonclinical group are consistent with those in previously reported general population samples at a similar latitude (12–14). Second, the patients with LLPDD were significantly older that the nonclinical subjects. However, the large epidemiologic survey conducted by Kasper et al. (13) found that seasonality scores of women declined significantly with age. In the present study, the greater age of the patients with LLPDD should therefore bias *against* finding greater seasonality among them than among the younger nonclinical subjects.

Mackenzie et al. (28) demonstrated an elevated lifetime prevalence of mood disorders in women with moderate to severe perimenstrual difficulties. These authors did not address seasonal depression per se. Our clinical group consisted of women referred by their family physicians to a subspecialty PMS clinic; hence, it is likely that most if not all of the patients would describe their illness as moderate or severe. It is possible that our finding of a greater prevalence of seasonal affective disorder merely reflects a general predisposition to endorse or experience mood symptoms in this population. Furthermore, we did not have systematic diagnoses for mood disorders in our study group. It is estimated that 10%–20% of patients with recurrent depression have seasonal affective disorder (29, 30); therefore, seasonal affective disorder may have been overrepresented in the LLPDD group simply because there was a higher prevalence of recurrent depression in that group than in the comparison group. Future studies would be enhanced by use of the Structured Clinical Interview for DSM-IV or another similar standardized diagnostic instrument.

Our findings, if replicable in other LLPDD study groups, have potential clinical significance in a number of domains. First, these results suggest that there may be a natural course of winter worsening and summer improvement in many patients with LLPDD, which is particularly important in clinical prognosis and treatment study design. Most LLPDD treatment studies require at least two menstrual cycles of prospective monitoring of symptoms followed by at least two cycles of treatment. Thus, many patients will be studied over the course of at least two seasons. Any improvement (or worsening) after treatment may not be due to the specific intervention but instead to natural seasonal variations in symptoms. For example, seasonal patients who start treatments in winter may improve spontaneously by spring. Therefore, treatment studies of LLPDD should take into account the substantial proportion of patients with seasonal variability of symptoms.

Second, it may be appropriate to use more intensive treatment modalities during the fall and winter months, when there are more symptoms. For example, drug holidays may be warranted during the summer months, when there are fewer symptoms.

Third, a common pathophysiology might underlie LLPDD and seasonal affective disorder, both of which are cyclical disorders with common symptom patterns ("atypical" depressive symptoms). For example, it has been proposed that serotonin is abnormally regulated in both LLPDD (31–35) and seasonal affective disorder (36–41). As well, serotonergic medications (including fluoxetine and *d*-fenfluramine) have been found to be effective in treating LLPDD (42–45) and seasonal affective disorder (46–48). The role of serotonin in seasonal syndromes is of particular interest, because serotonin demonstrates a clear seasonal pattern of metabolism in normal humans (49–53). However, it should be noted that nonserotonergic medications (e.g., bupropion [54]) may also have some benefit in seasonal affective disorder. The critical link between LLPDD and seasonal affective disorder may therefore not be serotonergic but, rather, an association between depression and LLPDD in a broader sense.

Fourth, the findings suggest novel treatments for LLPDD, such as light therapy. Preliminary studies using bright light treatment (7, 8) suggested that patients with LLPDD had beneficial responses. A subsequent study (9), however, did not find differences between conditions of bright light (morning and evening exposure) and dim light (a putative placebo) in a crossover study design. Those results must also be considered preliminary, since the study group was small (N=11) and each treatment condition was used during only one menstrual cycle; in fact, depression ratings improved after all three conditions. Also, all of these studies were conducted in San Diego, a location where seasonality may not be prevalent. It is possible that seasonal LLPDD patients may be even more likely to benefit from bright light treatment, especially during the winter season, when symptoms are greater.

In summary, this study presents evidence that patients with LLPDD experience substantial seasonal patterns in mood and premenstrual symptoms. This observation has potential clinical significance for the course, treatment, and pathophysiology of LLPDD.

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