Risk Factors for Premenstrual Dysphoric Disorder in a Community Sample of Young Women: The Role of Traumatic Events and Posttraumatic Stress Disorder

Axel Perkonigg, Ph.D.; Kimberly A. Yonkers, M.D.; Hildegard Pfister, Dipl.Inf.; Roselind Lieb, Ph.D.; and Hans-Ulrich Wittchen, Ph.D.

Background: There is some evidence that the onset and course of premenstrual syndrome is related to stress; however, few studies have explored the role of traumatic events and posttraumatic stress disorder (PTSD) as risk factors for the development of premenstrual dysphoric disorder (PMDD).

Method: A community cohort of 1488 women (aged 14–24 years at baseline) were prospectively and longitudinally evaluated up to 3 times over a period of about 42 months from 1995 to 1999. The DSM-IV version of the Munich-Composite International Diagnostic Interview was used to establish PMDD and PTSD diagnostic status; stressful life events and conditions were assessed with the Munich Events List and the Daily Hassles Scale. Prevalence and incidence of either threshold or subthreshold PMDD from baseline to the second follow-up were calculated. Risk factors, including prior comorbid mental disorders and traumatic events, were examined using logistic regression analysis.

Results: The incidence of threshold PMDD was 3.0%. The most powerful predictors were subthreshold PMDD at baseline (OR = 11.0, 95% CI = 4.7 to 25.9). Traumatic events greatly increased the odds of developing PMDD at follow-up (OR = 4.2, 95% CI = 1.2 to 12.0). Other predictors were a history of anxiety disorder (OR = 2.5, 95% CI = 1.1 to 5.5) and elevated daily hassles scores (OR = 1.6, 95% CI = 1.1 to 2.3). Both were also associated with the risk of developing subthreshold PMDD, although the association was less robust.

Conclusions: Traumatic events and preexisting anxiety disorders are risk factors for the development of PMDD. The underlying mechanisms are unknown, making further investigation necessary.

(J Clin Psychiatry 2004;65:1314–1322)

Received Oct. 28, 2003; accepted May 11, 2004. From the Technical University of Dresden, Institute of Clinical Psychology and Psychotherapy, Dresden, Germany (Drs. Perkonigg and Wittchen); Max Planck Institute of Psychiatry, Munich, Germany (Drs. Perkonigg, Lieb, and Wittchen and Ms. Pfister); and Yale University, School of Medicine, New Haven, Conn. (Dr. Yonkers).

This work is part of the Early Developmental Stages of Psychopathology (EDSP) Study and is funded by the German Federal Ministry of Education and Research, project no. 01 EB 9405/6 and 01 EB 9901/6. A complete list of the investigators and members of the EDSP Study can be found at the end of this article.

In the spirit of full disclosure and in compliance with all ACCME Essential Areas and Policies, the faculty for this CME activity were asked to complete a full disclosure statement. The information received is as follows: Dr. Yonkers is a consultant for and is on the advisory boards for Wyeth, GlaxoSmithKline, Pfizer, and Berlex and has received grant/research support from GlaxoSmithKline and Berlex. Drs. Wittchen, Perkonigg, Pfister, and Lieb have no significant commercial relationships to disclose relative to their presentations.

Corresponding author and reprints: Hans-Ulrich Wittchen, Ph.D., Technical University of Dresden, Institute of Clinical Psychology and Psychotherapy, Chemnitzer Str. 46, D-011187 Dresden, Germany (e-mail: wittchen@mpipsykl.mpg.de).

Luteal phase symptoms of depressed mood, anxiety, anger, or affective lability, together with physical symptoms, characterize women with premenstrual syndrome (PMS). Women with premenstrual dysphoric disorder (PMDD) experience a more severe form of PMS with recurrent mood and behavioral symptoms. The impairment in functioning found among women with PMDD is due to the increased number and severity of their symptoms.[1] Prevalence estimates suggest that premenstrual symptoms of any severity occur in up to 75% of all women.[2] PMDD is rare, with approximately 3% to 9% of women experiencing more severe premenstrual symptoms that would be consistent with such a diagnosis.[3–13] Community studies of women with PMS and clinical studies of women with PMDD uniformly show that women with premenstrual syndromes experience a high degree of comorbidity with other mental disorders. Although unipolar mood disorders are particularly common,[14] a high rate of comorbid anxiety disorders has also been observed.[15,16]

Clinical risk factors for the onset of PMDD have not yet been established, but several factors have been

© Copyright 2004 Physicians Postgraduate Press, Inc.

suggested in the literature on PMS. These include unmarried status, lower education, and lifestyle factors such as lack of exercise, cigarette smoking, and greater alcohol intake. There also is some evidence that genetic factors and stress increase a woman's susceptibility for developing a moderate to severe premenstrual condition. Although clinical reports also pointed to the role of sexual and physical abuse, no epidemiologic studies have been conducted to highlight the relevance of traumatic events and PTSD as potential risk factors for PMDD.[7,17–24,25]

Whereas information from studies of women with PMS and data culled from clinical cohorts of women with PMDD are useful, they fail to inform us about the expression of and risk factors associated with PMDD in the general community. Few studies have investigated PMDD incidence and prevalence,[26,27] and no study has explored risk factors, course, and comorbidity in a community cohort of women with PMDD. In this article, we attempt to address this gap by focusing on findings from a randomly sampled cohort of women who participated in a 42-month prospective, longitudinal study. Specifically, we follow up on a recently reported[25] cross-sectional association between traumatic events and PTSD with PMDD among young women in the community. Analyses of cross-sectional baseline data revealed a high odds ratio between PTSD and PMDD. We expand on these earlier findings by using longitudinal data and prospectively examining whether traumatic events or PTSD increase the risk for subsequent development of PMDD.

METHOD

Method and sample characteristics of the Early Developmental Stages of Psychopathology (EDSP) Study have been described in detail elsewhere.[13,28–30] The 1488 women participating in our study were followed up over 42 months within a prospective longitudinal design with up to 3 assessment points (approximately 21 months apart). The baseline assessment was conducted among this representative community sample in Munich, Germany, and surrounding areas in 1995. An intermediate first follow-up was carried out in a subset of this sample in 1996 and 1997, and a second follow-up was carried out in the full sample in 1998 and 1999.

Sample

The baseline sample consisted of 1488 women (response rate: 69.7%) aged 14 to 24 years. At final follow-up, 1251 women could be successfully reinterviewed (response rate: 84.1%). A subset of this sample, namely women aged 14 to 17 years at baseline (N = 591, response rate: 86.8%), participated in an additional intermediate follow-up investigation approximately 16 months after the baseline investigation. Of all participating women, 397 at baseline and 37 at both follow-up timepoints did not complete the PMDD symptom assessment due to the requirement of stable menstruation patterns. Thus, in calculating prevalence and incidence for each timepoint, these respondents were counted as having no diagnosis. Results include all women with a complete data set from baseline and second follow-up (N = 1251) in order to estimate cumulative incidence rates.

The women's age at the second follow-up ranged from 18 to 28 years. All baseline and follow-up sociodemographic characteristics have been reported previously.[13] Table 1 shows some of the more important characteristics.

At baseline, 36.4% of the respondents were in secondary school with the majority attending Gymnasium (secondary education between middle school and entrance to university). The majority were still living with their parents. At the time of the second follow-up interview, 12.6% were still attending a school other than university (25.0% attending university), 37.3% were employed, 35.2% lived with their parents, 28.7% lived with a partner, and 10.3% were married. At baseline, the majority were classified as middle class (58.9%) and 6.5% as lower social class. There was a slight tendency for movement to lower social classes at the second follow-up. At baseline, almost all women indicated having already had their first menstrual period, the majority prior to age 14. At the second follow-up, 45.8% had used contraceptives.

Assessment

At all 3 timepoints, the computer-assisted personal interview version of the Munich-Composite International Diagnostic Interview (M-CIDI) was used to derive diagnoses of mental disorders.[31] The M-CIDI allows for the standardized assessment of symptoms, syndromes, and diagnoses of a wide range of DSM-IV substance use and mental disorders along with information about onset, duration, and clinical and psychosocial severity (the complete M-CIDI is available on request). The M-CIDI findings reported here rely entirely on the subjects' self-reports and do not include the optional clinician's rating available for psychopathological syndromes. Lifetime and 12-month diagnoses were computed from the baseline assessment. For the 2 follow-up interviews, the M-CIDI was modified to cover the 12-month period prior to the follow-up interview as well as the remaining interval between the interviews with additional questions about the course since the preceding interview (12-month interval version).

In all assessments, the M-CIDI was supplemented by a separate respondents' booklet, which included several scales and questionnaires for assessing psychological constructs relevant to the study. For a complete overview, see Lieb et al.[28] For the purpose of this examination, we also analyzed a short self-competence scale,[32] which assesses the person's ability to cope with several problems

Table 1. Sociodemographic Variables at Baseline and Second Follow-Up for Women in the Early Developmental Stages of Psychopathology Study (N = 1251)

	Baseline			Second Follow-Up		
Variable	Unweighted N	Weighted %	95% CI	Unweighted N	Weighted %	95% CI
Employment						
School	651	36.4	33.7 to 39.2	269	12.6	11.1 to 14.3
University	244	27.1	24.2 to 30.2	268	25.0	22.3 to 27.8
Job training	114	9.5	7.9 to 11.4	181	10.4	8.9 to 12.1
Employed	193	21.8	19.1 to 24.7	370	37.3	34.2 to 40.4
Unemployed	4	0.4	0.2 to 1.1	17	1.6	0.9 to 2.7
Other	45	4.8	3.6 to 6.5	146	13.2	11.2 to 15.5
School type (among those attending school)						
Hauptschule[a]	39	1.6	1.2 to 2.2	1	0.1	0.0 to 0.3
Realschule[b]	131	6.3	5.2 to 7.6	11	0.4	0.2 to 0.8
Gymnasium[c]	443	26.1	23.7 to 28.6	208	9.6	8.3 to 11.1
Fachoberschule[d]	14	1.1	0.7 to 1.9	36	1.7	1.2 to 2.4
Other	24	1.3	0.8 to 2.0	13	0.8	0.5 to 1.5
No school	600	63.6	60.8 to 66.3	982	87.4	85.7 to 88.9
Living arrangements						
With parents	889	59.0	55.8 to 62.2	601	35.2	32.5 to 38.0
Alone	204	22.8	20.1 to 25.7	235	23.2	20.5 to 26.1
With partner	118	14.1	11.8 to 16.7	274	28.7	25.8 to 31.8
Other	40	4.1	3.0 to 5.7	141	12.9	10.9 to 15.3
Social class						
Lowest	5	0.5	0.2 to 1.3	6	0.5	0.2 to 1.1
Lower middle	64	6.0	4.6 to 7.7	103	9.1	7.4 to 11.1
Middle	760	58.9	55.8 to 62.0	783	61.8	58.8 to 64.8
Upper middle	360	29.9	27.2 to 32.9	311	24.8	22.2 to 27.6
Upper	39	3.2	2.3 to 4.6	19	1.5	0.9 to 2.4
None[e]	23	1.4	0.9 to 2.2	29	2.4	1.6 to 3.6
Financial situation[f]						
Very bad, bad	80	6.8	5.4 to 8.5	78	7.2	5.7 to 9.0
Not good nor bad	332	27.8	25.0 to 30.7	345	27.7	25.0 to 30.6
Good	695	53.9	50.8 to 57.0	701	56.4	53.2 to 59.4
Very good	144	11.5	9.7 to 13.7	108	8.8	7.1 to 10.8
Marital status						
Married	36	4.4	3.1 to 6.2	91	10.3	8.4 to 12.7
Separated	3	0.4	0.1 to 1.1	3	0.4	0.1 to 1.4
Divorced	1	0.1	0.0 to 1.0	8	1.0	0.5 to 2.1
Widowed	0	0.0	…	1	0.0	0.0 to 0.3
Single	1211	95.1	93.3 to 96.5	1148	88.2	85.7 to 90.3

[a]Lower secondary school leading to vocational school.
[b]Lower secondary school leading to advanced technical school.
[c]Upper secondary school leading to university.
[d]Advanced technical school.
[e]Respondents who could not decide on one of the categories.
[f]Subjective ratings by respondents; 19 respondents did not make a statement about their financial situation at the second follow-up.

(problems with partner, friends, parents, money, job, physical and mental health, and illicit drugs if applicable); the Munich Event List (MEL),[33] with 84 items covering 11 dimensions of life events (e.g., family dimension: parents separated); and the Daily Hassles Scale,[34] assessing the frequency of daily hassles in different areas (e.g., school or work). While the Munich Event List has established reliability and validity, the self-competence scale and the Daily Hassles Scale are short research instruments that have not yet been examined for validity and reliability. Detailed information on the validity and reliability of the M-CIDI has been described elsewhere.[29,30,35] Test-retest validity of the M-CIDI was fair to good, with kappa values ranging from 0.64 (Yule Y = 0.80) to 0.78 (Yule Y = 0.82).

Posttraumatic stress disorder. PTSD and all other mental disorders were defined according to DSM-IV. Details have been presented elsewhere.[36,37] The M-CIDI PTSD module consists of a set of screening questions and a respondent list with 10 groups of specified events, an open-ended question about any other traumatic events, a question for each event for the DSM-IV A2 criterion (intense fear, helplessness, or horror), and further probing for the most severe events as well as linkages between events. The question for the A2 criterion was used to determine the exact number of qualifying events. The event types and the responses to the open-ended question included horrific experience during war, imprisonment, being taken hostage or kidnapped, physical attacks and threats, sexual abuse, rape, serious accidents, experience of natural catastrophes, sudden (threat of) death of significant others, and witnessing any traumatic events as mentioned above happening to others. If a respondent indicated several qualifying events (A1 and

A2 criteria: events involving actual or threatened death or serious injury or a threat to the physical integrity of self or others and a response with intense fear, helplessness, or horror) that did not fall within a cluster, only the DSM-IV criteria for the worst and most distressing event were assessed.

As in our previous articles,[34,35] we specified a category of partial PTSD. Partial PTSD refers to persons who fulfilled the A, B (traumatic event, fear, and persistent reexperiencing), and E (duration) criteria of DSM-IV but did not fully meet the C (avoidance or numbing of general responsiveness) and D (increased arousal) criteria for the minimum time duration of more than 1 month. The DSM-IV criterion of impairment was not applied to this category. Rates of PTSD and associations with PMDD in this article concern full DSM-IV PTSD as well as partial PTSD. One-week test-retest reliability of PTSD was acceptable ($\kappa = 0.79$), as was the validity ($\kappa = 0.85$).

Premenstrual dysphoric disorder. In addition to the information on the respondents' menstruation history, anthropometric information (height, weight), and contraceptives use, each assessment timepoint included an identical assessment of PMDD conditions (full criteria or "threshold," less than full criteria or "subthreshold," or none) according to DSM-IV. It should be noted that the PMDD assessment did not include "charting of symptoms" and was based solely on retrospective self-reports. The PMDD module consisted of a series of questions pertaining to the past 12 months: (a) 11 questions to evaluate the presence of DSM-IV symptom criteria during that period and their presence during the majority of all menstrual cycles in the past 12 months (criterion A), (b) 1 question to ascertain whether these symptoms occurred consistently in the week before menstruation (criterion A), and (c) 3 questions to evaluate for impairment and psychosocial interference (criterion B). There was no PMDD-specific assessment for criterion C (differential diagnostic criteria) or criterion D (prospective ratings). For the purpose of this study, we specified threshold and subthreshold PMDD diagnoses. The latter is defined as falling short by only 1 DSM-IV criterion. Not meeting criterion B for impairment and psychosocial interference was, by far (72%), the most frequent reason for not meeting criteria for full diagnosis among women with subthreshold PMDD.

Interviewers and Interviewer Training

At each assessment timepoint, 57 clinical interviewers conducted personal interviews. All interviewers participated in at least 1 week of training for the M-CIDI and several follow-up trainings throughout each wave as well as at the beginning of each additional wave. This was followed by at least 10 practice interviews, which were closely monitored and supervised by the staff of the study.[28–30]

Weighting of Data

As the EDSP is designed with special interest in early stages of psychopathology, 14-to-15-year-olds were sampled at twice the probability of 16-to-21-year-olds, and 22-to-24-year-olds were sampled at half this probability. This sampling strategy allows particularly precise estimations of measures used for comparative analyses of the age group of primary interest—the 14-to-15-year-olds. Due to the different sampling probabilities, relative weights inversely proportional to the sampling fraction are applied to estimate the general sample. In addition, these weights also account for nonresponse according to the respondents' age and geographic distribution (urban vs. rural).

For the data from the first follow-up investigation that include only 14-to-17-year-olds, a special weight was computed for the subpopulation of the younger cohort. Weights were adjusted for dropout from baseline to first follow-up according to age, geographic distribution, and nonresponse. For the data from the second follow-up, under consideration here, the same weights as those of the baseline investigation were used because there was no selective attrition due to age and geographic distribution for which we needed to adjust.

Statistical Analysis

The Stata Software package[38] was used to calculate proportions and standard errors as well as robust confidence intervals for weighted data. Multiple logistic regressions with odds ratios (OR) were used to describe individual baseline risk factors of follow-up threshold and subthreshold PMDD excluding baseline 12-month threshold PMDD. In the first analysis, a subject's age at second follow-up was recognized as a confounding variable and was controlled for as a continuous variable. The second multiple regression analysis included all variables under consideration. Logistic regression, incorporating age as a covariate, was also used to analyze associations with specific types of events and threshold PMDD. In order to do this, cases up to the second follow-up were summed, and covariates in women who had an onset of threshold PMDD were compared with those in women who had no threshold PMDD.

RESULTS

Epidemiologic Findings

Table 2 illustrates the baseline 12-month prevalence, the follow-up incidence estimates, and the cumulated rates for PMDD at follow-up. The 12-month prevalence rate for threshold PMDD at baseline was 4.6%. Additionally, 15.9% met our criteria for subthreshold PMDD (total prevalence: 20.4%). Over the 42-month follow-up period, the increase of threshold PMDD was 3.0% resulting in a cumulative rate of 7.5% for threshold PMDD at follow-up.

Table 2. Prevalence and Incidence of PMDD and PTSD in the Total Sample and Subgroups for Women in the Early Developmental Stages of Psychopathology Study (N = 1251)

	Baseline 12-Month Prevalence			Second (42-month) Follow-Up Incidence[a]			Second Follow-Up Cumulated Assessment Incidence		
Variable	N[b]	%[c]	95% CI	N[b]	%[c]	95% CI	N[b]	%[c]	95% CI
Any PMDD	220	20.4	17.9 to 23.2	150	13.3	11.2 to 15.7	370	31.0	28.2 to 34.0
Subthreshold	171	15.9	13.6 to 18.4	137	12.3	10.3 to 14.7	326	27.1	24.4 to 29.9
Threshold	49	4.6	3.4 to 6.2	40	3.0	2.2 to 4.3	89	7.5	6.0 to 9.3
Any trauma	93	8.2	6.7 to 10.2	262	25.0	22.2 to 28.0	350	28.9	26.2 to 31.8
Any PTSD	78	6.9	5.4 to 8.7	73	5.7	4.5 to 7.4	151	12.2	10.3 to 14.4
Subgroups[d]									
Pure PMDD (without PTSD/trauma)									
Subthreshold	136	12.7	10.7 to 15.1	82	7.4	5.8 to 9.4	149	12.5	10.6 to 14.8
Threshold	37	3.2	2.2 to 4.5	20	1.6	1.0 to 2.6	40	3.3	2.3 to 4.6
PMDD + PTSD									
With subthreshold PMDD	21	1.8	1.2 to 2.9	10	1.0	0.5 to 1.9	45	3.8	2.8 to 5.2
With threshold PMDD	9	0.9	0.4 to 1.8	7	0.5	0.2 to 1.1	25	2.0	1.3 to 3.1
PMDD + traumatic events									
With subthreshold PMDD	14	1.3	0.8 to 2.2	40	3.6	2.6 to 5.0	87	7.2	5.8 to 9.0
With threshold PMDD	3	0.5	0.2 to 1.7	13	1.0	0.5 to 1.7	24	2.2	1.4 to 3.4
Neither PMDD nor PTSD	983	75.4	72.5 to 78.1	…	…	…	800	62.6	59.5 to 65.7

[a]Prevalence at second follow-up without baseline cases.
[b]Unweighted N.
[c]Weighted percentage.
[d]Cumulated rates for combinations of PMDD and PTSD/trauma subgroups are computed independently of pure PMDD status at baseline. Women with pure PMDD might belong to the cumulated group of those with trauma or PTSD if they had experienced trauma or PTSD during follow-up but no incident PMDD. Follow-up PMDD incidence accounting for baseline status of PTSD/trauma among those without baseline PMDD: Threshold PMDD = 19.2% (N = 8) and subthreshold PMDD = 3.49% (N = 5); for new PMDD among baseline trauma cases without baseline PMDD: Threshold PMDD = 38.1% (N = 14) and subthreshold PMDD = 14.5% (N = 17).
Abbreviations: PMDD = premenstrual dysphoric disorder, PTSD = posttraumatic stress disorder.

Prevalence rates are also presented for pure PMDD with or without PTSD or trauma, PMDD with PTSD, and PMDD with trauma. These rates revealed that the majority of women with threshold PMDD (total rate: 7.5%) had either PTSD (2.0%) or at least traumatic events (2.2%) at second follow-up. Pure threshold PMDD without PTSD or trauma was found in 3.3%. At baseline, the rates of threshold PMDD with either trauma (0.5%) or PTSD (0.9%) were lower than those of pure PMDD (3.2%). This indicates that up to the second follow-up, a modest increase of comorbid trauma/PTSD and PMDD cases occurred. In fact, comparisons with the prevalence and incidence patterns of pure PMDD showed that almost 50% of all incident follow-up cases of threshold PMDD occurred among women with trauma or PTSD. For subthreshold PMDD, these patterns tend to be similar overall.

Predictors of PMDD

Table 3 shows the results of logistic regression models with several baseline variables as predictors of follow-up threshold PMDD in the first 2 columns and those of subthreshold PMDD in the third and fourth columns. To avoid confounding with age, separate analyses for each predictor variable in the first and third column were controlled for age. The results in the second and fourth columns are based on a multiple logistic regression analysis with all predictor variables including age. To be strictly prospective, the analyses were computed in a subsample of women who did not have PMDD at baseline.

Controlling only for age at the second follow-up evaluation, the strongest baseline predictor of threshold PMDD at follow-up was subthreshold PMDD at baseline (OR = 12.9, 95% CI = 6.0 to 27.5). The odds ratio for women who experienced traumatic events was 3.6 (95% CI = 1.6 to 7.9), indicating a substantial contribution in risk of PMDD for this factor. Women with baseline anxiety disorders also had a high risk of subsequently developing PMDD (OR = 3.4, 95% CI = 1.7 to 6.9). Furthermore, lower self-competence (OR = 1.5, 95% CI = 1.1 to 2.2), negative life events (OR = 1.3, 95% CI = 1.1 to 1.6), and daily hassles (OR = 1.7, 95% CI = 1.2 to 2.5) seem to play a role.

Despite including baseline subthreshold PMDD in the multiple logistic regression model (OR = 11.0, 95% CI = 4.7 to 25.9), any qualifying traumatic event (OR = 4.2, 95% CI = 1.2 to 12.0) increased the odds of developing PMDD. The risk for those with an antecedent anxiety disorder was still significant, but it diminished (OR = 2.5, 95% CI = 1.1 to 5.5) as did the effect of daily hassles (OR = 1.6, 95% CI = 1.1 to 2.3).

An interesting finding is that the results for subthreshold PMDD were different. We found no significant association with traumatic events or PTSD. Here, the strongest associations with the development of new subthreshold PMDD was nicotine dependence (OR = 2.4, 95% CI = 1.4 to 4.1), anxiety disorders (OR = 2.0, 95% CI = 1.3 to 3.0), and daily hassles (OR = 1.4, 95% CI = 1.2 to 1.7). These baseline predictors also remained significant in the mul-

Table 3. Predictors of New-Onset (incident) Threshold and Subthreshold PMDD in the Sample of Women in the Early Developmental Stages of Psychopathology Study (N = 1251)

	Incident Threshold PMDD Versus No PMDD				Incident Subthreshold PMDD Versus No PMDD			
	Controlled for Age		Multiple[a]		Controlled for Age		Multiple[a]	
Baseline Predictors	OR[b]	95% CI[b]	OR[b]	95% CI[b]	OR[b]	95% CI[b]	OR[b]	95% CI[b]
Age at final follow-up	0.8*	0.7 to 0.9	0.8*	0.7 to 0.9	0.9	0.9 to 1.0	0.9	0.9 to 1.0
Subthreshold PMDD	12.9*	6.0 to 27.5	11.0*	4.7 to 25.9	…	…	…	…
Any qualifying trauma	3.6*	1.6 to 7.9	4.2*	1.2 to 12.0	1.2	0.7 to 2.2	1.6	0.8 to 3.3
Diagnosis of PTSD at baseline	2.6*	1.0 to 6.6	0.7	0.1 to 2.8	0.7	0.2 to 1.8	0.3	0.1 to 1.2
Low self-competence[c]	1.5*	1.1 to 2.2	1.1	0.7 to 1.8	1.2	0.9 to 1.4	1.0	0.8 to 1.2
No. of negative life events	1.3*	1.1 to 1.6	0.9	0.7 to 1.3	1.1	0.9 to 1.3	0.9	0.8 to 1.2
Increased daily hassles	1.7*	1.2 to 2.5	1.6*	1.1 to 2.3	1.4*	1.2 to 1.7	1.4*	1.1 to 1.7
Substance use disorder[d]	0.9	0.3 to 2.6	0.4	0.1 to 1.6	1.2	0.6 to 2.6	0.8	0.3 to 1.7
Nicotine dependence	2.2	0.9 to 5.5	1.7	0.6 to 4.5	2.4*	1.4 to 4.1	2.2*	1.3 to 3.9
Any anxiety disorder	3.4*	1.7 to 6.9	2.5*	1.1 to 5.5	2.0*	1.3 to 3.0	1.7*	1.1 to 2.7
Any mood disorder	2.2	0.9 to 5.0	1.1	0.4 to 3.2	1.5	0.9 to 2.6	1.2	0.7 to 2.3
Any somatoform disorder/syndrome	1.1	0.5 to 2.6	0.8	0.3 to 2.1	1.2	0.7 to 2.2	1.0	0.6 to 1.9
Any eating disorder	2.4	0.7 to 7.9	2.2	0.8 to 6.9	1.7	0.6 to 5.1	1.4	0.5 to 4.0

[a]Multiple logistic regression model with all predictor variables.
[b]From logistic regression.
[c]Standardized values; higher values are associated with lower self-competence.
[d]Without nicotine dependence.
*p < .05.
Abbreviations: PMDD = premenstrual dysphoric disorder, PTSD = posttraumatic stress disorder.

Table 4. Frequency of DSM-IV PTSD and Traumatic Events Among Women With and Without Threshold PMDD in the Follow-Up Sample (N = 1251)

	No Threshold PMDD (cumulative lifetime)[a]			Threshold PMDD (cumulative lifetime)[a]			Comparison[c]	
PTSD and Trauma	N	%[b]	95% CI	N	%[b]	95% CI	OR	95% CI
PTSD	81	9.2	7.3 to 11.6	25	27.2	18.3 to 38.6	3.7*	2.1 to 6.5
Any trauma[d]	320	37.5	34.0 to 41.2	49	56.3	44.6 to 67.3	2.1*	1.3 to 3.5
War, combat-related trauma	3	0.5	0.2 to 1.6	0	0.0	…	…	…
Physical threat (with weapon)	54	5.4	4.0 to 7.2	14	15.6	9.0 to 25.8	3.3*	1.6 to 6.7
Rape, sexual assault	23	3.0	1.9 to 4.7	5	5.5	2.2 to 13.4	1.9	0.6 to 5.5
Sexual abuse during childhood	29	3.4	2.3 to 5.0	13	19.1	11.1 to 30.8	6.7*	3.2 to 14.1
Natural disaster	6	0.6	0.3 to 1.4	2	2.2	0.5 to 8.3	3.8	0.7 to 20.0
Severe accident (involved)	41	4.9	3.5 to 6.7	10	10.3	5.3 to 19.0	2.3*	1.0 to 5.0
Witnessed any of the above	234	27.9	24.8 to 31.4	35	39.2	28.6 to 50.9	1.6	0.9 to 2.7
Other types of trauma	29	2.8	1.8 to 4.0	4	4.7	1.7 to 12.4	1.8	0.6 to 5.6

[a]Cumulated data from baseline, first follow-up, and second follow-up among those who completed second follow-up.
[b]Weighted percentage.
[c]OR and 95% CI from logistic regression.
[d]Qualifying for DSM-IV traumatic events according to DSM-IV PTSD criteria A1 and A2.
*p < .05.
Abbreviations: PMDD = premenstrual dysphoric disorder, PTSD = posttraumatic stress disorder.

tiple logistic regression model with nicotine dependence as strongest association (OR = 2.2, 95% CI = 1.3 to 3.9) followed by anxiety disorders (OR = 1.7, 95% CI = 1.1 to 2.7) and daily hassles (OR = 1.4, 95% CI = 1.1 to 1.7).

Not shown in Table 3 is an additional analysis in which the predictive power of traumatic events for PMDD was compared with that for other depressive disorders (major depressive disorder, dysthymic disorder). Results differed markedly. The group comparison based on a multiple logistic regression model with all variables from Table 3 showed that traumatic events were a more powerful predictor for the onset of PMDD (OR = 5.1, 95% CI = 1.2 to 21.3) than they were for the onset of other depressive disorders.

Specific Types of Traumatic Events and PMDD

In a further step, we investigated whether any particular type of traumatic event was more frequent among women with threshold PMDD. Table 4 shows a comparison between women with and without PMDD up to the second follow-up, using logistic regression models controlling for age.

Compared to women without PMDD, those with threshold PMDD were significantly more likely to have experienced physical threat (5.4% vs. 15.6%; OR = 3.3, 95% CI = 1.6 to 6.7), sexual abuse during childhood (3.4% vs. 19.1%; OR = 6.7, 95% CI = 3.2 to 14.1), and severe accidents (4.9% vs. 10.3%; OR = 2.3,

95% CI = 1.0 to 5.0). A large proportion of women with PMDD had experienced more than 1 trauma.

DISCUSSION

The key finding of this study is the remarkably strong association between threshold PMDD and traumatic events. The association was particularly marked for women with threshold PMDD in the individual predictor analysis and was maintained even after controlling for preexisting subthreshold PMDD, other mental disorders, and daily hassles. The nonsignificant results for PTSD might be due to the small number of women with full PTSD and PMDD.

Although this is, to our knowledge, the first investigation to explore the role of trauma and PTSD as risk factors for the onset of PMDD in an epidemiologic sample, it is consistent with our previous reports and observations and the work of others suggesting that stress may be a risk factor for the development of moderate to severe premenstrual conditions. In a community study of women with premenstrual stress, Deuster et al.[7] found that women with the highest stress scores were more likely to be classified as having premenstrual disorder. Our findings also extend the work of others who have noted high rates of abuse in women with PMDD.[39] In our report, we suggest that a sequela of such abuse is not limited to PTSD but that it can also include PMDD. Furthermore, our results indicate that, prospectively, there is a significant risk for developing PMDD after other traumatic events. Prolonged stress responses after traumatic events might be involved in this pathogenic association. Neurobiological markers suggesting an abnormal stress response support this role of stress and trauma in the pathophysiology of PMDD.[24]

It is also worth noting that baseline anxiety disorders increased the risk of developing PMDD. This is consistent with a number of provocation studies that have predictably produced panic attacks in patients with PMDD.[40,41] On the other hand, antecedent mood disorders did not significantly increase the risk of subsequent PMDD. Whereas much of the focus on PMDD has been its possible association with mood disorders,[16,42–44] in a genetic study great stability has been found for premenstrual symptoms but only a modest association between risk factors for premenstrual symptoms and major depressive disorder.[23] In line with these findings are our additional results showing that the effects of traumatic events might differ in predicting PMDD and other depressive disorders. We found a much stronger and significant effect of trauma on the development of threshold PMDD. We refrain from discussing the full spectrum of comorbid patterns, because this issue was discussed comprehensively in our previous publication.[13]

With regard to subthreshold and threshold PMDD, it is noteworthy that there are differences in the predictors, especially with regard to traumatic events and PTSD. Although the association with threshold PMDD was strong, we found no significant association between subthreshold PMDD and traumatic events in the individual predictor analysis. Because the majority of women with subthreshold PMDD had simply missed the impairment criterion, a certain severity might be an important aspect moderating the observed effect. It may also be that the criterion for threshold PMDD defines a cohort of women who are more homogenous in terms of the biological underpinnings of and risk factors for the illness. Further studies might also need to explore alternative ways for defining subthreshold PMDD by lowering the threshold of symptoms required for the diagnosis.

The current study has a number of strengths, including the longitudinal nature of the data and the representative sample; however, some limitations should be noted. Besides the significant association between traumatic events and threshold PMDD, our results also show that the strongest predictor of threshold PMDD at follow-up is subthreshold PMDD at baseline. Therefore, women with subthreshold PMDD may possibly be more likely to experience traumatic events. We cannot exclude this interpretation, although if such a hypothesis were correct, it would suggest a strong cross-sectional association between subthreshold PMDD and traumatic events or PTSD. However, our baseline data had not shown a significant cross-sectional association between PTSD and subthreshold PMDD,[25] and the additional case-by-case review showed that a high proportion of the women with threshold PMDD experienced traumatic events before the onset of menses.

A second limitation might be that our definition of PMDD does not account for criteria C and D of the DSM-IV and was based solely on retrospective self-report without the "charting" during menstrual cycles as required by DSM-IV criteria. Third, we only examined women aged 14 to 24 years at baseline and followed them up over a period of 42 months. Thus, the results refer to adolescents and young adults and not to women above this age cutoff.

Furthermore, our findings from this relatively young urban German community sample, consisting of a well-educated, relatively high socioeconomic group, might not be representative of other populations, especially with regard to traumatic events. A final limitation is that our data refer to self-reports that require recall of events and symptoms. Some recall bias can thus not be excluded, although this is less likely given the close period of follow-up and our capacity to evaluate incident cases.

To conclude, our findings suggest that traumatic events might be an important pathogenic pathway to PMDD and may aggravate subthreshold PMDD, leading to full expression of the disorder. Whereas the underlying mechanisms are still unknown and require further investigation,

  © Copyright 2004 Physicians Postgraduate Press, Inc.

this poses an intriguing lead in our understanding the illness of PMDD and may be relevant for prevention and treatment of PMDD among women after traumatic events.

Disclosure of off-label usage: The authors of this article have determined that, to the best of their knowledge, no investigational information about pharmaceutical agents has been presented in this article that is outside U.S. Food and Drug Administration–approved labeling.

Principal investigators of the Early Developmental Stages of Psychopathology (EDSP) Study: Hans-Ulrich Wittchen, Ph.D., and Roselind Lieb, Ph.D. Current or former staff members of the EDSP group are Kirsten von Sydow, Ph.D., Gabriele Lachner, Dr.Rer.Biol.Hum., Axel Perkonigg, Ph.D., Peter Schuster, Dr.Rer.Nat., Franz Gander, Ph.D., Michael Höfler, Dipl.Stat., Holger Sonntag, Dipl.Psych., and Petra Zimmermann, Dr.Rer.Nat., as well as Esther Beloch, Mag.Phil., Martina Fuetsch, Ph.D., Elzbieta Garczynski, Dipl.Psych., Alexandra Holly, Dipl.Psych., Barbara Isensee, Dr.Rer.Nat., Marianne Mastaler, Ph.D., Chris Nelson, Ph.D., Hildegard Pfister, Dipl.Inf., Victoria Reed, Ph.D., Andrea Schreier, Dipl.Psych., Dilek Türk, Dipl.Psych., Antonia Vossen, Dipl.Psych., and Ursula Wunderlich, Ph.D. Scientific advisors are Jules Angst, M.D., Dr.Hc. (University of Zürich, Zürich, Switzerland); Jürgen Margraf, Dr.Rer.Nat. (University of Basel, Basel, Switzerland); Günther Esser, Ph.D. (University of Potsdam, Potsdam, Germany); Kathleen Merikangas, Ph.D. (National Institute of Mental Health, Bethesda, Md.); and Ron Kessler, Ph.D. (Harvard Medical School, Boston, Mass.).

REFERENCES

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Washington, DC: American Psychiatric Association; 1994
2. Banhart KT, Freeman EW, Sondheimer SJ. A clinician's guide to the premenstrual syndrome. Med Clin North Am 1995;79:1457–1472
3. Andersch B, Wendestam C, Hahn L, et al. Premenstrual complaints, 1: prevalence of premenstrual symptoms in a Swedish urban population. J Psychosom Obstet Gynaecol 1986;5:39–49
4. Angst J, Sellaro R, Merikangas KR, et al. The epidemiology of perimenstrual psychological symptoms. Acta Psychiatr Scand 2001;104:110–116
5. Boyle CA, Berkowitz GS, Kelsey JL. Epidemiology of premenstrual symptoms. Am J Public Health 1987;77:349–350
6. Cleckner-Smith CS, Doughty AS, Grossman JA. Premenstrual symptoms. Prevalence and severity in an adolescent sample. J Adolesc Health 1998;22:403–408
7. Deuster PA, Adera T, South-Paul J. Biological, social, and behavioral factors associated with premenstrual syndrome. Arch Fam Med 1999; 8:122–128
8. Harlow B, Wise L, Otto M, et al. Depression and its influence on reproductive endocrine and menstrual cycle markers associated with perimenopause: the Harvard Study of Moods and Cycles. Arch Gen Psychiatry 2003;60:29–36
9. Hurt SW, Schnurr PP, Severino S, et al. Late luteal phase dysphoric disorder in 670 women evaluated for premenstrual complaints. Am J Psychiatry 1992;149:525–530
10. Johnson SR, McChesney C, Bean JA. Epidemiology of premenstrual symptoms in a nonclinical sample, 1: prevalence, natural history and help-seeking behavior. J Reprod Med 1988;33:340–346
11. Merikangas KR, Foeldenyi M, Angst J. The Zurich study, 19: patterns of menstrual disturbance in the community: results of the Zurich Cohort Study. Eur Arch Psychiatry Clin Neurosci 1993;243:23–32
12. Mongale L, Dan A, Krogh V, et al. Perimenstrual symptom prevalence rates: an Italian-American comparison. Am J Epidemiol 1993;138: 1070–1081
13. Wittchen H-U, Becker E, Lieb R, et al. Prevalence, incidence and stability of premenstrual dysphoric disorder in the community. Psychol Med 2002;32:119–132
14. Bailey JW, Cohen LS. Prevalence of mood and anxiety disorders in women who seek treatment for premenstrual syndrome. J Womens Health Gend Based Med 1999;8:1181–1184
15. Landén M, Eriksson E. How does premenstrual dysphoric disorder relate to depression and anxiety disorders? Depress Anxiety 2003;17:122–129
16. Yonkers K. The association between premenstrual dysphoric disorder and other mood disorders. J Clin Psychiatry 1997;58:19–25
17. Ramcharan S, Love EJ, Fick GH, et al. The epidemiology of premenstrual symptoms in a population-based sample of 2650 urban women: attributable risk and risk factors. J Clin Epidemiol 1992;45:377–392
18. DeLongis A, Coyne JC, Dakof G, et al. Relationship of daily hassles, uplifts, and major life events to health status. Health Psychol 1982;1:119–136
19. Friedman D, Jaffe A. Influence of life-style on the premenstrual syndrome: analysis of a questionnaire survey. J Reprod Med 1985;30: 715–719
20. Gannon L, Luchetta T, Pardie L, et al. Perimenstrual symptoms: relationship with chronic stress and selected life-style variables. Behav Med 1989;15:149–159
21. Woods NF, Mitchell ES, Lentz MJ. Social pathways to premenstrual symptoms. Res Nurs Health 1995;18:225–237
22. Kendler KS, Silberg JL, Neale MC, et al. Genetic and environmental factors in the aetiology of menstrual, premenstrual and neurotic symptoms: a population-based twin study. Psychol Med 1992;22:85–100
23. Kendler KS, Karkowski LM, Corey LA, et al. Longitudinal population-based twin study of retrospectively reported premenstrual symptoms and lifetime major depression. Am J Psychiatry 1998;155:1234–1240
24. Girdler SS, Pedersen CA, Straneva PA, et al. Dysregulation of cardiovascular and neuroendocrine responses to stress in premenstrual dysphoric disorder. Psychiatry Res 1998;81:163–178
25. Wittchen H-U, Perkonigg A, Pfister H. Trauma and PTSD: an overlooked pathogenic pathway for premenstrual dysphoric disorder? Arch Women Ment Health 2003;6:293–297
26. Rivera-Tovar AD, Franke E. Late luteal phase dysphoric disorder in young women. Am J Psychiatry 1990;147:1634–1636
27. Soares C, Cohen L, Otto M, et al. Characteristics of women with premenstrual dysphoric disorder (PMDD) who did or did not report history of depression: a preliminary report from the Harvard Study of Moods and Cycles. J Womens Health Gend Based Med 2001;19:873–878
28. Lieb R, Isensee B, von Sydow K, et al. The Early Developmental Stages of Psychopathology Study (EDSP), 1: methodology: an update. Eur Addict Res 2000;6:170–182
29. Wittchen H-U, Perkonigg A, Lachner G, et al. Early developmental stages of psychopathology study (EDSP): objectives and design. Eur Addict Res 1998;4:18–27
30. Wittchen H-U, Lachner G, Wunderlich U, et al. Test-retest reliability of the computerized DSM-IV version of the Munich-Composite International Diagnostic Interview (M-CIDI). Soc Psychiatry Psychiatr Epidemiol 1998b;33:568–578
31. Wittchen H-U, Pfister H, eds. DIA-X-Interviews: Manual für Screening Verfahren und Interview; Interviewheft Längsschnittuntersuchung (DIA-X-Lifetime); Ergänzungsheft (DIA-X-Lifetime); Interviewheft Querschnittuntersuchung (DIA-X-12 Monate); Ergänzungsheft (DIA-X-12 Monate); PC Programm zur Durchführung des Interviews (Längs- und Querschnittuntersuchung); Auswertungsprogramm, Frankfurt: Swets & Zeitlinger; 1997
32. Perkonigg A, Wittchen H-U. Skala zu Problemlösekompetenzen. München: Max-Planck-Institut, Eigendruck; 1995
33. Friis RH, Wittchen H-U, Pfister H, et al. Life events and changes in the course of depression in young adults. Eur Psychiatry 2002;17:241–253
34. Perkonigg A, Wittchen H-U. The Daily-Hassles Scale: Research Version. München: Max-Planck-Institut für Psychiatrie, Eigendruck; 1995
35. Reed V, Gander F, Pfister H, et al. To what degree the Composite International Diagnostic Interview CIDI correctly identifies DSM-IV disorders? testing validity issues in a clinical sample. Int J Methods Psychiatr Res 1998;7:142–155
36. Perkonigg A, Kessler RC, Storz S, et al. Traumatic events and posttraumatic stress disorder in the community: prevalence, risk factors and comorbidity. Acta Psychiatr Scand 2000;101:46–59
37. Stein MB, Hoefler M, Perkonigg A, et al. Patterns of incidence and psychiatric risk factors for traumatic events. Int J Methods Psychiatr Res 2002;11:143–153
38. StataCorp [computer program]. Stata Statistical Software: Release 6.0. College Station, Tex: Stata Corp; 1999
39. Golding JM, Taylor DL, Menard L, et al. Prevalence of sexual abuse

history in a sample of women seeking treatment for premenstrual syndrome. J Psychosom Obstet Gynaecol 2000;21:69–80
40. Gorman JM, Kent J, Martinez J, et al. Physiological changes during carbon dioxide inhalation in patients with panic disorder, major depression, and premenstrual dysphoric disorder: evidence for a central fear mechanism. Arch Gen Psychiatry 2001;58:125–131
41. Harrison WM, Sandberg D, Gorman JM, et al. Provocation of panic with carbon dioxide inhalation in patients with premenstrual dysphoria. Psychiatry Res 1989;27:183–192
42. Endicott J. Affective disorder and premenstrual depression. In: Osofsky HJ, Blumenthal SJ, eds. PMS: Current Findings and Future Directions. New York, NY: American Psychiatric Association Press; 1985:3–11
43. Graze KK, Nee J, Endicott J. Premenstrual depression predicts future major depressive disorder. Acta Psychiatr Scand 1990;81:201–205
44. Hsiao M, Liu C. Antidepressant-related hypomania in a patient with premenstrual dysphoric disorder. J Clin Psychopharmacol 2002;22: 534–535

For the CME Posttest for this article, see pages 1437–1388

