Original contribution

Trauma and PTSD – An overlooked pathogenic pathway for Premenstrual Dysphoric Disorder?

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Summary

Background: A recent epidemiological analysis on premenstrual dysphoric disorder (PMDD) in the community revealed increased rates of DSM-IV posttraumatic stress disorder (PTSD) among women suffering from PMDD.
Aims: To explore whether this association is artifactual or might have important pathogenic implications.
Methods: Data come from a prospective, longitudinal community survey of an original sample of N = 1488 women aged 14–24, who were followed-up over a period of 40 to 52 months. Diagnostic assessments are based on the Composite International Diagnostic Interview (CIDI) using the 12-month PMDD diagnostic module. Data were analyzed using logistic regressions (odds ratios) and a case-by-case review.
Results: The age adjusted odds ratio between PTSD and threshold PMDD was 11.7 (3.0–46.2) at baseline. 10 women with full PTSD and at least subthreshold PMDD were identified at follow-up. Most reported an experience of abuse in childhood before the onset of PMDD. Some had experienced a life-threatening experience caused by physical attacks, or had witnessed traumatic events experienced by others. 3 women reported more than one traumatic event.
Conclusions: A case-by-case review and logistic regression analyses suggest that women with traumatic events and PTSD have an increased risk for secondary PMDD. These observations call for more in-depth analyses in future research.

Keywords: Premenstrual Dysphoric Disorder; Posttraumatic Stress Disorder; traumatic events; comorbidity; epidemiology.

Introduction

The existence of cyclically recurring premenstrual symptoms of clinical significance has been recognised for decades, and has been labelled premenstrual syndrome (PMS). Subsequent studies in clinical settings and a few in the community have underlined that PMS symptoms are widespread, with significant attendant clinical, public health and socio-economic implications. (Logue and Moos, 1988; Woods et al., 1982). More stringent attempts to define and operationalize diagnostic criteria for severe premenstrual conditions, however, have been a more recent event. The revised 3rd edition of DSM (DSM-III-R; APA, 1987) suggested in its appendix for conditions requiring further study, the category of late luteal phase dysphoric disorder (LLPDD) for severe forms of PMS with criteria predominantly characterized by mood symptoms. In DSM-IV (APA, 1994) the diagnosis was retained under the name "Premenstrual Dysphoric Disorder (PMDD) in the appendix, with more refined and slightly different criteria along with the suggestion to diagnose and code this condition as "depressive disorders not otherwise specified".

Despite an abundance of clinical research on premenstrual and menstrual symptoms, there are only few reliable and comprehensive epidemiological data available that do provide estimates about the prevalence, incidence, risk factors and correlates of both LLPDD and PMDD in the community and in clinical settings. In particular, data on patterns of comorbidity are rare. Most of the available epidemiological evidence is confined to numerous studies that used questionnaire data to describe the frequency and the type of PMS symptoms as well as selected correlates in both adolescent and

adult women (Van Keep and Lehert, 1981; Logue and Moos, 1986; Johnson, 1987; Johnson et al., 1988; Cleckner-Smith et al., 1998; Monagle et al., 1993; Ramcharan et al., 1992). Despite considerable variation in instruments, sampling and design of these studies, there is considerable evidence that the vast majority of women have at least some PMS symptoms. Yet, the prevalence of more severe PMS symptoms seems to be considerably lower. Estimates for variably defined severe PMS symptomatology vary between 1% and 9%. There are three community studies available that have used stricter epidemiological standards concerning PMS as a syndrome and that have provided prevalence estimates for clinically relevant PMS conditions. Results from the Zurich cohort studies (Merikangas et al., 1993; Angst et al., 2001) suggest that according to their study instrument 8.1% could be regarded as having severe and 13.6% as having moderate perimenstrual syndromes in their community cohort of 299 women, aged 21 to 35. Deuster et al. (1999) have performed the most powerful survey in the community to date. Using telephone interview survey data incorporating the administration of the Menstrual Distress Questionnaire in a sample of 874 women in Virginia, US, they reported a cross-sectional prevalence of 8.3% (95 confidence interval 6.4%–10.2%) for females aged 18–44. This study is also the only one examining associations between a number of social and behavioural factors including nutritional, physical exercise, stress and affective state. The third and the most recent study is the Early Developmental Stages of Psychopathology Study (EDSP), a prospective-longitudinal community survey in Munich, Germany (Wittchen et al., 2002).

Findings from the EDSP revealed a 12-month prevalence of 5.8% of DSM-IV PMDD and an additional 18.6% with "near-threshold" PMDD among younger women aged 14–24 years old at baseline. The cumulative incidence after 42 months was 7.4%. 12-month and lifetime comorbidity of PMDD with other mental disorders namely anxiety disorders 47.4%, mood disorders 22.9%, somatoform disorders 28.4% were high and the unexpectedly strong association between posttraumatic stress disorder (PTSD) and PMDD was particularly noteworthy. Because of the strength of this association and the potential pathogenic implications, the present study will explore this association in greater detail, by examining:

1. whether this association is artifactual and
2. the temporal patterns of PMDD and PTSD by means of case-by-case review.

Methods

The Early Developmental Stages of Psychopathology Study (EDSP) has been described in greater detail elsewhere (Lieb et al., 2000; Wittchen et al., 1998a, b). Briefly, the study is based on a 4-year prospective-longitudinal design with up to three assessment points (approximately 20 months apart). As part of a representative community sample of $N = 3021$, adolescents and young adults living in the Munich area, at baseline (T0) in 1995, $N = 1488$ females aged 14 to 24 years were enrolled. For all subjects written informed consent was obtained.

Due to the requirement of stable menstruation patterns, only 1091 (73.3%) women completed the PMS assessment at baseline (T0). At the first follow-up (T1), only the younger cohort aged 14–17 at baseline was contacted. $N = 586$ (99.2%) out of the total of 591 females completed the PMS assessment. At the second follow-up (T2), among all baseline participants recontacted, $N = 1233$ (99.5%) out of 1251 women completed the PMS assessment an average of 42 months after T0. Baseline and follow-up sociodemographic characteristics of this representative German community sample have been reported in the previous PMDD-paper (Wittchen et al., 2002).

Assessment of adolescents and young adults

In all three waves of investigation, symptom and diagnostic assessment were based on the computer-assisted version of the Munich-Composite International Diagnostic Interview (M-CIDI; Wittchen and Pfister, 1997). 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, clinical and psychosocial severity[1]. Detailed information of the M-CIDI has already been described elsewhere (Wittchen et al., 1998a). Detailed analyses covering validity and reliability of single diagnostic criteria and age-, frequency- and quantity-information have also been provided elsewhere (Reed et al., 1998; Wittchen et al., 1998b). In the baseline investigation, the lifetime version of the M-CIDI was used to assess lifetime and 12-month information. For the two follow-up investigations, 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 investigations (12-month-interval-version).

Assessment of PTSD

Posttraumatic stress disorder as well as all other disorders is defined here as one meeting DSM-IV criteria per the M-CIDI diagnostic algorithm. Details have been presented elsewhere (Perkonigg et al., 2000). Briefly, to match DSM-IV criteria and to take into account more recent methodological innovations, the PTSD module consisted of a screening question and a respondent list with 10 groups of specified events, an open-ended question about any other traumatic events to avoid speaking about embarrassing and stigmatising traumas, 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 latter was used to

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[1] The complete M-CIDI is available on request.

determine exactly the number of qualifying events. Ten traumatic event types plus the open category were presented on the list: horrific experience during war, being imprisoned, or taken hostage or kidnapped, physical attacks and threats, sexual abuse, rape, serious accidents, experience of natural catastrophes, sudden (threat of) death of associates and witnessing traumatic events experienced by others. If the respondent indicated several qualifying events (A1 and A2 criterion: 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 cluster, DSM-IV criteria for the worst and most distressing event were assessed with all DSM-IV criteria questions. One-week test-retest reliability of PTSD is acceptable (kappa = 0.79) as was the validity (kappa = 0.85).

M-CIDI-PMDD module

In addition to the information concerning the respondents' menstruation history, anthropometrical information as well as contraceptives use, each wave included an identical assessment of premenstrual syndromes according to criteria of DSM-IV PMDD. The PMDD module was only administered in females with at least 3 years' history of regular menstruation and 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 the past 12 months, respectively their presence during the majority of all menstrual cycles in the past 12 months (DSM-IV criteria A), b) one question to ascertain whether these symptoms occur consistently in the week before onset of menstruation (A), c) as well as three questions to evaluate criterion B for impairment and psychosocial interference. There was no PMDD specific assessment for criterion C (differential diagnostic criteria) nor of criterion D (prospective ratings). Besides this DSM-IV PMDD threshold diagnosis (without criteria C and D) we also specified a subthreshold PMDD diagnosis defined by falling short of just one of the several other DSM-IV criteria.

Weighting of data and statistical analysis

As the EDSP is designed with special interest in early stages of psychopathology, 14- to 15-year-olds were sampled at twice this 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 for the age group of primary interest, i.e., 14- to 15-year-olds. Due to the different sampling probabilities, relative weights inversely proportional to the sampling fraction are used in the estimation of measures that are generalized to the sampling frame. In addition, these weights also account for non-response according to age and geographic distribution (urban vs. rural) of the respondents to that of the registered sampling frame. The Stata Software package (Stata Corp., 1999) was used to calculate proportions and standard errors as well as robust confidence intervals for weighted data. Logistic regressions controlling for age with odds ratios (OR) were used to describe associations between other 12-month DSM-IV baseline disorders and threshold PMDD as well as subthreshold PMDD. An OR of 1.0 or indistinguishable from 1.0 as bounded by the 95% confidence interval is hereby considered as insignificant.

Results

Associations of other disorders and PTSD with PMDD

Table 1 reports the frequency of other selected mental disorders and especially PTSD among non-PMDD cases and compares their rates to the frequencies among threshold and subthreshold PMDD cases. These comparisons result in an OR which should be distinguishable from 1.0 if there is any association.

Most frequent significant associations were between threshold PMDD and (a) anxiety disorders (OR = 3.1; CI, 1.7–5.5), (b) all mood disorders (OR = 3.0; CI, 1.6–5.7), including bipolar I and II, and (c) somatoform disorders (pain, and SSI-4/6; OR = 3.4; CI, 1.8–6.6). Among anxiety disorders, the strongest association was found with PTSD (OR = 11.7; CI, 3.0–46.2). Associations of subthreshold PMDD appear to be relatively similar, however the associations were generally weaker and due to the lower number of PTSD cases and the

Table 1. 12-month comorbidity of threshold and subthreshold PMDD cases at baseline

Other 12-month DSM-IV disorders	No PMDD N = 828		PMDD N = 62				Subthreshold PMDD N = 201			
	N	%w[1]	N	%w[1]	OR[2]	(95% CI)	N	%w[1]	OR[2]	(95% CI)
Any substance use disorder	141	17.7	23	38.3	**2.9**	**(1.6–5.3)****	55	26.3	**1.66**	**(1.1–2.5)**
Any mood disorder	97	12.3	20	29.8	**3.0**	**(1.6–5.7)****	43	21.0	**1.9**	**(1.2–2.9)***
Any anxiety disorder	187	22.5	30	47.4	**3.1**	**(1.7–5.5)*****	70	34.6	**1.8**	**(1.3–2.6)***
- PTSD	7	0.8	4	8.3	**11.7**	**(3.0–46.2)*****	3	1.9	2.5	(0.6–11.2)
Any somatoform disorder	90	10.4	17	28.4	**3.4**	**(1.8–6.6)*****	26	12.4	1.2	(0.7–2.0)
Any eating disorder	16	2.1	4	5.2	2.6	(0.8–8.7)	9	5.5	**2.7**	**(1.1–6.7)***

[1] = weighted %.
[2] = odds ratio and 95% confidence intervals from logistic regression controlled for by age.
* = p < .05; ** = p < .01; *** = p < .001.

higher number of subthreshold PMDDs, this association was not significant.

Not shown in Table 1, we further examined whether baseline PTSD predicted the onset of PMDD during the follow-up period. While we found 13.8% of women with PTSD among new threshold PMDD cases resulting in a significant OR of 8.7 (1.3–57.9) PTSD was not significantly associated with subthreshold PMDD (OR = 0.2; CI, 0.0–1.4).

Case by case review of PMDD and PTSD cases

At baseline and first follow-up 10 women fulfilled DSM-IV criteria for PTSD and had suffered from threshold or subthreshold PMDD. A case by case review of these 10 women showed the following pattern up to the second follow-up:

Five women with full PTSD at baseline had been abused or reported a rape. All 5 women had also suffered from threshold PMDD. 3 of them had an early age at trauma between 11 and 12 years, which precedes PMDD symptoms. At the second follow-up, one of them still reported symptoms qualifying for threshold PMDD 13 years after the trauma. Another one still reported subthreshold PMDD at the second follow-up. One woman with a preceding abuse experience did not fulfil criteria of subthreshold or threshold PMDD. The remaining two women reported no symptoms or had dropped out by the follow-up investigation.

Three women fulfilled our criteria of subthreshold PMDD at baseline. One of them had been raped later during follow-up and suffered from full PMDD at follow-up. The second woman with subthreshold PMDD at baseline reported of a threat trauma after or at the same time as the onset of subthreshold PMDD, and the third had experienced multiple traumas with an earlier onset at the age of 11. At the second follow-up investigation, this woman fulfilled criteria for threshold PMDD.

Findings for primary traumatic events also came from two women who reported an earlier age at abuse and rape before baseline at the age of 12 and 15 years and had suffered from PMDD after baseline, assessed at the first follow-up at the age of 18 years.

Findings for other types of events preceding PMDD are unclear. Threat events also preceded PMDD in two women at the age of 12 and 14 years, but one of them had reported a rape at the age of 15. Witnessing traumatic events experienced by others also seem to precede but were only reported by women who had experienced more than one trauma.

Discussion

This is to our knowledge the first epidemiological study demonstrating associations between PMDD and PTSD. The fact that these associations were confirmed in prospective longitudinal follow-ups, and were also sustained in case-by-case reviews, lends further support to the possibility that this association might bear important nosological implications.

To our knowledge, this association has not been examined in great detail until now. There are a small number of clinical studies among sexually abused women (Girdler et al., 1998; Golding et al., 2000) that showed that many abused women had symptoms of PMDD. Golding et al. (2000) also reported that these women were abused earlier in life, more frequently and by similar types of offenders. But no previous study has used strict diagnostic criteria in a large community study, based on a standardized diagnostic interview, instead of questionnaires. Furthermore, a broader range of traumatic events qualifying for PTSD has not been studied.

Our prospective-longitudinal design allowed us to show that there might be causal effects of traumatic events on PMDD. The fact that the majority of triggering traumatic events leading to PTSD appears before menstruation started supports this speculation. Further, indirect support comes from our previous analyses on incident comorbid conditions (Wittchen et al., 2002), suggesting that after the onset of PMDD, women reveal a decreased risk for further incident anxiety disorders as well as no elevated risk for PTSD and traumatic events.

Still, the specificity of effects of traumatic events for PMDD is unclear. Comorbidity rates of both PMDD and PTSD with other mental disorders and also other physical symptoms (McCauley et al., 1997) are high and one might speculate a nonspecific dysregulation of the stress response in association with traumatic events, which might also influence menstruation. In further research into our prospective data we will include more complex models with a broader range of preceding factors to clarify the role of traumatic events and PTSD in PMDD.

Among the limitations of the study, one should keep in mind that traumatic event reports might be influenced by recall bias and could also have influenced self-ratings of PMDD. Furthermore, in diagnosing PMDD we did not take into account all diagnostic exclusions and we were also unable to fulfil the DSM-IV requirement of using prospective diaries across at least 2 menstrual cycles. Another important limitation of the study is that we exclusively examined PMDD cases aged 14–24

years at baseline, and followed them up over a period of 38 months. Thus, the results refer to adolescents and young adults and not to women above this age cut-off, for which a second high incidence period after the age of 35 has been suggested in previous literature. It is also noteworthy that the number of cases especially with both full threshold PTSD and PMDD is relatively small.

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