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ORIGINAL ARTICLE

Premenstrual symptoms are associated with psychological and physical symptoms in early pregnancy

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Abstract The reproductive life of women is characterised by a number of distinct reproductive events and phases (e.g. premenstrual phase, peripartum, perimenopause). The hormonal transitions during these phases are often associated with both psychological and physical symptoms. Associations between these reproductive phases have been shown by numerous studies. However, the relationship between symptoms during the premenstrual phase and during early pregnancy has received little attention thus far, although early pregnancy is a time of dramatic hormonal as well as physical adaptation. Findings are based on a prospective longitudinal study with N=306 pregnant women (MARI study). Three hundred five women that had menstrual bleeding in the year before pregnancy rated the severity of psychological and physical symptoms during premenstrual phases in the year preceding pregnancy. Besides this, they rated the severity of the same symptoms during early pregnancy (weeks 10 to 12 of gestation). The overall severity of premenstrual symptoms was significantly associated with the overall severity of early pregnancy symptoms (b=0.4, 95 % CI=0.3–0.5; p<0.001). The overall severity of early pregnancy symptoms was best predicted by the severity of premenstrual irritability. The best predictor for a particular symptom in early pregnancy mostly was the corresponding premenstrual symptom. The associations between premenstrual and early pregnancy symptoms support the reproductive hormone sensitivity hypothesis that some women are prone to repeatedly experience specific psychological and physical symptoms during different reproductive phases. The findings further imply that the nature of symptoms might be rather consistent between different reproductive phases.

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Introduction

During their reproductive life, women undergo different phases of intense shifts in levels of gonadal hormone. The levels of estrogens and progesterone significantly change, especially during menstrual cycle, pregnancy, postpartum and perimenopause. Many women cope with these hormonal changes with minimal psychological disturbances, but some women suffer mild to severe psychological symptoms and disorders during these phases (Soares and Zitek 2008; Steiner et al. 2003).

It has been hypothesised that these women have a heightened sensitivity to hormonal changes and are therefore more prone than others to experience psychological symptoms or psychological disorders during different reproductive phases (Halbreich 2010; Payne et al. 2007; Soares 2010; Soares and Zitek 2008). Numerous clinical and a few population-based studies support this "reproductive hormone sensitivity" hypothesis (Soares and Zitek 2008). Associations have, for example, been shown between premenstrual symptoms and postpartum depression (Bloch et al. 2005; Warner et al. 1991; Pearlstein et al. 1990) and also between premenstrual and perimenopausal symptoms (Binfa et al. 2004; Freeman et al. 2004).

The reproductive hormone sensitivity hypothesis is further supported by experimental studies. Schmidt et al. (1998) showed that women with a premenstrual syndrome, but not women without a premenstrual syndrome, experienced psychological and physical symptoms when their ovarian function was suppressed by leuprolide while estrogens or progesterone were administered. Similarly, Bloch et al. (2000) showed that women with a history of postpartum

depression, compared to women without, experienced significant psychological symptoms when hormonal changes of pregnancy and postpartum were simulated by administration and abrupt discontinuation of estrogens and progesterone.

Based on these observations, it has been suggested that different reproductive-related symptoms and disorders share a common aetiology (Halbreich 2003, 2005): A main aetiological factor might be a genetic predisposition which includes the hypersensitivity of women to changes in gonadal hormones. A second aetiological factor may be a predisposition for specific symptom constellations so that symptom patterns may not only be similar, e.g. from menstrual cycle to menstrual cycle (Bloch et al. 1997), but also in different reproductive phases.

Associations between premenstrual phases and early pregnancy have received little attention thus far. To our knowledge, there is only one study on this subject. Sugawara et al. (1997) found that women who reported irritability during premenstrual phases experienced more depressive and anxiety symptoms during early pregnancy. However, irritability was the only premenstrual symptom investigated in this study.

Due to this lack of knowledge, the aim of the present study was to investigate the association between premenstrual symptoms in the year preceding pregnancy and psychological and physical symptoms during early pregnancy. Secondly, it was investigated which premenstrual symptom is the best predictor for psychological and physical conditions during early pregnancy. A third aim of this study was to analyse if women experience similar or different symptom patterns during the premenstrual phases and early pregnancy.

Methods

Procedure

The sample consisted of women who participated in the Maternal Anxiety in Relation to Infant Development Study (MARI study), a prospective longitudinal study that investigates the course of mental disorders during pregnancy and postpartum and the association to early development of the offspring. The participants were recruited during early pregnancy. Recruitment was conducted by personal contact in outpatient settings in the area of Dresden (Germany). To be eligible for the study, women were required to be between 18 and 40 years old. Exclusion criteria were: (a) multiple pregnancy, (b) history of more than three spontaneous abortions/(induced) terminations of pregnancy/still births or child impairment, (c) invasive infertility treatment, (d) severe physical disease/microsomia/skeletal malformation of the expectant mother, (e) severe psychiatric illness, (f) substance abuse of psychoactive substances (e.g. stimulants, hypnotics, opiates) or heroin substitution during the past 6 months, (g) desire to leave the area of Dresden during assessment period or (h) insufficient mastery of German language. Data of the first assessment point during early pregnancy (weeks 10 to 12 of gestation) were used for the present study. The assessments took place at the Institute for Clinical Psychology and Psychotherapy of Technische Universität Dresden or at the participants' homes. Ethics for MARI study have been approved by the Ethics Committee of the Medical Faculty of the Technische Universität Dresden (no: EK 94042007).

Diagnostic assessment

The symptoms that were assessed for the premenstrual phases and during early pregnancy are the 11 symptoms that are listed in the DSM-IV Premenstrual Dysphoric Disorder (PMDD) criteria (APA 2000) as these symptoms are expected to be triggered by gonadal hormone changes and represent a broad range of psychological and physical symptoms: (1) depressed mood, (2) anxiety/tension, (3) tearfulness/increased sensitivity to rejection, (4) irritability/anger, (5) decreased interest, (6) difficulty concentrating, (7) fatigability, (8) appetite/craving, (9) sleep disturbance, (10) feeling overwhelmed, (11) physical complaints (like breast tenderness, headaches, joint/muscle pain, bloating and weight gain). Items were rated on a four-point Likert scale as "not at all", "mild", "moderate" and "severe". Data were collected during early pregnancy (weeks 10 to 12 of gestation). The questionnaire to assess premenstrual symptoms during the year preceding pregnancy was introduced with the question "During the 12 months before your current pregnancy, did you experience any of the following premenstrual symptoms that started before your menstruation and stopped within a few days of bleeding?" The questionnaire that assessed symptoms during early pregnancy (weeks 10 to 12 of gestation) was introduced with "Did you experience any of the following symptoms during your current pregnancy?"

To ensure that associations between premenstrual symptoms and early pregnancy symptoms cannot be attributed to an underlying mental disorder, results were controlled for any DSM-IV anxiety, depressive and somatoform disorder within the last 12 months. The assessment of these DSM-IV disorders was based on the standardised Composite International Diagnostic Interview for Women (CIDI-V; Martini et al. 2009) that was conducted by trained and supervised psychologists. The CIDI-V is a modified version of the World Health Organization-CIDI (Kessler and Ustün 2004) and a highly structured interview for the assessment of mental disorders based on DSM-IV that was enriched by women-specific diagnostic modules. The CIDI has established reliability and validity (Reed et al. 1998; Wittchen et al. 1998).

Statistical analysis

Frequency and severity of symptoms were analysed descriptively. Dependent *t* tests were used to compare differences between severity of symptoms in the premenstrual phases in the year preceding pregnancy and symptoms in early pregnancy. Linear regression analyses were used to examine bivariate relationships between premenstrual symptoms and symptoms in early pregnancy. Multiple linear regression analyses were used to test and compare the predictive value of each premenstrual symptom for symptoms in early pregnancy. Multicollinearity among the predictor variables was assessed using variance inflation factors (VIF). The VIF of the predictor variables (premenstrual symptoms) ranged from 1.0 to 1.8, indicating that there were no multicollinearity concerns (Rawlings et al. 1998). Associations were controlled for age and any DSM-IV anxiety, depressive and somatoform disorder within the last 12 months. Statistical tests were conducted at the 5 % level. STATA version 12.1. (StataCorp. 2011) was used for data analysis.

Results

Sample

In the MARI study, a total of *N*=306 women participated in the first assessment during the first trimester of pregnancy (weeks 10 to 12 of gestation). The mean age of the sample was 28.0 years (SD=4.4) and ranged from 19 to 40 years. Two hundred eighty-five (93.1 %) lived together with a partner. The current occupation status of *N*=173 (56.5 %) was employment, *N*=66 (21.6 %) were students, *N*=30 (9.8 %) were unemployed, *N*=17 (5.6 %) were housewives and *N*=20 (6.5 %) were otherwise occupied (like freelancing). For *N*=149 women (48.7 %), it was the first pregnancy. In the present study, one case was excluded. This woman had no menstrual bleeding in the year before pregnancy because she was pregnant with an older child and breast-feeding, respectively. So a total of *N*=305 cases was left for analysis.

Premenstrual symptoms and symptoms during early pregnancy

In the 12 months preceding their current pregnancy, the women of the sample had on average 5.7 mild to severe symptoms (SD=3.6) during their premenstrual phases. The average severity scores of the individual premenstrual symptoms are shown in Table 1. Physical complaints were rated highest (mean=2.5, SD=1.0), followed by irritability/anger (mean=2.2, SD=0.9) and fatigability (mean=1.9, SD=0.9). The ratings of all premenstrual symptoms were converted into a mean global severity score. For premenstrual symptoms, this score was 1.6 (SD=0.5).

During early pregnancy, women reported an average of 7.2 mild to severe symptoms (SD=3.1). The average severity scores of the individual early pregnancy symptoms are shown in the second column of Table 1. During early pregnancy, the symptoms with the highest severity were fatigability (mean=2.5, SD=0.9), physical complaints (mean=2.4, SD=0.8), irritability/anger (mean=2.1, SD=0.9) and sleep disturbances (mean=2.1, SD=0.6). The global severity score of early pregnancy symptoms was 1.8 (SD=0.4).

The *t* tests revealed that the total number as well as the global severity of symptoms was significantly higher for early pregnancy than for the premenstrual phase ($t=-6.9$, $p<0.001$ and $t=-6.7$, $p<0.001$, respectively). The *t* tests for

Table 1 Severity of premenstrual symptoms and early pregnancy symptoms, dependent *t* test for differences (*N*=305)

	Premenstrual symptoms		Early pregnancy symptoms		*t* test for differences	
	Mean severity[a]	SD	Mean severity[a]	SD	*t*	*p*
1. Depressed mood	1.6	0.8	1.4	0.6	4.3	<0.001
2. Anxiety/tension	1.4	0.7	1.6	0.8	−4.5	<0.001
3. Tearfulness/sensitivity to rejection	1.7	0.9	1.8	0.9	−1.3	n.s.
4. Irritability/anger	2.2	0.9	2.1	0.9	1.2	n.s.
5. Decreased interest	1.5	0.6	1.6	0.7	−3.4	<0.001
6. Difficulty concentrating	1.4	0.7	1.5	0.7	−3.4	<0.001
7. Fatigability	1.9	0.9	2.5	0.9	−10.0	<0.001
8. Appetite/craving	1.7	0.9	1.6	0.9	0.7	n.s.
9. Sleep disturbance	1.4	0.6	2.1	0.6	−18.4	<0.001
10. Feeling overwhelmed	1.2	0.6	1.2	0.5	1.6	n.s.
11. Physical complaints	2.5	1.0	2.4	0.8	1.5	n.s.

n.s. not significant

[a]Severity of symptoms: 1 = not at all, 2 = mild, 3 = moderate, 4 = severe

differences between the ratings of individual symptoms during the premenstrual phase and early pregnancy are shown in the right column of Table 1. Compared to the premenstrual phase, the severity of anxiety/tension, decreased interest, difficulty concentrating, fatigability and sleep disturbances was rated significantly higher during early pregnancy. The severity of depressed mood was rated significantly lower. Other symptoms showed no significant differences.

Associations between premenstrual symptoms and early pregnancy symptoms

The total numbers of symptoms during the premenstrual phase and during early pregnancy were significantly associated (linear regression; b=0.4; 95 % CI=0.3–0.5; p<0.001). To ensure that the association cannot be attributed to the age of the women or underlying DSM-IV mental disorders associations were controlled for age and any anxiety, depressive and somatoform disorder within the last 12 months and it revealed a similar result (b=0.3, 95 % CI=0.2–0.4, p<0.001). Likewise, the global severities of symptoms during the premenstrual phases and during early pregnancy were significantly associated (linear regression; b=0.4; 95 % CI=0.3–0.6, p<0.001). The same association controlled for age or any DSM-IV anxiety, depressive and somatoform disorder within the last 12 months was also significant (b=0.4, 95 % CI=0.3–0.5, p<0.001).

Table 2 shows the bivariate associations between each premenstrual symptom and each early pregnancy symptom. There are numerous significant associations between premenstrual and early pregnancy symptoms ranging from 0.1 to 0.4. All associations between equal symptoms during premenstrual phases and early pregnancy were significant.

A multiple linear regression model was calculated for each early pregnancy symptom; however, only the premenstrual symptoms that were significantly associated in the bivariate regression analyses were included. As shown in Table 3, predominantly the associations between equal symptoms remained significant.

Table 4 shows the bivariate associations between each premenstrual symptom and the global severity of symptoms in early pregnancy. All premenstrual symptoms were significantly associated with the global severity score of early pregnancy symptoms, except for appetite/craving. Again, only the significantly associated symptoms were included in a multiple linear regression model. As presented in the right column of Table 4, only irritability/anger remained as a significant predictor for severity of early pregnancy symptoms.

Discussion

In this study, the associations between premenstrual and early pregnancy symptoms were analysed. At first the frequencies of these symptoms were compared. During early pregnancy, the number of symptoms as well as the average severity of symptoms was significantly higher than during premenstrual phases. Of course, the different time frames of the reproductive phases have to be considered: The premenstrual phase is a short cyclic reoccurring period, whereas

Table 2 Associations between premenstrual and early pregnancy symptoms (bivariate linear regression analyses) (N=305)

	Early pregnancy symptoms										
Premenstrual symptoms	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.
1. Depressed mood	*0.2**	0.1*	0.3*	0.2*	0.1*	0.2*	0.3*	n.s.	0.2*	0.1*	0.2*
2. Anxiety/tension	0.2*	*0.3**	0.2*	0.3*	0.1*	0.2*	0.2*	n.s.	0.1*	0.2*	0.2*
3. Tearfulness/sensitivity to rejection	0.1*	0.2*	*0.4**	0.2*	n.s.	0.1*	0.2*	n.s.	0.1*	n.s.	0.1*
4. Irritability/anger	0.2*	0.1*	0.3*	*0.4**	0.2*	0.2*	0.2*	n.s.	0.1*	0.1*	0.2*
5. Decreased interest	0.1*	n.s.	0.2*	0.2*	*0.3**	0.3*	0.3*	n.s.	0.2*	n.s.	n.s.
6. Difficulty concentrating	n.s.	n.s.	n.s.	0.3*	0.2*	*0.3**	0.1*	n.s.	0.2*	0.1*	0.2*
7. Fatigability	n.s.	0.1*	0.1*	0.2*	0.1*	0.2*	*0.2**	n.s.	0.1*	0.1*	0.1*
8. Appetite/craving	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	*0.2**	n.s.	n.s.	n.s.
9. Sleep disturbance	n.s.	n.s.	n.s.	n.s.	n.s.	0.2*	n.s.	n.s.	*0.3**	0.2*	0.2*
10. Feeling overwhelmed	0.2*	n.s.	n.s.	0.4*	n.s.	0.2*	n.s.	n.s.	0.2*	*0.2**	n.s.
11. Physical complaints	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	0.1*	n.s.	*0.3**

Controlled for age and any DSM-IV anxiety, depressive and somatoform disorder during the last 12 months

n.s. not significant

*p<0.05 significant

In italics: Associations between same symtoms during premenstrual phases and early pregnancy

Table 3 Final multiple regression models of premenstrual symptoms for severity of early pregnancy symptoms (N=305)

	Early pregnancy symptoms										
Premenstrual symptoms	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.
1. Depressed mood	*0.1**	n.s.	0.2*	n.s.	n.s.	n.s.	n.s.		n.s.	n.s.	n.s.
2. Anxiety/tension	n.s.	*0.3**	n.s.	n.s.	n.s.	n.s.	n.s.		n.s.	0.1*	n.s.
3. Tearfulness/sensitivity to rejection	n.s.	n.s.	*0.3**	n.s.		n.s.	n.s.		n.s.		n.s.
4. Irritability/anger	n.s.	n.s.	n.s.	*0.3**	0.1*	n.s.	n.s.		n.s.	n.s.	n.s.
5. Decreased interest	n.s.		n.s.	n.s.	*0.2**	n.s.	n.s.		n.s.	n.s.	
6. Difficulty concentrating				n.s.	n.s.	*0.3**	n.s.		n.s.	n.s.	n.s.
7. Fatigability		n.s.	n.s.	n.s.	n.s.	n.s.	*n.s.*		n.s.	n.s.	n.s.
8. Appetite/craving								*0.2**			
9. Sleep disturbance						n.s.			*0.1**	n.s.	n.s.
10. Feeling overwhelmed	n.s.			n.s.		n.s.			n.s.	*n.s.*	
11. Physical complaints									n.s.		*0.2**

Controlled for age and any DSM-IV anxiety, depressive and somatoform disorder during the last 12 months

n.s. not significant

*p<0.05 significant

In italics: Associations between same symtoms during premenstrual phases and early pregnancy

early pregnancy is an ongoing condition. Interestingly, in both reproductive phases, the same symptoms were rated highest. During premenstrual phases, the rank order was physical complaints, irritability/anger and fatigability. During early pregnancy, the rank order was fatigability, physical complaints and irritability/anger, therefore showing a higher dominance of symptoms which might be attributed to physical adaptation processes of pregnancy.

Most importantly, our results show that the examined reproductive phases are not independent from each other. The severity of symptoms during the premenstrual phases is significantly associated with the severity of symptoms during early pregnancy. To our knowledge, the only study that investigated a similar research question was conducted by Sugawara et al. (1997) who reported that premenstrual irritability was correlated with depressive and anxiety symptoms during early pregnancy. While their investigation assessed only one single premenstrual symptom, we considered 11 premenstrual symptoms and corresponding symptoms in early pregnancy. Our results suggest that not only premenstrual irritability but also the severity of a broad range of premenstrual psychological and physical symptoms indicates the severity of early pregnancy symptoms. Our results are in line with studies investigating the relationship of premenstrual symptoms with symptoms during other reproductive phases for example with depression during postpartum as well as during perimenopause (Binfa et al. 2004; Bloch et al. 2005; Freeman et al. 2004; Harlow et al. 2003). They therefore

Table 4 Bivariate linear regression analyses of premenstrual symptoms for global severity of early pregnancy symptoms and multiple regression model

	Bivariate linear regressions			Multiple regression		
Premenstrual symptoms	*b*	95 % CI	*p*	*b*	95 % CI	*p*
1. Depressed mood	0.2	0.1–0.2	<0.001			n.s.
2. Anxiety/tension	0.2	0.1–0.3	<0.001			n.s.
3. Tearfulness/sensitivity to rejection	0.1	0.1–0.2	<0.001			n.s.
4. Irritability/anger	0.2	0.1–0.2	<0.001	0.1	0.0–0.2	0.002
5. Decreased interest	0.2	0.1–0.3	<0.001			n.s.
6. Difficulty concentrating	0.2	0.1–0.3	<0.001			n.s.
7. Fatigability	0.1	0.1–0.2	<0.001			n.s.
8. Appetite/craving			n.s.			
9. Sleep disturbance	0.1	0.1–0.2	0.001			n.s.
10. Feeling overwhelmed	0.1	0.0–0.3	0.012			n.s.
11. Physical complaints	0.1	0.0–0.1	0.033			n.s.

Controlled for age and any DSM-IV anxiety, depressive and somatoform disorder during the last 12 months

n.s. not significant

further support the reproductive hormone sensitivity hypothesis that some vulnerable women are prone to develop symptoms during phases of intense hormonal changes (Soares and Zitek 2008).

The associations between premenstrual symptoms within the 12 months preceding pregnancy and early pregnancy symptoms in the present study were statistically controlled for age and any DSM-IV depressive, anxiety and somatoform disorder during the last 12 months. They therefore cannot be attributed to the age or an underlying disorder. However, the reported symptoms cannot exclusively be explained by the hormonal changes of the reproductive phases because accompanying psychosocial factors, like stress and changes of the family structure or the professional role, may lead to psychological burden below the threshold of a mental disorder. But, in the concept of reproductive hormone sensitivity, symptoms in a reproductive phase are always the result of an interaction between hormonal and psychosocial factors (Halbreich 2003, 2005; Soares 2010).

The detailed analysis of the relationships between the individual symptoms showed that almost all symptoms during early pregnancy were best predicted by the corresponding symptom in the premenstrual phases. Although the maximum beta weights are 0.3 only, this indicates a certain intraindividual stability of predominant symptoms in different reproductive phases. It has already been shown that the nature of symptoms is consistent from menstrual cycle to menstrual cycle (Bloch et al. 1997) and that premenstrual symptoms predict the same symptoms during the perimenopause 10 years later (Abraham et al. 1995). Thus, the results correspond to these findings and show that the nature of symptoms is also consistent between premenstrual phase and early pregnancy. This means that women who had difficulties coping with specific premenstrual symptoms will probably be confronted with the same symptoms during early pregnancy and possibly during other reproductive phases, too. It therefore supports the hypothesis that an aetiological factor of reproductive-related symptoms may be a predisposition for specific symptom patterns (Halbreich 2003, 2005).

A comparison of the importance of premenstrual symptoms for symptoms during early pregnancy showed that irritability/anger was most important. Taking into account that irritability is known as one of the most prominent and most compromising symptoms during premenstrual, perinatal and perimenopaual phases and is hardly considered in questionnaires and interviews (Born and Steiner 1999; Born et al. 2008), further research on the specific meaning of hormonal sensitivity on irritability and anger is clearly necessary.

A limitation of the present investigation is that the premenstrual symptoms were assessed retrospectively for the year preceding pregnancy. They are therefore subject to recall bias and may be influenced by the current mood of the respondents. This could have lead to an overestimation of the strength of associations. Also, our data do not imply causality. However, a prospective study with women who were recruited before pregnancy and prospectively investigated during pregnancy would be associated with methodological problems also as becoming pregnant is subject to a selection bias itself. Finally, the study sample may not be considered representative of the general population of pregnant women, as the sample was recruited in the area of Dresden in Germany.

To conclude, despite the fact that each reproductive phase is characterised by individual neuroendocrine and psychosocial changes, our results show that women who suffer from psychological and physical premenstrual symptoms are prone to develop the same symptoms during early pregnancy. This suggests that a kind of phenotype predisposition might be involved in women's reproductive hormone sensitivity. Even though this means that a certain set of symptoms may repeatedly accompany some women throughout their reproductive life, our results also imply the necessity of effective therapy because interventions helping women to cope with their premenstrual symptoms could also help them to deal with symptoms in pregnancy and therefore significantly and sustainable increase their quality of life.

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