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# Prevalence of hormone-related mood disorder symptoms in women with ADHD

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ABSTRACT

This is the first study to assess the prevalence of symptoms of premenstrual dysphoric disorder (PMDD), episodes of postpartum depression symptoms (PPD) after first childbirth, and climacteric mood symptoms in Attention-Deficit/Hyperactivity Disorder (ADHD). 209 consecutive women (18–71 years) with ADHD completed the PMDD chapter of the Neuropsychiatric Interview Plus version 5.0.0 to assess PMDD, the Edinburgh Postnatal Depression Scale to assess PPD, and the Greene Climacteric Scale to assess climacteric symptoms. Comorbid psychiatric disorders, medication use, and chronobiological sleep characteristics were also assessed. The prevalence of PMDD and PPD were high in ADHD, compared to the general population. PMDD symptoms were associated with less use of contraceptives. Antidepressants were associated with more PMDD symptoms. The following GCS scores were significant increased: anxiety, depression, and sexual dysfunction, vasomotor and somatic complaints. No significant differences were found in sleep characteristics or current comorbidity between the groups with and without PPD or PMDD, or increased climacteric scores. The prevalences of PMDD, PPD and climacteric scores were high in women with ADHD. This is the first study in women with ADHD that suggests that female ADHD patients suffer from significant PMDD symptoms, experience PPD during the first child birth, and experience more severe climacteric symptoms.

## 1. Introduction

In women with attention-deficit/hyperactivity disorder (ADHD), depression and anxiety is generally more prevalent than in men with ADHD (Rucklidge, 2010). Women with ADHD have an earlier onset, longer episodes of depression, and higher rates of suicidality in comparison with women without ADHD (Biederman et al., 2008; Fuller-Thomson et al., 2016). The median age of onset for depression is higher than for ADHD, suggesting that ADHD increases the risk for depression (Kessler et al., 2005). The increased prevalence of depression in women starting after puberty and temporal associations between changes in female hormones, suggest a window of vulnerability during times of female hormone fluctuations throughout the life span (Kessler et al., 1993; Soares and Zitek, 2008; Steiner et al., 2003). Research on female mood disorders like premenstrual dysphoric disorder (PMDD), postpartum depression (PPD) and depressive symptoms during the menopausal transition is scarce. However, one study showed higher depression risk in pregnant women with increased ADHD symptoms (Jones et al., 2018). Another study showed that ADHD had an increased prevalence and was associated with worse clinical outcomes in women with bipolar disorder and PMDD (Slyepchenko et al., 2017).

This study focused on three phases of hormonal change in women's life with increased risk for depression: PMDD during the premenstrual period with a prevalence of 3–8%, postpartum depression (PPD) with estimated prevalences of 14–19% in the general population, and depressive symptoms during the menopausal transition (Barentsen et al., 2001; Bromberger and Kravitz, 2011; Gavin et al., 2005; Gelaye et al., 2016; Halbreich et al., 2003; O'Hara and McCabe, 2013).

Clinical experience has suggested that women with ADHD often experience more severe mood changes during episodes of hormonal

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changes. Studies with prevalence rates of PMDD, PPD and climacteric symptoms in ADHD were, however, lacking. Beside these episodes of mood changes, we also assessed the sleep-wake rhythm preference (i.e. 'chronotype') in order to examine any associations between sleep characteristics, ADHD, and the mood symptoms (APA, 2013; Khazaie et al., 2016; Van Veen et al., 2010). Results will give a first insight into self-reported mood symptoms in women with ADHD during the premenstrual period, the postpartum period, and the menopausal transition.

## 2. Methods

### 2.1. Participants

Participants were female patients from the PsyQ outpatient clinic for Adult ADHD in The Hague, The Netherlands, who were in care in April and May 2016. They were at least 18 years of age and met the DSM-IV criteria for ADHD. In total 316 patients were approached, of whom 209 (66%; mean age 34.5, SD 11.5 years) completed the study. As this study only involved a few questionnaires and existing data from the patient's electronic records on comorbidity and medication use, medical ethical evaluation was not needed following the Dutch Medical Research Involving Human Subjects Act (WMO) regulations. All respondents were informed that by filling out the questionnaires they consented to the use of their anonymized data for the current study.

### 2.2. Design

The PMDD and PPD symptoms reported in this study were not statistically compared to the prevalence rates reported in studies among the general population, as this would be majorly affected by selection bias. The prevalence rates from general population studies were however

**Table 1**
General characteristics of women with ADHD in PMDD-group and non PMDD-group, N = 209.

| Characteristics | Total study group, $N = 209$ | No PMDD $n = 114$ | PMDD $n = 95$ | No PMDD vs. PMDD: value | No PMDD vs. PMDD: $p$ | Number of PMDD symptoms: value | Number of PMDD symptoms: $p$ |
|---|---|---|---|---|---|---|---|
| Age in years[a], *M (SD)* | 34.5 (11.5) | 34.5 (12.2) | 34.4 (10.6) | $F = 0.001$ | .978 | $F = 0.063$ | .802 |
| Reproductive status[a], *n* (%) | | | | $\chi^2 = 0.134$ | .714 | $t = 0.582$ | .561 |
| Of reproductive age | 174 (83.3) | 94 (82.5) | 80 (84.2) | | | | |
| Peri- or postmenopausal | 35 (16.7) | 20 (17.5) | 15 (15.8) | | | | |
| Educational level[a] ($n = 208$), *n* (%) | | | | $\chi^2 = 6.744$ | .081 | $F = 0.619$ | .603 |
| Elementary school | 10 (4.8) | 9 (7.9) | 1 (1.1) | | | | |
| Lower vocational training/lower prof. education | 37 (17.7) | 22 (19.3) | 15 (15.8) | | | | |
| Higher secondary school/ intermediate prof. education | 91 (43.5) | 48 (43.0) | 42 (44.2) | | | | |
| Higher prof. education/University | 71 (34.0) | 34 (29.8) | 37 (38.9) | | | | |
| Use of (psychiatric) medication[c], *n* (%) | | | | | | | |
| ADHD medication | 143 (68.4) | 79 (71.8) | 63 (66.3) | $\chi^2 = 0.725$ | .395 | $t = 1.147$ | .253 |
| Antidepressants | 66 (31.6) | 29 (26.4) | 35 (36.8) | $\chi^2 = 2.607$ | .106 | $t = -1.991$ | **.048** |
| Melatonin | 47 (22.5) | 25 (22.7) | 22 (23.2) | $\chi^2 = 0.005$ | .942 | $t = -1.217$ | .225 |
| Anti-anxiety medication | 3 (1.4) | 1 (0.9) | 2 (2.1) | $\chi^2 = 0.506$ | .477 | $t = 0.485$ | .628 |
| Use of hormonal contraceptives[a,e], *n* (%) | 105 (50.2) | 64 (68.1) | 41 (50.6) | $\chi^2 = 5.531$ | **.019** | $t = 2.515$ | **.013** |
| Menstrual regularity[a,e], *n* (%) | | | | $\chi^2 = 0.241$ | .886 | $F = 0.211$ | .810 |
| Regular menstrual cycle | 115 (55.0) | 63 (55.3) | 52 (54.7) | | | | |
| Irregular menstrual cycle | 70 (33.5) | 39 (34.2) | 31 (32.6) | | | | |
| Unknown | 24 (11.5) | 12 (10.5) | 12 (12.6) | | | | |
| At least one biological child[a], *n* (%) | 85 (40.7) | 45 (41.3) | 38 (40.0) | $\chi^2 = 0.035$ | .852 | $t = 0.105$ | .917 |
| Any complications ante/peri/ postpartum[a,b], *n* (%) | 53 (62.4) | 25 (55.6) | 26 (68.4) | $\chi^2 = 1.439$ | .230 | $F = 1.227$ | .271 |
| Medical comorbidity[c], *n* (%) | | | | $\chi^2 = 0.241$ | .886 | | |
| Hypertension | 12 (5.7) | 6 (5.3) | 6 (6.3) | $\chi^2 = 0.079$ | .779 | | |
| Hypothyroidism | 8 (3.8) | 3 (2.6) | 5 (5.1) | $\chi^2 = 0.904$ | .342 | | |
| Diagnosed DSM-IV disorders[c,d], *n* (%) | | | | | | | |
| Current mood disorder | 48 (23.0) | 27 (23.7) | 21 (22.1) | $\chi^2 = -0.169$ | .787 | $t = 0.681$ | .496 |
| Mood disorder in remission | 81 (38.8) | 39 (34.2) | 42 (44.2) | $\chi^2 = 2.183$ | .140 | $t = -2.500$ | **.013** |
| Current anxiety disorder | 51 (24.4) | 24 (21.1) | 27 (28.4) | $\chi^2 = 1.525$ | .217 | $t = -1.289$ | .199 |
| Anxiety disorder in remission | 24 (11.5) | 12 (10.5) | 12 (12.6) | $\chi^2 = 0.226$ | .635 | $t = -0.294$ | .769 |
| Current Seasonal Affective Disorder | 2 (1.0) | 2 (1.8) | 0 (0) | $\chi^2 = 1.683$ | .195 | $t = 1.584$ | .115 |
| Seasonal Affective Disorder in remission | 11 (5.3) | 6 (5.5) | 5 (5.3) | $\chi^2 = 0.004$ | .952 | $t = -0.670$ | .504 |
| Personality disorder | 10 (4.8) | 7 (6.1) | 3 (3.2) | $\chi^2 = 1.012$ | .314 | $t = -0.986$ | .326 |
| Current substance abuse disorder (alcohol/drugs) | 29 (13.9) | 15 (13.2) | 13 (13.7) | $\chi^2 = 0.914$ | .633 | $t = -0.575$ | .566 |
| Substance abuse disorder (alcohol/drugs) in remission | 43 (20.6) | 26 (23.7) | 17 (17.9) | $\chi^2 = 0.853$ | .653 | $t = 0.446$ | .656 |
| Delayed Sleep Phase Syndrome (DSPS) | 81 (38.8) | 45 (39.5) | 32 (33.7) | $\chi^2 = 0.746$ | .388 | $t = 0.195$ | .846 |

[a] Self-report.
[b] Multiple options could be chosen.
[c] Assessed by a therapist extracted from electronic patient files.
[d] At the time of assessment.
[e] Reported retrospectively by menopausal women.

reported for an overall impression of any differences in prevalence rates. Studies among the general population from similar countries using the same methodology were lacking, or had only small sample sizes. The odds ratios and effect sizes are reported to provide a general impression of the differences between the PMDD, PPD, and climacteric symptoms in women with ADHD, and in those from the general population.

### 2.3. Measures

The standard diagnostic assessment consisted of the validated Diagnostic Interview for ADHD in adults 2.0 (Kooij and Francken, 2010) based on DSM-IV criteria (Pettersson et al., 2015; Ramos-Quiroga et al., 2016). Second, the Neuropsychiatric Interview Plus version 5.0.0 (the M.I.N.I. Plus) was used to assess comorbidity, a 20-30-min structured assessment of 23 major DSM-IV psychiatric conditions (Sheehan et al., 1998; Van Vliet and De Beurs, 2007). The precursor of the M.I.N.I. Plus, the M.I.N.I., had good to very good kappa values in comparisons with other widely used diagnostic measures, and high sensitivity and specificity (Sheehan et al., 1998). Other data, such as medication use, from the initial assessment was extracted from the electronic patient files. Adherence to pharmacologic treatment could not be assessed. The questionnaire of the study consisted of the background characteristics (see Table 1), and four existing questionnaires about PMDD, PPD, and climacteric symptoms, as well as sleep characteristics. These questionnaires are discussed below.

#### 2.3.1. PMDD

To define clinically relevant symptoms of PMDD, 13 premenstrual dysphoria questions from the M.I.N.I. Plus were used that assess changes in mood, anxiety, activities, sensitivity, concentration, energy, irritability, appetite, sleep, being in control, and physical complaints that they regularly experience during the pre-menstrual week. Peri- or postmenopausal women filled out the questions retrospectively about their complaints during their reproductive age. A clinical diagnosis of PMDD in accordance to the DSM-5 classification includes additional confirmation of premenstrual symptoms from daily self-reports during two consecutive menstrual cycles. This was however not possible. Hence only a PMDD indication was assessed, which is termed PMDD in this article to enhance readability.

The PMDD symptoms in this study was compared with caution to a study using women from the general population that used a comparable definition of PMDD (defined as 'severe premenstrual symptomatology') and a similar data collection (Hylan et al., 1999). In this study, the PMDD symptoms of 1405 women aged 18–49 years from the United States, the United Kingdom and France were assessed by telephone interviews. Of these mostly married women, approximately two thirds had children, and more than half of them had some level of education beyond high school or its equivalent (Hylan et al., 1999). Psychiatric comorbidity was not assessed. The PMDD prevalence rates among the various countries varied between 23.0% and 31.0%, with an overall prevalence of 28.7%.

#### 2.3.2. PPD

The postpartum period after the birth of the first biological child was assessed for a prevalence of PPD symptoms, using the Edinburgh Postnatal Depression Scale (EPDS) (Cox et al., 1987). The EPDS consisted of 10 items and the used cut-off for PPD was 10 points. The PPD symptoms in this study were compared with two systematic reviews about PPD. The first systematic review included 53 studies about PPD with a mean prevalence of 19.6% (16.8–22.6%) among 38,142 participants in low- and middle-income countries (Gelaye et al., 2016). Demographics of the participants from these low- and middle-income countries were unfortunately not provided. The second review included 28 studies in high-income countries with a PPD prevalence of 14.5% (Gavin et al., 2005). The reported demographics of the participants were limited, but it was reported that included studies represented a wide array of developed nations with a limited racial/ethnic mix.

#### 2.3.3. Climacteric symptoms

Following the Stages of Reproductive Aging Workshop (STRAW) criteria (Soules et al., 2001), 'perimenopause' was described as experiencing changes in the cycle length of at least seven days longer or shorter than the regular cycle for at least two cycles, or amenorrhea for a maximum of 11 months. 'Postmenopause' was described as amenorrhea for at least one year. In both the peri- and postmenopausal participants, climacteric symptoms were assessed using the Greene Climacteric Scale (GCS) which consist of 21 symptoms (Greene, 1998). The GCS gave a total score, and sub-scores for psychological symptoms, which was subdivided into sexual dysfunction, and anxiety, depressive, somatic, and vasomotor symptoms. Norm scores from 504, mostly married women aged 45–65 years from the Dutch population were used for comparison (Barentsen et al., 2001). The researchers report that the women were a representative group of the Dutch female population aged 45–65 years, in regards to age, married status, having children, income, education, work situation and household size (Barentsen et al., 2001).

#### 2.3.4. Sleep and psychiatric characteristics

The validated Munich Chronotype Questionnaire (MCTQ) assessed times of falling asleep and waking up to calculate mid-sleep timing on nights before workdays and on free days (Roenneberg et al., 2003). Mid-sleep on free days corrected for possible sleep debt on work days (MSFsc) is a validated outcome of the MCTQ that can be used as a continuous parameter for chronotype (Allebrandt and Roenneberg, 2008). Participants were categorized as a late chronotype when their MSFsc was 05:00 a.m. or later (Juda et al., 2013).

### 2.4. Analysis

Categorical variables were compared between groups using chi-square and odds ratios. For continuous variables, t-tests and ANOVAs were used. Linear regression was used to examine associations between sleep characteristics and PMDD and PPD. We used SPSS 25.0 (Chicago, IL) for data analysis. An α-level of $\leq 0.05$ was used for statistical significance.

## 3. Results

### 3.1. Demographics

Table 1 shows the demographics and characteristics of (psychiatric and somatic) comorbidity for the total ADHD study group, PMDD-group and for those with PMDD symptoms separately (last two columns). Of the participating women, $n = 174$ (83.3%) were of reproductive age, and $n = 35$ (16.7%) were peri- or postmenopausal. Half of the participants used, or have used in the past, hormonal contraceptives during their reproductive years. An irregular menstrual cycle was reported by 33.5%. Of the participants with at least one biological child (40.7%), 62.4% reported to have had complications antepartum, peripartum and/or postpartum after their first child birth. Adherence to any medical treatment was not assed.

### 3.2. PMDD

Indication for PMDD was present in $n = 95$ (45.5%) participants, from now on referred to as the PMDD-group, which seems high in comparison with the prevalence of 28.7% in the general population (Hylan et al., 1999). Even though Hylan et al. used a comparable definition of PMDD among their women from the general population, this comparison should however, be made with caution considering that this and the current study relies on data from self-report questionnaires and therefore only can give an indication for PMDD.

Within our sample, the PMDD-group used significantly less contraceptives compared to the no-PMDD-group (50.6% vs. 68.1%, $\chi^2$ (1) = 5.82; $p$ = .016, OR = 2.09). The presence of premenstrual symptoms in the PMDD-group was the main reason (39.0%) for using contraceptives. This reason was almost significantly more reported than in the no-PMDD-group (39.0% vs. 21.9%, $\chi^2$ (1) = 3.601; $p$ = .058, OR = 0.44). Current and past comorbidities were not significantly related to an indication of PMDD. However, exploring the PMDD-symptoms shows a significant relationship with the use of antidepressants ($t$ = −1.991, $p$ = .048), contraceptives ($t$ = 2.515, $p$ = .013), complications during pregnancy ($F$ = 5.385, $p$ = .008), and a mood disorder in remission ($t$ = −2.500, $p$ = .013), see Table 1. In order to examine the associations between PMDD symptoms and any of the covariates, these variables, except for reported complications during pregnancy (due to a smaller sample size, i.e. only women with a biological child), were entered as covariates in a regression analysis, correcting for age and education level, see Table 2. Use of contraceptives was associated with a lower number of PMDD symptoms, and using antidepressants was associated with a higher number of PMDD symptoms.

### 3.3. PPD

Of the $n$ = 85 women who had least one biological child, 49 (57.6%) met criteria for an indication for PPD in the postpartum period after the first childbirth. This prevalence was much higher compared to the prevalences of two systematic reviews, which found a prevalence of 19.6% among low-to middle-income countries and a prevalence of 14.5% in high-income countries (Gavin et al., 2005; Gelaye et al., 2016). Reported current and past comorbidity was not significant different between the PDD-groups. In this study, the PMDD symptoms were significant higher in the PPD-group compared to the no-PPD-group, with a medium effect size, (M = 7.38, SD = 3.28 vs. M = 5.53, SD = 4.07; $t$ (81) = −2.30, $p$ = .024, d = 0.50). The PPD-group used significantly more antidepressants than the no-PPD-group (49.0% vs. 25.0%, $\chi^2$ = 6.330; $p$ = .010).

### 3.4. Climacteric symptoms

Of the $n$ = 37 women beyond their reproductive age, 18 (48.6%) were perimenopausal, and 19 (51.4%) postmenopausal. One participant was excluded from analyses due to too many missings. Table 3 shows the comparison of the CGS scores of the participants to the Dutch norm scores (Barentsen et al., 2001). In order to correct for multiple testing, a Bonferroni-correction was applied, which did not alter the outcomes. Peri- and postmenopausal participants reported significantly more symptoms on all GCS subscales compared to the norm groups, with (very) large effect sizes (see Table 3).

No differences were found between the peri- and postmenopausal group on any of the GCS scores (not tabulated). Between the PMDD ($n$ = 11) and no PMDD-group ($n$ = 14) significant differences were found on the GCS subscores for depression ($F$ (1) = 5.105, $p$ = .030) and sexual dysfunction ($F$ (1) = 5.191, $p$ = .029). Significant correlations were found between a higher number of PMDD symptoms and a higher total scores of GCS ($r$ = 0.511, $n$ = 38, $p$ = .001), and the subscores psychosocial ($r$ = 0.441, $n$ = 38, $p$ = .006), anxiety ($r$ = 0.381, $n$ = 38, $p$ = .020), depression ($r$ = 0.0418, $n$ = 38, $p$ = .010) and somatic ($r$ = 0.425, $n$ = 38, $p$ = .009) complaints. The PPD-group ($n$ = 18) showed significantly higher GCS scores (vs. no PPD, $n$ = 8) on the total score ($F$ = 7.18 (1), $p$ = .013), the subscores psychosocial ($F$ = 6.01 (1), $p$ = .021), anxiety ($F$ = 5.84 (1), $p$ = .023), depression ($F$ = 4.51 (1), $p$ = .043), vasomotor ($F$ = 7.03 (1), $p$ = .013) and sexual dysfunction ($F$ = 4.56 (1), $p$ = .043).

**Table 2**
Linear regression analysis for variables associated with symptoms of PMDD, N = 171.

| | PMDD symptoms | | |
|---|---|---|---|
| Variable | $\beta$ | $SE\ \beta$ | $p$ |
| Age | 0.014 | 0.033 | .683 |
| Education level | 0.309 | 0.320 | .336 |
| Use of contraceptives | −1.525 | 0.546 | .006 |
| Mood disorder in remission | 0.507 | 0.570 | .375 |
| Use of antidepressants | 1.372 | 0.627 | .030 |

### 3.5. Sleep timing

Complete MCTQ data of 188 participants gave a MSFsc of 4:48 a.m. (SD 1:25 h). No significant MSFsc differences were found between the PMDD- and no-PMMD-group ($F$ (1) = 0.209, $p$ = .648) or PPD ($F$ (1) = 0.010, $p$ = .991). A late chronotype, defined as mid-sleep later than 5:00 a.m., was present in 47.4% ($n$ = 54) participants. No significant differences were found between MSFsc and PPD, PMDD symptoms or any of the CGS scales.

## 4. Discussion

The prevalence of hormone-related mood disorders is unknown and studies are lacking in women with ADHD, while shared pathophysiology and clinical experience suggest that they are at risk for more severe mood changes lifetime during episodes of hormonal fluctuations. This is the first study known to date to explore hormone-related mood symptoms such as PMDD, PPD and climacteric symptoms in ADHD. The results suggest a possible elevated presence of hormone-related mood symptoms throughout the lives of women with ADHD. The prevalences assessed with self-report questionnaires were compared with caution, to prevalence rates from the general population. The supposed PMDD prevalence in this study was 45.5%, which seems high compared to the prevalence of 28.7% in the general population (Hylan et al., 1999). The prevalence of PPD after the first childbirth was 57.6% in our sample which, again, is higher than the prevalence of 19.6% in low- and middle-income countries and 14.5% in high-income countries (Gavin et al., 2005; Gelaye et al., 2016). Peri- and postmenopausal participants reported more climacteric symptoms than the general population, with a very large effect size of 3.71 (1.33–4.94). Contraceptive users reported less PMDD symptoms. Participants using antidepressants reported more PMDD symptoms. PPD after the first childbirth was related to the current use of antidepressants, increased PMDD symptoms and increased climacteric mood symptoms. Sleep timing was not related to PMDD, PPD or climacteric symptoms. This is the first study that explores prevalences of PDD, PMDD and climacteric mood symptoms in women with ADHD, suggesting that they could be more vulnerable to hormone-related mood disorders during their lifespan.

It is believed that in ADHD, levels of dopamine are reduced across several brain regions compared to healthy controls, which not only elicit the ADHD symptoms, but also play a role in reduced mood (Volkow et al., 2009). This may be the reason that hormonal fluctuations across the lifespan have more impact on women with ADHD. The changing hormone levels throughout the menstrual cycle are also suggested to play a role in ADHD symptom severity (Haimov-Kochman and Berger, 2014). In brief, the intracellular signalling systems that are suggested to be abnormal in ADHD seem to able to be regulated by sex hormones like estrogen and progesterone (Haimov-Kochman and Berger, 2014).

The results of our current preliminary study need to be interpreted with caution because of the use of self-report compared with data from community-based studies as a control group. Provided demographics from the general population studies were scarce, which limited the quality of the comparison between women with ADHD and the general population. Comparing our results to the general population could generate a selection bias because psychiatric patients in general may have more symptoms in comparison with the general population. Prevalence rates in other psychiatric populations are unavailable but an

**Table 3**
Comparison of mean CGS scores of the peri- and postmenopausal women (n = 36) to Dutch norm scores (n = 296).

| | Perimenopausal women, mean (SD) | | | | Postmenopausal women, mean (SD) | | | |
|---|---|---|---|---|---|---|---|---|
| GCS domains | ADHD, *n* = 17 | Norms, *n* = 99 | *p* | Cohen's d | ADHD, *n* = 19 | Norms, *n* = 198 | *p* | Cohen's d |
| Total score | 50.06 (3.02) | 15.78 (9.09) | <.001 | 5.06 | 48.02 (2.56) | 15.33 (9.01) | <.001 | 4.94 |
| Psychosocial | 27.83 (1.53) | 7.67 (5.27) | <.001 | 5.20 | 26.97 (1.66) | 7.44 (5.48) | <.001 | 4.82 |
| - Sub-score Anxiety | 5.50 (0.88) | 3.89 (2.84) | .019 | 0.77 | 14.34 (0.82) | 4.07 (2.94) | <.001 | 4.76 |
| - Sub-score Depression | 12.33 (0.77) | 3.78 (2.85) | <.001 | 4.10 | 12.63 (1.02) | 3.37 (2.84) | <.001 | 4.34 |
| Somatic | 14.94 (1.25) | 4.53 (3.76) | <.001 | 3.71 | 14.13 (1.06) | 4.23 (3.43) | <.001 | 3.90 |
| Vasomotor | 4.83 (0.48) | 2.82 (1.75) | <.001 | 1.57 | 4.53 (0.47) | 2.67 (1.92) | <.001 | 1.33 |
| Sexual dysfunction | 2.44 (0.27) | 0.79 (0.88) | <.001 | 2.54 | 2.37 (0.27) | 1.06 (0.94) | <.001 | 1.89 |

elevated risk for PMDD is found in major depression, generalized anxiety disorder, bipolar disorder, posttraumatic stress disorder, trauma and suicidal ideation (Accortt et al., 2013; Pilver et al., 2011; Slyepchenko et al., 2017; Yen et al., 2020). In addition, in female suicide attempters (n = 232) the prevalence of PMDD was 23% (Ducasse et al., 2016). Due to the lack of known prevalence rates of these hormone related mood disorders in other psychiatric populations it is not possible to conclude that the prevalence rates found in this study are specific for ADHD or just in general for women with psychiatric disorders. Secondly, prospective daily ratings during at least two menstrual cycles as required for a classification of PMDD according to DSM-5 were not possible; only the self-report of DSM-5 criteria for PMDD was used as an indication of PMDD (APA, 2013). Furthermore, concerning PPD, only an estimation of the PPD prevalence after the first childbirth was established. Other studies assessed PPD either prospectively or retrospectively in women who recently gave birth (Halbreich and Karkun, 2006). Due to the retrospective self-reports, no distinction could be made between the possible presence of depressive disorder symptoms before pregnancy, prenatally or postpartum. In addition, our study may be subject of recall bias. In previous research in women with premenstrual symptoms, recall bias varied in accordance with the weeks in their menstrual cycle (Schneider et al., 2013). Finally, in contract with other studies, we did not find significant associations between a broad spectrum of psychiatric disorders and PMDD (de Carvalho et al., 2018; Hong et al., 2012; Wittchen et al., 2002). This could be because comorbidity in our sample may be underreported or less severe. Clinicians should be aware of the possibility that a majority of their female ADHD patients of reproductive age experience significant PMDD symptoms. Women with a history of PPD and ADHD could experience more PMDD symptoms and climacteric mood symptoms. Also, more severe climacteric symptoms seem to be present in women with ADHD during and after their menopausal transition. Existing treatments consist of antidepressants, contraceptives or hormonal suppletion therapy (Sepede et al., 2016). A temporary increase of the stimulant medication dosage during the premenstrual week, or light therapy in the last week of the menstrual cycle may as well be helpful for women with ADHD. However, studies on the efficacy of such treatments are still lacking.

Despite these limitations, this is the first study exploring the presence of mood symptoms during hormonal transitions over the lifespan in women with ADHD. The suggested differences in prevalence rates with the general population are, despite the limitations, large, but should be interpreted with caution. Further studies should focus on the use of control groups, prospective monitoring during 2 menstrual cycles of mood symptoms in case of PMDD, the role of discontinued pharmacological treatment for ADHD during pregnancy on the prevalence of prenatal depression and PPD, the pathophysiology, prevention, and treatment of PMDD, PPD, and climacteric symptoms in women with ADHD.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## References


Accortt, E.E., Kogan, A.V., Allen, J.J.B., 2013. Personal history of major depression may put women at risk for premenstrual dysphoric symptomatology. J. Affect. Disord. 150 (3), 1234–1237.

Allebrandt, K.V., Roenneberg, T., 2008. The search for circadian clock components in humans: new perspectives for association studies. Braz. J. Med. Biol. Res. 41 (8), 716–721.

APA, 2013. Diagnostic and Statistical Manual of Mental Disorders - DSM 5, fifth ed. American Psychiatric Publishing, Washington, DC.

Barentsen, R., van de Weijer, P.H., van Gend, S., Foekema, H., 2001. Climacteric symptoms in a representative Dutch population sample as measured with the Greene Climacteric Scale. Maturitas 38 (2), 123–128.

Biederman, J., Ball, S.W., Monuteaux, M.C., Mick, E., Spencer, T.J., McCreary, M., Cote, M., Faraone, S.V., 2008. New insights into the comorbidity between ADHD and major depression in adolescent and young adult females. J. Am. Acad. Child Adolesc. Psychiatry 47 (4), 426–434.

Bromberger, J.T., Kravitz, H.M., 2011. Mood and menopause: findings from the study of women's health across the nation (SWAN) over 10 years. Obstet. Gynecol. Clin. N. Am. 38 (3), 609–625.

Cox, J.L., Holden, J.M., Sagovsky, R., 1987. Detection of postnatal depression. Development of the 10-item Edinburgh postnatal depression scale. Br. J. Psychiatry 150, 782–786.

de Carvalho, A.B., Cardoso, T.A., Mondin, T.C., da Silva, R.A., Souza, L.D.M., Magalhaes, P., Jansen, K., 2018. Prevalence and factors associated with Premenstrual Dysphoric Disorder: a community sample of young adult women. Psychiatr. Res. 268, 42–45.

Ducasse, D., Jaussent, I., Olie, E., Guillaume, S., Lopez-Castroman, J., Courtet, P., 2016. Personality traits of suicidality are associated with premenstrual syndrome and premenstrual dysphoric disorder in a suicidal women sample. PloS One 11 (2), e0148653.

Fuller-Thomson, E., Lewis, D.A., Agbeyaka, S.K., 2016. Attention-deficit/hyperactivity disorder casts a long shadow: findings from a population-based study of adult women with self-reported ADHD. Child Care Health Dev. 42 (6), 918–927.

Gavin, N.I., Gaynes, B.N., Lohr, K.N., Meltzer-Brody, S., Gartlehner, G., Swinson, T., 2005. Perinatal depression: a systematic review of prevalence and incidence. Obstet. Gynecol. 106 (5 Pt 1), 1071–1083.

Gelaye, B., Rondon, M.B., Araya, R., Williams, M.A., 2016. Epidemiology of maternal depression, risk factors, and child outcomes in low-income and middle-income countries. Lancet Psychiatry 3 (10), 973–982.

Greene, J.G., 1998. Constructing a standard climacteric scale. Maturitas 29 (1), 25–31.

Haimov-Kochman, R., Berger, I., 2014. Cognitive functions of regularly cycling women may differ throughout the month, depending on sex hormone status; a possible explanation to conflicting results of studies of ADHD in females. Front. Hum. Neurosci. 8, 191.

Halbreich, U., Borenstein, J., Pearlstein, T., Kahn, L.S., 2003. The prevalence, impairment, impact, and burden of premenstrual dysphoric disorder (PMS/PMDD). Psychoneuroendocrinology 28 (Suppl. 3), 1–23.

Halbreich, U., Karkun, S., 2006. Cross-cultural and social diversity of prevalence of postpartum depression and depressive symptoms. J. Affect. Disord. 91 (2–3), 97–111.

Hong, J.P., Park, S., Wang, H.R., Chang, S.M., Sohn, J.H., Jeon, H.J., Lee, H.W., Cho, S.J., Kim, B.S., Bae, J.N., Cho, M.J., 2012. Prevalence, correlates, comorbidities, and suicidal tendencies of premenstrual dysphoric disorder in a nationwide sample of Korean women. Soc. Psychiatr. Psychiatr. Epidemiol. 47 (12), 1937–1945.

Hylan, T.R., Sundell, K., Judge, R., 1999. The impact of premenstrual symptomatology on functioning and treatment-seeking behavior: experience from the United States, United Kingdom, and France. J Womens Health Gend Based Med 8 (8), 1043–1052.

Jones, H.A., Eddy, L.D., Bourchtein, E., Parks, A.M., Green, T.L., Karjane, N.W., Svikis, D. S., 2018. Attention-deficit/hyperactivity disorder symptoms, depression risk, and quality of life in black pregnant women. J Womens Health (Larchmt) 27 (10), 1263–1270.

Juda, M., Vetter, C., Roenneberg, T., 2013. The Munich ChronoType questionnaire for shift-workers (MCTQShift). J. Biol. Rhythm. 28 (2), 130–140.

Kessler, R.C., Berglund, P., Demler, O., Jin, R., Merikangas, K.R., Walters, E.E., 2005. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the national comorbidity survey replication. Arch. Gen. Psychiatr. 62 (6), 593–602.

Kessler, R.C., McGonagle, K.A., Swartz, M., Blazer, D.G., Nelson, C.B., 1993. Sex and depression in the national comorbidity survey. I: lifetime prevalence, chronicity and recurrence. J. Affect. Disord. 29 (2–3), 85–96.

Khazaie, H., Ghadami, M.R., Khaledi-Paveh, B., Chehri, A., Nasouri, M., 2016. Sleep quality in university students with premenstrual dysphoric disorder. Shanghai Arch Psychiatry 28 (3), 131–138.

Kooij, J.J.S., Francken, M.H., 2010. Diagnostisch Interview Voor ADHD Bij Volwassenen Versie 2.0 (DIVA 2.0). DIVA Foundation, The Hague, The Netherlands. Available online at: www.divacenter.eu.

O'Hara, M.W., McCabe, J.E., 2013. Postpartum depression: current status and future directions. Annu. Rev. Clin. Psychol. 9, 379–407.

Pettersson, R., Soderstrom, S., Nilsson, K.W., 2015. Diagnosing ADHD in adults: an examination of the discriminative validity of neuropsychological tests and diagnostic assessment instruments. J. Atten. Disord. 22 (11), 1019–1031. https://doi.org/10.1177/1087054715618788.

Pilver, C.E., Levy, B.R., Libby, D.J., Desai, R.A., 2011. Posttraumatic stress disorder and trauma characteristics are correlates of premenstrual dysphoric disorder. Arch Womens Ment Health 14 (5), 383–393.

Ramos-Quiroga, J.A., Nasillo, V., Richarte, V., Corrales, M., Palma, F., Ibanez, P., Michelsen, M., Van de Glind, G., Casas, M., Kooij, J.J.S., 2016. Criteria and concurrent validity of diva 2.0: a semi-structured diagnostic interview for adult ADHD. J. Atten. Disord. 23 (10), 1126–1135.

Roenneberg, T., Wirz-Justice, A., Merrow, M., 2003. Life between clocks: daily temporal patterns of human chronotypes. J. Biol. Rhythm. 18 (1), 80–90.

Rucklidge, J.J., 2010. Gender differences in attention-deficit/hyperactivity disorder. Psychiatr. Clin. 33 (2), 357–373.

Schneider, S., Broderick, J.E., Junghaenel, D.U., Schwartz, J.E., Stone, A.A., 2013. Temporal trends in symptom experience predict the accuracy of recall PROs. J. Psychosom. Res. 75 (2), 160–166.

Sepede, G., Sarchione, F., Matarazzo, I., Di Giannantonio, M., Salerno, R.M., 2016. Premenstrual dysphoric disorder without comorbid psychiatric conditions: a systematic review of therapeutic options. Clin. Neuropharmacol. 39 (5), 241–261.

Sheehan, D.V., Lecrubier, Y., Sheehan, K.H., Amorim, P., Janavs, J., Weiller, E., Hergueta, T., Baker, R., Dunbar, G.C., 1998. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J. Clin. Psychiatr. 59 (Suppl. 20), 22–33.

Slyepchenko, A., Frey, B.N., Lafer, B., Nierenberg, A.A., Sachs, G.S., Dias, R.S., 2017. Increased illness burden in women with comorbid bipolar and premenstrual dysphoric disorder: data from 1 099 women from STEP-BD study. Acta Psychiatr. Scand. 136 (5), 473–482.

Soares, C.N., Zitek, B., 2008. Reproductive hormone sensitivity and risk for depression across the female life cycle: a continuum of vulnerability? J. Psychiatry Neurosci. 33 (4), 331–343.

Soules, M.R., Sherman, S., Parrott, E., Rebar, R., Santoro, N., Utian, W., Woods, N., 2001. Executive summary: Stages of reproductive aging Workshop (STRAW). Climacteric 4 (4), 267–272.

Steiner, M., Dunn, E., Born, L., 2003. Hormones and mood: from menarche to menopause and beyond. J. Affect. Disord. 74 (1), 67–83.

Van Veen, M.M., Kooij, J.J.S., Boonstra, A.M., Gordijn, M.C.M., van Someren, E.J.W., 2010. Delayed circadian rhythm in adults with attention-deficit/hyperactivity disorder and chronic sleep-onset insomnia. Biol. Psychiatr. 67 (11), 1091–1096.

Van Vliet, I.M., De Beurs, E., 2007. [The MINI-International Neuropsychiatric Interview. A brief structured diagnostic psychiatric interview for DSM-IV en ICD-10 psychiatric disorders]. Tijdschr Psychiatr. 49 (6), 393–397.

Volkow, N.D., Wang, G.J., Kollins, S.H., Wigal, T.L., Newcorn, J.H., Telang, F., Fowler, J. S., Zhu, W., Logan, J., Ma, Y., Pradhan, K., Wong, C., Swanson, J.M., 2009. Evaluating dopamine reward pathway in ADHD: clinical implications. J. Am. Med. Assoc. 302 (10), 1084–1091.

Wittchen, H.U., Becker, E., Lieb, R., Krause, P., 2002. Prevalence, incidence and stability of premenstrual dysphoric disorder in the community. Psychol. Med. 32 (1), 119–132.

Yen, J.Y., Lin, P.C., Huang, M.F., Chou, W.P., Long, C.Y., Ko, C.H., 2020. Association between generalized anxiety disorder and premenstrual dysphoric disorder in a diagnostic interviewing study. Int. J. Environ. Res. Publ. Health 17 (3).