Title

Stress and Rumination in Premenstrual Syndrome (PMS): identifying stable and menstrual cycle-related differences in PMS symptom severity

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All corresponding data and analysis scripts are made openly available through https://osf.io/j5ynz/.

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Abbrev.: PMS: Premenstrual Syndrome; PMDD: Premenstrual Dysphoric Disorder; DASS: Depression, Anxiety, Stress Scale; PSST: Premenstrual Symptoms Screening Tool; PSS: Perceived Stress Scale; RRS: Ruminative Response Scale; PTQ: Perseverative Thinking Questionnaire

Abstract

Since the inclusion of Premenstrual Dysphoric Disorder (PMDD) as a mood disorder in the DSM-5, Premenstrual Syndrome (PMS) symptoms have received more attention from researchers and clinicians. In this large-scale study, we investigated core psychological concepts relevant to mood disorder vulnerability between people with 1) no to mild, 2) moderate to severe, and 3) PMDD levels of PMS symptoms. Several trait measures related to mood disorders including depressive symptoms, feelings of stress and anxiety, and ruminative thinking were measured (single measurement, $N = 380$) along with state (momentary) reports of stress and stress-related perseverative thinking (measured twice, once in the follicular and once in the premenstrual/luteal phase, $N = 237$). We consistently observed that participants with higher severity of PMS symptoms also scored higher on depression, anxiety, stress, and rumination (trait measures). We also found consistent increases in momentary stress and stress-related perseverative ruminative thinking with increased PMS symptoms at each of our two test moments (in the middle of the follicular and premenstrual/luteal phase respectively). Interestingly, we did not find significant differences between our two test moments for any group, despite PMS being characterized by specific systems in the premenstrual/luteal phase. However, this could be due to noise surrounding the testing moments due to the temporal resolution of the questionnaires and the menstrual cycle estimation method. Nevertheless, these results suggest that stress and rumination are important psychological mechanisms to consider in PMS. Future PMS research studying stress and rumination on a day-to-day basis in combination with hormonal measures is warranted.

keywords: PMS, PMDD, Stress, Rumination, Depression, Anxiety, Menstrual Cycle

Introduction

The COVID-19 pandemic has exacerbated major challenges regarding mental health, demonstrating the importance of research into stress-related mental and somatic disorders (Brantley & Jones, 1993; Cullen et al., 2020; Talevi et al., 2020). In this context, clinicians and scientists increasingly highlight the importance of the menstrual cycle, as hormones can directly influence our mental health, even if this influence is periodic and linked to the monthly cycle (Barron et al., 2008; Jang & Elfenbein, 2019). Indeed, a large portion of the menstruating population experiences different mood, behavioral, and physical symptoms in the week prior to menses (during the premenstrual/luteal phase), which decrease at the start of menstruation (during the follicular phase) (Hofmeister & Bodden, 2016). When substantially impacting daily life, these symptoms are referred to as premenstrual syndrome (PMS; Braverman, 2007). Common physical complaints are joint pain, muscle aches, lower back pain, sensitive breasts, bloating, headaches, skin conditions, and weight gain (Kadian & O'Brien, 2012). Common psychological and behavioral complaints are changes in appetite, energy, exhaustion, mood swings, irritability, anger, restlessness, insomnia/hypersomnia, inability to concentrate, social withdrawal, lack of interest in usual activities, loneliness, rumination, depressive complaints, feelings of helplessness, confusion, and tension (Kadian & O'Brien, 2012). Despite 70 to 90% of menstruating adults reporting occasional PMS symptoms and 12% reporting symptoms that impact daily life (Braverman, 2007; Potter et al., 2009), PMS remains understudied (England, 2016) and PMS complaints are often not understood or recognized by healthcare workers (Osborn et al., 2020). Besides people suffering from PMS, 3 to 8% of the menstruating population is estimated to meet the diagnostic criteria for Premenstrual Dysphoric Disorder (PMDD)(Grady-Weliky, 2003). PMDD was included in the DSM-5 as a mood disorder and is a more extreme version of PMS, where the symptoms heavily affect daily life and often demand medical care to cope (American Psychiatric Association, 2013; Hartlage et al., 2014).

Past research has suggested that core psychological mechanisms associated with mood disorders, such as perceived stress, rumination, sustained negative mood, and anxiety, are higher for people with PMS and PMDD, and worsen during the premenstrual phase (Cahill, 1998; Craner et al.,

2014; Gollenberg et al., 2010; Hou & Zhou, 2021; Landén & Eriksson, 2003; Liu et al., 2017; Nillni et al., 2011; Pearlstein, 1995; Rapkin, 1992, p. 19; Sigmon et al., 2009; Ussher & Wilding, 1992; Welz et al., 2016; Yonkers & White, 1992). PMS symptoms might be explained as caused by a sensitivity to progesterone, a hormone that rises during the premenstrual phase (see Appendix A for a schematic overview) (Hawkins & Matzuk, 2008). Several studies have found evidence suggesting that progesterone might increase mood disorder related vulnerabilities such as stress (reactivity), anxiety, negative mood, and rumination through the increase of amygdala/hippocampal activity in PMS and PMDD patients (Chung et al., 2016; Gingnell et al., 2012; Lin et al., 2013; Lisofsky et al., 2015; van Wingen et al., 2008). Stress sensitivity and rumination are especially important factors in the etiology of mood disorders (Apazoglou et al., 2019; Bale, 2006; Kovács et al., 2020). However, research on the link between stress and rumination in regards to PMS symptoms remains relatively scarce. As such, it is still not fully understood how these core concepts related to mood disorders differ exactly between people with different levels of PMS symptoms, and if these vulnerabilities are stable traits or if they fluctuate in a cycle-dependent way (Beck et al., 1990; Craner et al., 2014; Gollenberg et al., 2010; Liu et al., 2017). Because of this, the menstrual cycle rarely gets taken into account when studying mood disorder-related concepts.

In the current study, we compared core psychological measures relevant to mood disorders between three groups depending on the severity of PMS symptoms as defined by an official screening questionnaire (no/mild, moderate/severe, and PMDD levels of PMS symptoms). Core psychological measures were assessed on a trait level (habitual characteristic) as well as on a momentary state level (between the two phases of the cycle). We investigated 1) whether there are differences between people with no to mild PMS symptoms, people with PMS, and people with PMDD in terms of depressive symptoms, feelings of anxiety and stress, and rumination on a trait level (i.e., between-groups) and 2) how stress and rumination changes (i.e., state-induced changes) during the premenstrual/luteal phase as compared to the follicular phase (i.e., within-groups). We recruited a large sample in order to test these hypotheses, generating unique insights into these mood-related psychological vulnerabilities in relation to (menstrual-phase specific) PMS.

Methods

Data is made openly availably through Open Science Framework (https://osf.io/j5ynz/) as well as all analysis scripts, software and package usage, and more details concerning the methodology.

Participants

A total of 549 healthy, Dutch-speaking participants (recruited in Belgium and The Netherlands) aged 18 to 45 took part in this study. 169 participants used hormonal contraception methods (123 pill, 10 hormonal coil, 36 other methods such as NuvaRing) and were therefore excluded for the between-group analyses of the **trait** questionnaires resulting in a final sample of 380 participants (*M* age = 33.04, *SD* age = 7.03). Of these participants, 196 (51%) fell within the category of no-mild PMS (called the 'noPMS' group), 138 (36%) fell within the moderate to severe ('PMS) category and 46 (12%) within the PMDD category based on the PSST results. They were comparable in terms of age (*M* = 32.40, 33.78, and 33.13; *SD* = 7.20, 6.68, and 7.30)..

If a participant did not complete all questionnaires at either the follicular or luteal testing moment, they were excluded from the within-subject analysis. Due to a diversity of reasons (e.g. missed moment, the start of hormonal contraceptive, technical limitations), 123 participants were excluded, resulting in a total of 237 participants for the within-participant **state** questionnaire analysis (*M* age = 33.56, *SD* age = 7.15). Of these participants, 128 (54%) fell within the category of no-mild PMS, 74 (31%) fell within the moderate to severe category, and 35 (15%) within the PMDD category. They were comparable in terms of age (*M* = 33.58, 33.86, and 32.83; *SD* = 7.16, 6.89, and 7.67). Full descriptives can be found in the supplemental materials (Appendix C).

Ethics

The study was part of a larger project investigating emotion regulation and arousal processes in the menstruating population. This study was approved by the Medical Ethics Committee of The Ghent University Hospital (reference BC-07212 & BC-07212 E01), all participants gave informed consent before participating, and the study was conducted in accordance with the Declaration of Helsinki Ethical Principles and Good Clinical Practice.

Inclusion Criteria

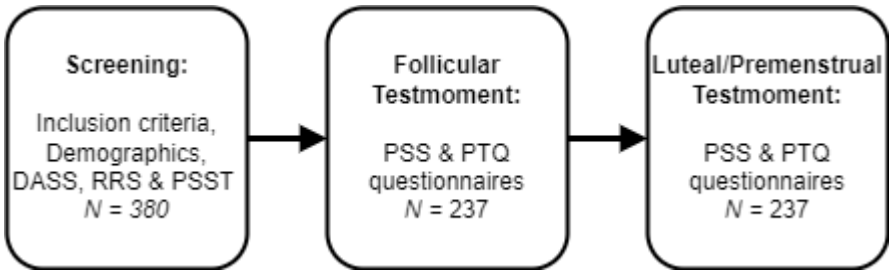
Solely participants that had a regular cycle, meaning consistently between 21 and 35 days (Fehring et al., 2006) and were menstruating at the time of participation were included in the study. This was crucial because the calculation of the two test moments was based on an accurate calculation of the timing of the follicular and premenstrual/luteal phases of the menstrual cycle. Participants who were pregnant, three months post-partum, in or past menopause, breastfeeding or breastfeeding up until six months before testing were excluded to avoid added hormonal fluctuations. In addition, given that hormonal contraception methods are often prescribed to diminish PMS symptoms and their effects on PMS symptoms differ widely (Lundin et al., 2017; Sanders et al., 2001; Simmons et al., 2019), participants who took any form of hormones or hormonal contraceptives were excluded.

Procedure

Participants were recruited through social media, press articles, blogs, and flyers. This was done between June 2020 and September 2021 in the midst of the COVID-19 pandemic. Via a hyperlink on the Ghent Experimental Psychiatry Lab website (www.gheplab.ugent.be), participants were directed to LimeSurvey (Schmitz, 2017) to fill in a screening questionnaire and informed consent. The study was completely executed online.

Figure 1

Flowchart of the study design.



Note. Depression, Anxiety and Stress Scale (DASS), Ruminative Response Scale (RRS), Premenstrual Symptoms Screening Tool (PSST), Perceived Stress Scale (PSS), and Perseverative Thinking Questionnaire (PTQ) at the different test moments.

Screening

After providing informed consent, participants indicated that they met all the inclusion criteria, after which they filled in questions about demographics, questionnaires assessing the Premenstrual Symptoms Screening Tool (PSST), the Depression Anxiety Stress Scale (DASS), and the Ruminative Response Scale (RRS).

Follicular Test Moment

On the estimated first day of a participant's menstruation (based on their self-reported menstrual cycle length and timing of last menstruation), an email was sent. Here, participants were asked only to respond when this date was incorrect, and inform us when their menstruation had started. One day after this first email was sent, participants received an email containing the dates of the two test moments. Participants were asked to indicate whether or not they would be available to fill in the tests at these dates. If not, the procedure would be repeated in the next menstrual cycle.

The email with the link to the first test moment was sent in the middle of the follicular phase. Because the follicular phase is on average 14 days long, this date was calculated as seven days after the start of menstruation.. At both the follicular and premenstrual/luteal test phase participants had to fill in the Perceived Stress Scale (PSS), Perseverative Thinking Questionnaire (PTQ), and the Brief State Rumination Inventory (BSRI). If after 24 hours the test was not filled in, a reminder email was sent which gave the participant an additional 24 hours to fill in the questionnaires. If this time limit was passed, no more reminders were sent and a new confirmation of menstruation would be sent on the first day of the next cycle, restarting the aforementioned procedure.

Premenstrual/Luteal Test Moment

The email with the link to the second test moment was sent in the middle of the premenstrual/luteal phase. The date was calculated by subtracting seven days from the expected start of the next cycle (i.e. first day of current cycle plus participant's cycle length). If the test moment was not filled in by the participant after 24 hours, a reminder email was sent which gave them an additional 48 hours to fill in the questionnaires. If they surpassed this 72-hour time limit, they were excluded, because the participant had already participated in the first (follicular) test moment by then, and prior knowledge and hence bias would exist if we would try again in the next menstrual cycle. The procedures for the premenstrual/luteal and the follicular test moments were exactly the same, with the same questionnaires.

Questionnaires

All questionnaires showed excellent internal consistency (Cronbach's $\alpha > .90$). For more detailed descriptions of the questionnaires, see Appendix G.

Trait Questionnaires

Premenstrual Symptoms Screening Tool (PSST). The Dutch translation of the PSST (Steiner et al., 2003b) was used to assess the severity of PMS symptoms. The PSST allocates people into three groups: a group with no to mild PMS symptoms, here referred to as the 'noPMS' group, a group with moderate to severe PMS symptoms, here referred to as the 'PMS' group, and a group with PMDD levels of PMS symptoms, here the 'PMDD' group.

Depression, Anxiety and Stress Scale (DASS). The DASS (Lovibond & Lovibond, 1995) contains three self-report scales designed to measure negative emotional states of Depression, Anxiety, and Stress. The DASS scale characterizes Depression as a loss of self-esteem and incentive, anhedonia, dysphoria, self-deprecation, and hopelessness. It characterizes Anxiety by autonomic arousal, skeletal musculature effects, situational anxiety, and the subjective experience of anxiety. Lastly, it defines Stress as a state of persistent arousal and tension, and impatience with a low threshold for becoming upset or agitated (Lovibond, 1995).

Ruminative Response Scale (RRS). The RRS (Treynor & Gonzalez, 2003) is a self-report measure for ruminative thoughts and actions for adults. Rumination is defined here as the process of

pervasive thinking about one's emotions or problems without actively problem-solving or changing the circumstances for the better (Nolen-Hoeksema et al., 2008).

State Questionnaires

These questionnaires were collected twice per participant; once during the follicular phase, and once during the premenstrual/luteal phase of the menstrual cycle.

Perceived Stress Scale (PSS). The PSS is a self-report questionnaire about the subjective experience of stress (Cohen et al., 1994). Whereas the original version asked participants to report on these statements over the last month, the current study asked participants to report on these statements over the last week.

Perseverative Thinking Questionnaire (PTQ)[1]. The PTQ (Ehring et al., 2011) is a content-independent measure of repetitive negative thinking in the last week (worry and rumination). The PTQ evaluates the repetitiveness, intrusiveness, difficulty disengaging, perceived unproductiveness, and the capturing of mental resources of Ruminative Negative Thinking (RNT).

Data Analyses

All data was preprocessed and analyzed using R3.9.6 (R Core Team, 2021). To make sure our models were parsimonious, we bottom-up tested if adding certain independent variables to the model improved the model fit. For each dependent variable, we compared models that included and excluded *Age* and *Contraception*. Either factor was only included in the model if it showed to be a significant contributor after comparing models with reducing complexity using $\chi 2$ goodness-of-fit tests within the 'anova()' function. The statistical significance level was set to $p < .05$. *Contraception* as a factor (non-hormonal, copper IUD) showed no significant contributor to any model. Due to some discussion in the literature with regard to the inclusion of women with copper IUD, we also performed an additional analysis whilst excluding these, which can be found in the supplemental materials (Appendix D). We concluded, in accordance with the literature, that there is no effect on our dependent variables for copper

[1] In addition to the PTQ we collected the Brief State Rumination Inventory (BSRI). Considering both measure similar constructs, similar results were expected and observed. Since the PTQ has a better validity, only the PTQ results will be described in the manuscript and the BSRI results are added to supplemental materials (Appendix K)

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IUDs. *Age* showed to be a significant contributor for *trait* dependent variables; *Rumination*, *Anxiety*, and *Stress*, and for the *Stress state* variable. *Age* was therefore added to these models as a fixed effect and was excluded from the other models.

Model factors were then analyzed using ANOVA. The sum of squares was estimated using the 'type III' approach with the 'car' package (Fox & Weisberg, 2019), and the statistical significance level was set to $p < .05$. Follow-up tests with pairwise comparisons of the estimated marginal means (EMMs) were performed with the 'emmeans' package (Searle et al., 1980), using false discovery rate (FDR) to correct for multiple comparisons (Lenth et al., 2021). Lastly, Cohen's *d* was calculated for each test as a measure of internal consistency using the 'lsr' R package.

Trait variables

Analyses were conducted by fitting (generalized) linear models ([G]LMs) for each dependent trait variable. Model selection was done by comparing the Akaike Information Criterion (AIC) for different distributions of the dependent variable (i.e. normal, gamma, inverse-gaussian) (Akaike, 1998). The (G)LMs were fitted with 'lm()' and 'glm()' functions from the 'lme4' R package (Bates et al., 2015). Each [G]LM was defined as *DV* (dependent variable) ~ *PMS* (group; noPMS, PMS, PMDD) and *Age* was added as a fixed effect depending on its priorly determined relevance. Each individual formula will also be defined in the results section.

State variables

Analysis was conducted by fitting linear mixed models (LMMs) for each dependent state variable. No other distributions were used in modeling due to the presence of non-positive values in the dependent variables. Models were fit using the 'lme4' R package (Bates et al., 2015) using the 'lmer' function. Each LMM was defined as *DV* ~ *PMS* (group; noPMS, PMS, PMDD) * *Moment* (follicular, premenstrual/luteal), + *Subject* as a random intercept. Depending on whether it showed a significant contribution, *Age* was also included in the model as a fixed effect. Each dependent variable's individual formula will also be defined in the results section.

Full analysis scripts, detailed software descriptions can be found in the supplemental materials, OSF (https://osf.io/j5ynz/).

Results

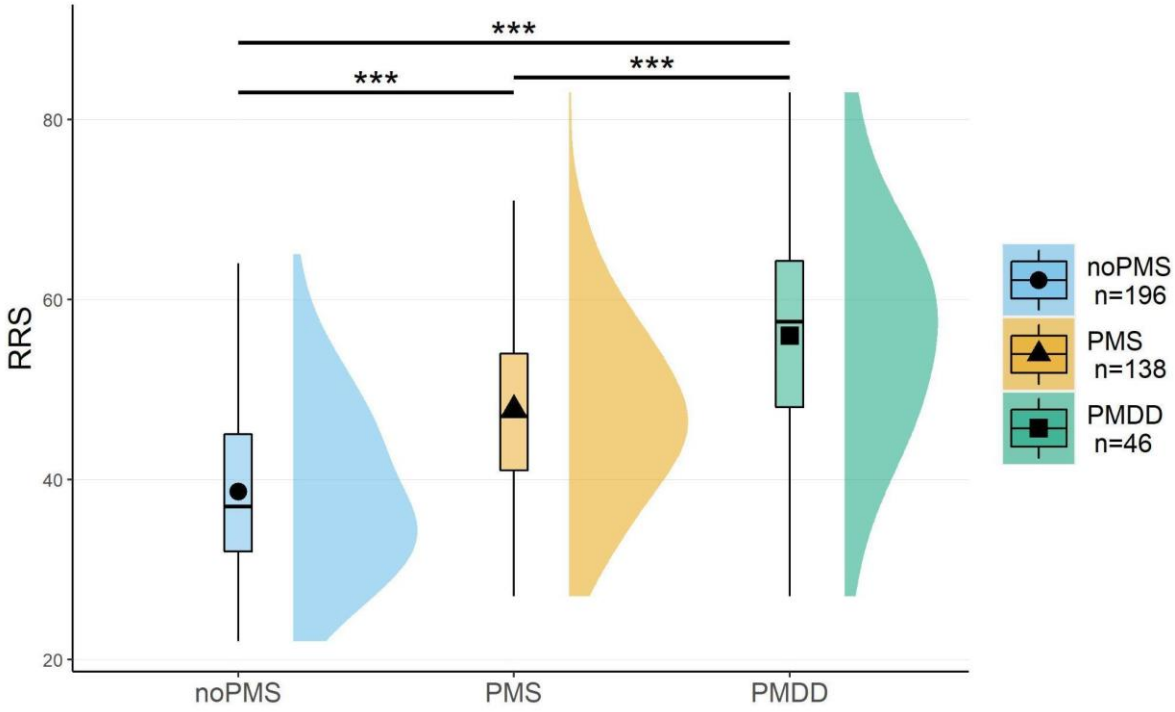
Trait questionnaires

Ruminative Response Scale.

RRS, with formula *RRS ~ PMS + Age*, was best represented by a GLM with Gamma distribution and identity link (AIC = 2789) showing a significant main effect for the PMS group after controlling for age, $\chi 2(2, N = 380) = 145.63$, $p < .001$. Follow-up pairwise comparisons showed significant differences between every group, with PMS having higher RRS values than the noPMS group, $b = 9.30$, $SE = 1.08$, $t = 8.58$, $p < .001$, $d = .93$, 95% CI [0.69, 1.16], PMDD having higher RRS values than the PMS group, $b = 8.01$, $SE = 2.02$, $t = 3.96$, $p < .001$, $d = .80$, 95% CI [0.45, 1.14], and PMDD having higher RRS values than the noPMS group, $b = 17.32$, $SE = 1.92$, $t = 9.04$, $p < .001$, $d = 1.75$, 95% CI [1.39, 2.12], see Figure 2.

Figure 2

Differences in trait rumination levels between the PMS groups.



Note. Estimated marginal means based on the GLM with RRS as outcome measure are represented with black dots. Descriptive data are shown per group (boxplot, density plot) to display underlying distributions. Black horizontal lines display significant contrasts between the different PMS groups with

corresponding significance levels. *** indicates $p < .001$. Abbrev.: GLM, General Linear Model; RRS, Ruminative Response Scale; PMS, Premenstrual Syndrome; PMDD, Premenstrual Dysphoric Disorder.

Depression, Anxiety, Stress Scale.

The DASS Depression subscale, with formula *DASS_Depression ~ PMS*, was best represented by a GLM with an inverse Gaussian distribution and identity link (AIC = 1963) and showed a significant main effect for PMS, $\chi 2(2, N = 380) = 151.59$, $p < .001$. Follow-up pairwise comparisons showed significant differences between every group, with PMS having higher Depression values than the noPMS group, $b = 3.43$, $SE = .38$, $t = 8.97$, $p < .001$, $d = 1.07$, 95% CI [0.83, 1.32], PMDD having higher Depression values than the PMS group, $b = 2.41$, $SE = .81$, $t = 2.99$, $p = .003$, $d = .57$, 95% CI [0.23, 0.91], and PMDD having higher Depression values than the noPMS group, $b = 5.83$, $SE = .76$, $t = 7.72$, $p < .001$, $d = 1.82$, 95% CI [1.45, 2.19], see Figure 3A.

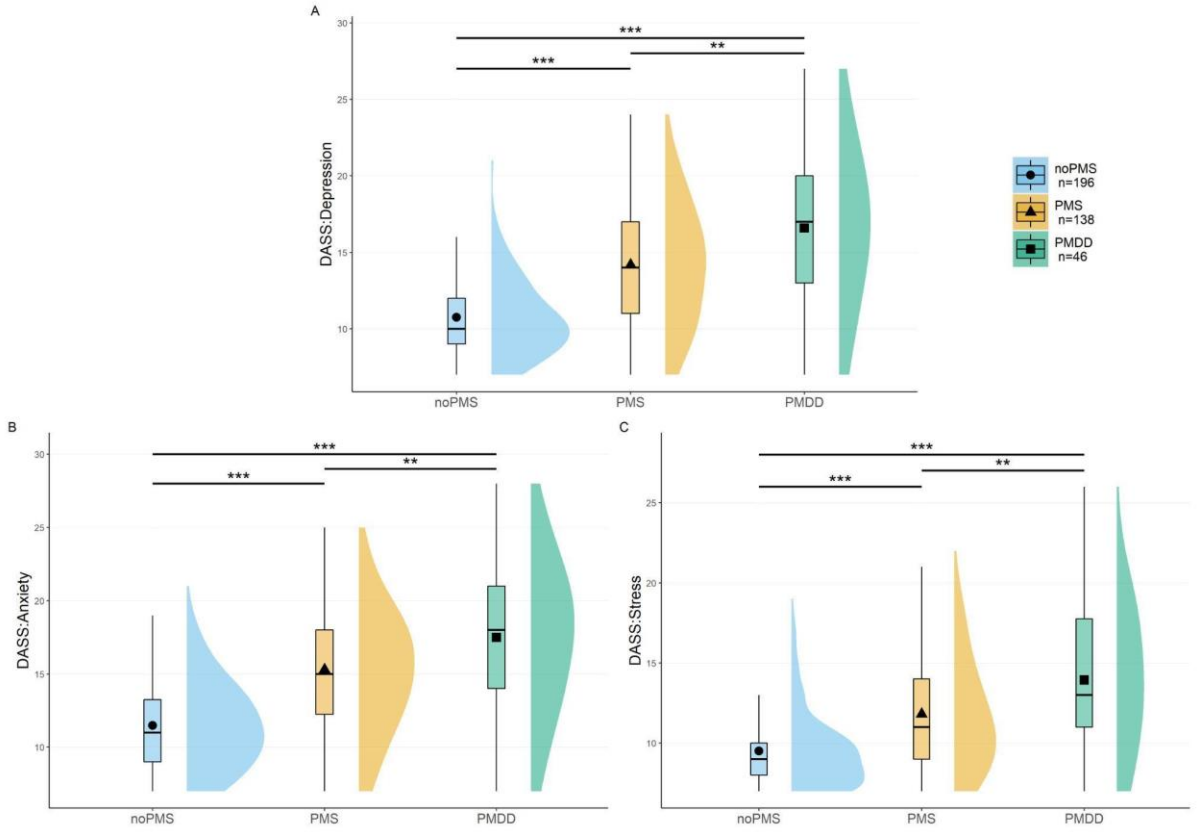
The DASS Anxiety subscale, with formula *DASS_Anxiety ~ PMS + Age*, was best represented by a GLM with a gamma distribution and identity link (AIC = 2041) and showed a significant main effect for the PMS group after controlling for age, $\chi 2(2) = 150.35$, $p < .001$. Follow-up pairwise comparisons showed significant differences between every group, with PMS having higher Anxiety values than the noPMS group, $b = 3.80$, $SE = .40$, $t = 9.41$, $p < .001$, $d = 1.07$, 95% CI [0.83, 1.31], PMDD having higher Anxiety values than the PMS group, $b = 2.21$, $SE = .76$, $t = 2.91$, $p = .004$, $d = .53$, 95% CI [0.19, 0.87], and PMDD having higher Anxiety values than the noPMS group, $b = 6.01$, $SE = .71$, $t = 8.46$, $p < .001$, $d = 1.75$, 95% CI [1.38, 2.11], see Figure 3B.

The DASS Stress subscale, with formula *DASS_Stress ~ PMS + Age*, was best represented by a GLM with an inverse Gaussian distribution and identity link (AIC = 1831) and showed a significant main effect for the PMS group after controlling for age, $\chi 2(2) = 101.08$, $p < .001$. Follow-up pairwise comparisons showed significant differences between every group, with PMS having higher Stress values than the noPMS group, $b = 2.30$, $SE = .33$, $t = 7.00$, $p < .001$, $d = .76$, 95% CI [0.53, 0.99], PMDD having higher Stress values than the PMS group, $b = 2.13$, $SE = .69$, $t = 3.11$, $p = .002$, $d = .60$, 95% CI [0.26, 0.94], and PMDD having higher Stress values than the noPMS group, $b = 4.43$, $SE = .65$,

t = 6.83, p < .001, d = 1.53, 95% CI [1.17, 1.88], see Figure 3C. For a table depicting the statistics see supplemental material (Appendix F).

Figure 3

Differences in DASS Depression (A), Anxiety (B) and Stress (C) scores between the PMS groups.



Note. Estimated marginal means based on the GLM, with each of the subscales of the DASS as outcome measure, are represented with black dots. Descriptive data is shown per group (boxplot, density plot) to display underlying distributions. Black horizontal lines display significant contrasts between the different PMS groups with corresponding significance levels. ** indicates p <.01*** indicates p < .001. Abbrev.: Abbrev.: GLM, General Linear Model; DASS, Depression Anxiety Stress Scale; PMS, Premenstrual Syndrome; PMDD, Premenstrual Dysphoric Disorder.

State Questionnaires

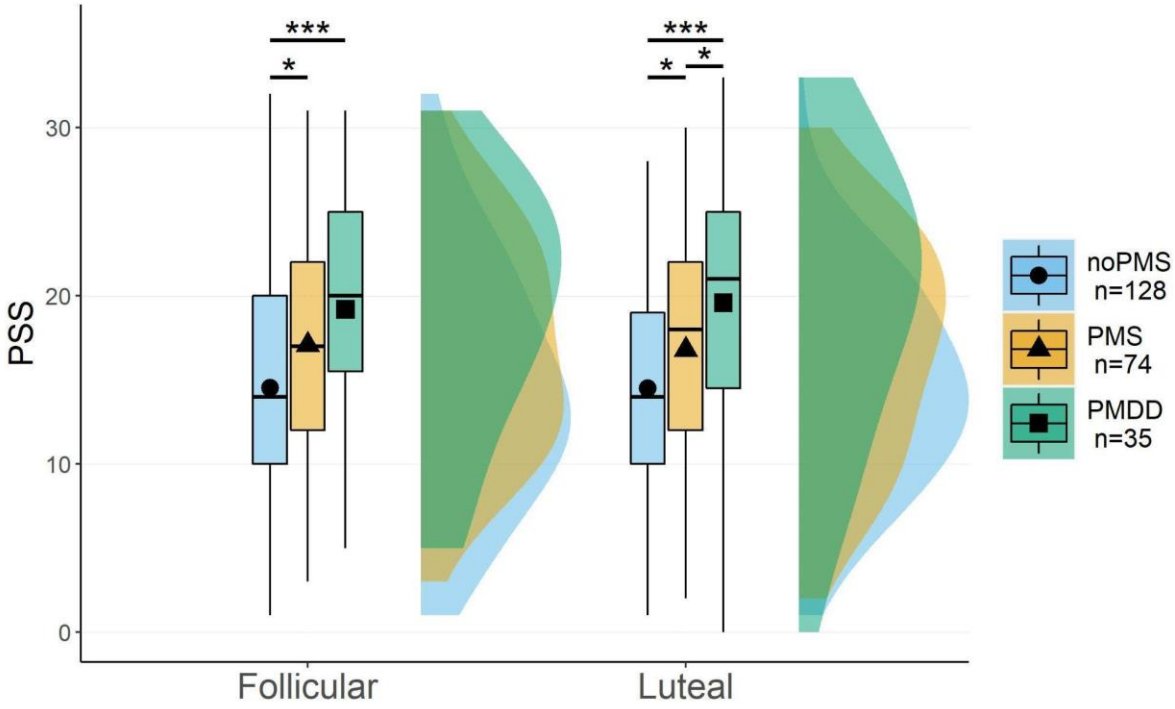
Perceived Stress Scale.

The LMM with formula *PSS ~ PMS * Moment + Age + (1|ID)*, showed that PMS was positively associated with PSS (main effect) after controlling for age, $\chi 2(2, N = 237) = 26.69$, p < .001. No

significant main effect for Moment was found, $\chi 2(1) < .01$, $p = .956$, nor a PMS x Moment interaction $\chi 2(2) = .17$, $p = .919$. Despite the lack of a significant interaction effect, due to specifically described prior hypotheses, follow-up pairwise comparisons of the EMMs are executed to better understand the results. These analyses were executed both at the group level (noPMS vs PMS vs PMDD) and moment level (follicular vs premenstrual/luteal per group). At the follicular test moment, PMS had higher PSS values than the noPMS group, $b = 2.55$, $SE = .98$, $t = 2.61$, $p = .014$, $d = .37$, 95% CI [0.08, 0.66], and PMDD had higher PSS values than the noPMS group, $b = 4.66$, $SE = 1.27$, $t = 3.66$, $p < .001$, $d = .67$, 95% CI [0.29, 1.06], but PMDD did not have higher PSS values than the PMS group, $b = 2.11$, $SE = 1.37$, $t = 1.54$, $p = .124$, $d = .32$, 95% CI [-0.07, 0.74]. At the premenstrual/luteal test moment, PMS had higher PSS values than the noPMS group, $b = 2.28$, $SE = .98$, $t = 2.34$, $p = .030$, $d = .36$, 95% CI [0.07, 0.65], PMDD had higher PSS values than the noPMS group, $b = 5.08$, $SE = 1.27$, $t = 3.99$, $p < .001$, $d = .79$, 95% CI [0.4, 1.18], and PMDD had higher PSS values than the PMS group, $b = 2.80$, $SE = 1.37$, $t = 2.04$, $p = .042$, $d = .41$, 95% CI [0, 0.82]. For a table see Appendix F. No significant effects were found for moment (follicular vs premenstrual/luteal) tested within each group: noPMS; $b = .02$, $SE = .72$, $t = .02$, $p = .983$, $d < .01$, 95% CI [-0.25, 0.24], PMS; $b = .28$, $SE = .95$, $t = .3$, $p = .765$, $d = -.04$, 95% CI [-0.37, 0.28], PMDD; $b = .40$, $SE = 1.38$, $t = .29$, $p = .772$, $d = .05$, 95% CI [-0.42, 0.52].

Figure 4

Differences in stress between the PMS groups at the two test moments.



Note. Estimated marginal means based on the LMM with PSS at the outcome measure are represented with black dots. Descriptive data is shown per group (boxplot, density plot) to display underlying distributions. Black horizontal lines display significant contrasts between the different PMS groups with corresponding significance levels. * indicates $p < .05$, *** indicates $p < .001$. Abbrev.: LMM, Linear Mixed Model; PSS, Perceived Stress Scale; PMS, Premenstrual Syndrome; PMDD, Premenstrual Dysphoric Disorder.

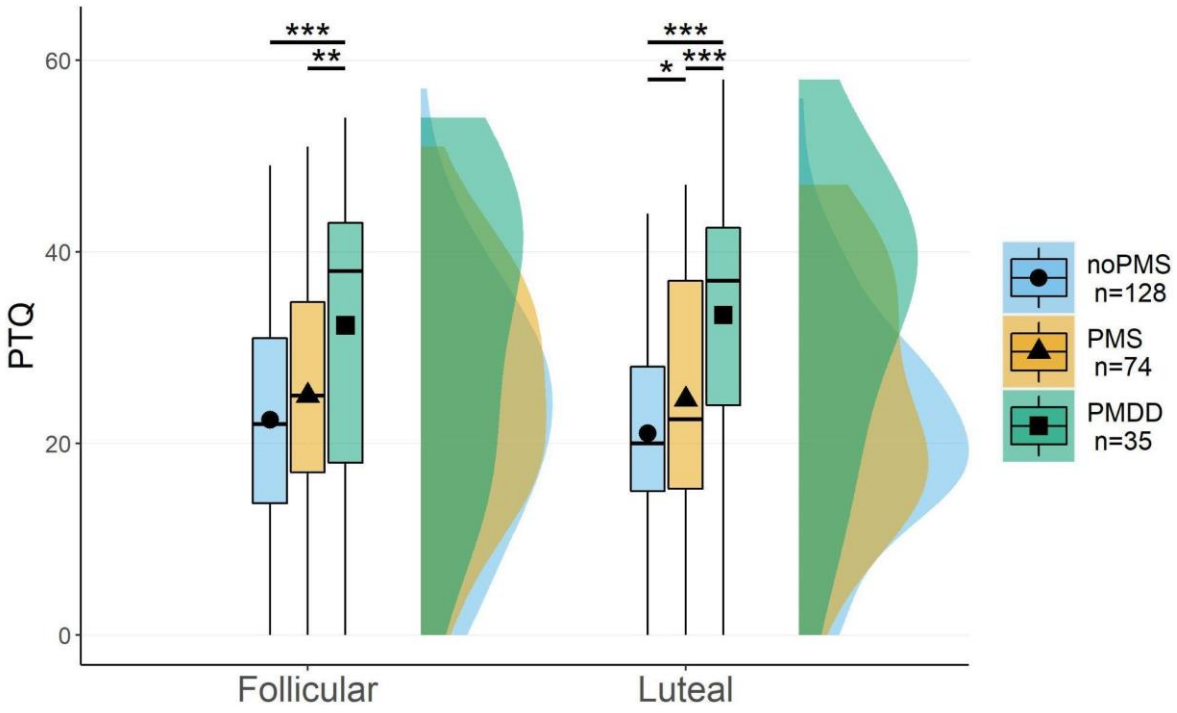
Perseverative Thinking Questionnaire.

The LMM, formula *PTQ ~ PMS * Moment + (1|ID)*, showed that PMS was positively associated with PTQ, $\chi 2(2, N = 237) = 31.71$, $p < .001$. No significant main effect for Moment was found, $\chi 2(1) = .06$, $p = .809$, nor a PMS x Moment interaction $\chi 2(2) = 1.06$, $p = .590$. Despite the lack of a significant interaction effect, due to specifically described prior hypotheses, follow-up pairwise comparisons of the EMMs are executed both at the group level (noPMS vs PMS vs PMDD) and moment level (follicular vs premenstrual/luteal per group). At the follicular test moment, PMS did not have higher PTQ values than the noPMS group, $b = 2.51$, $SE = 1.80$, $t = 1.40$, $p = .163$, $d = .21$, 95% CI [-0.08, 0.49], PMDD had higher PTQ values than the PMS group, $b = 7.34$, $SE = 2.53$, $t = 2.91$, $p = .006$, $d = .57$, 95% CI [0.16, 0.98], and PMDD had higher PTQ values than the noPMS group, $b = 9.85$, $SE = 2.35$, $t = 4.20$,

$p < .001$, $d = .76$, 95% CI [0.38, 1.15]. At the premenstrual/luteal test moment, PMS had higher PTQ values than the noPMS group, $b = 3.56$, $SE = 1.80$, $t = 1.98$, $p = .049$, $d = .31$, 95% CI [0.02, 0.6], PMDD had higher PTQ values than the PMS group, $b = 8.81$, $SE = 2.53$, $t = 3.49$, $p < .001$, $d = .68$, 95% CI [0.27, 1.1], and PMDD had higher PTQ values than the noPMS group, $b = 12.36$, $SE = 2.35$, $t = 5.26$, $p < .001$, $d = 1.05$, 95% CI [0.65, 1.44]. For a table see Appendix F. No significant effects were found for moment (follicular vs premenstrual/luteal), noPMS; $b = 1.42$, $SE = 1.17$, $t = 1.21$, $p = .226$, $d = .-12$, 95% CI [-0.37, 0.12], PMS; $b = .38$, $SE = 1.54$, $t = .25$, $p = .806$, $d = -.03$, 95% CI [-0.35, 0.29], PMDD; $b = 1.086$, $SE = 2.24$, $t = .484$, $p = .629$, $d = .07$, 95% CI [-0.39, 0.54], see Figure 5.

Figure 5

Differences in stress-related perseverative thinking between the PMS groups at the two test moments.



Note. Estimated marginal means based on the LMM with PTQ as the outcome measure are represented with black dots. Descriptive data is shown per group (boxplot, density plot) to display underlying distributions. Black horizontal lines display significant contrasts between the different PMS groups with corresponding significance levels. * indicates $p < .05$, *** indicates $p < .001$. Abbrev.: LMM, Linear Mixed Model; PTQ, Perseverative Thinking Questionnaire; PMS, Premenstrual Syndrome; PMDD; Premenstrual Dysphoric Disorder.

Discussion

Since the inclusion of PMDD in the DSM-5 as a mood disorder, premenstrual symptoms have gained increasing attention. We compared core psychological measures relevant to mood disorders between different levels of PMS symptoms (no/mild, moderate/severe, PMDD) as measured by the Premenstrual Symptoms Screening Tool (PSST). Core measures of mood disorders were assessed at the trait level for 380 participants, measuring habitual feelings of depression, anxiety, stress (using the Depression, Anxiety and Stress Scale; DASS), and recurring ruminative thinking (using the Ruminative Response Scale; RRS). Of these participants, 237 also reported their perceived momentary (state) stress (using the Perceived Stress Scale; PSS) and repetitive negative stress-related thoughts (using the Perseverative Thinking Questionnaire; PTQ) at two points during (the two phases of) the menstrual cycle.

First, we consistently found increased habitual tendencies to ruminate while being in a sad mood, as well as higher trait measures of depression, anxiety, and stress with increased premenstrual symptoms, thus confirming our first hypotheses. Secondly, we found that momentary stress and perseverative stress-related thinking were consistently higher (at both the follicular and premenstrual/luteal test moment) with increased premenstrual symptoms. Some exceptions were found at the follicular test moment, where participants with PMDD level symptoms did not report higher perceived stress scores than the group with moderate/severe PMS symptoms, and the group with moderate/severe PMs symptoms did not report higher levels of momentary perseverative thinking than the group with no/mild PMS symptoms. The latter result hints at a clear distinction in PTQ for PMDD levels of PMS, whereas the differences between PMS and noPMS are less pronounced. This is especially clinically relevant, as this clear distinction in high PTQ scores for PMDD participants could be relevant in early interventions for the development of PMDD or in the development of other affective disorders in addition to PMDD, with perseverative thinking being a common vulnerability factor. Despite observing differences between the groups at each individual moment, we did not find evidence that perceived stress or stress-related perseverative thinking was higher in the premenstrual/luteal phase compared to the follicular phase, nor an interaction effect between test moment and PMS group. This

was unexpected because PMS is characterized by its periodic increase in various symptoms during the premenstrual/luteal phase.

The categorization of no/mild, moderate/severe, and PMDD levels of PMS symptoms was based on a questionnaire (the PSST) of self-reported higher physical, emotional, and behavioral PMS symptoms during the premenstrual/luteal phase. Despite the PSST containing several psychological symptoms, stress and rumination are not identified as core symptoms of PMS. Yet, our results indicate consistent differences between groups with no/mild, moderate/severe, and PMDD levels of PMS symptoms, despite no differences between the menstrual phases.

Our findings confirm past findings that individuals reporting PMS experience more stress in general (Gollenberg et al., 2010) as well as a continuous abnormality in emotional state, anxiety, and stress reactivity, irrespective of the menstrual cycle (Landén & Eriksson, 2003; Liu et al., 2017). This has also been observed in different cortisol levels among people with low, mild, and severe levels of premenstrual symptoms during the premenstrual/luteal phase (Cahill, 1998). Prolonged stress is one of the biggest causing factors of depression and other affective disorders (Bale, 2006; Yang et al., 2015), which might also explain the large and significant differences in depression and anxiety scores between the three groups. Moreover, stress exposure has been shown to be a risk factor for PMDD and PMS (Hantsoo & Epperson, 2015; Potter et al., 2009). The act of rumination, according to the response styles theory (Nolen-Hoeksema, 1991), can increase the effect of mood on cognitive processing, leading one to stay focused on negative thoughts and memories and using them to interpret new events. Rumination is thus an important factor in the development of mood disorders (Apazoglou et al., 2019; Kovács et al., 2020). Based on retrospective and prospective studies, rumination seems to act as a partial mediator, along with sensitivity to anxiety, that contributes to the onset of PMS symptoms (Craner et al., 2014; Graham et al., 2018) and acts as a moderator of the association between the menstrual cycle and mood variables such as irritability and mood deterioration towards the end of the cycle (Sigmon et al., 2009; Welz et al., 2016). This leaves the question: why and how are these core psychological mechanisms associated with the severity of PMS? Hormonal fluctuations might be important to consider in this context.

People with PMS seem to have an increased sensitivity to hormonal fluctuations (Cunningham et al., 2009) as well as to anxiety and depressive symptoms. The premenstrual/luteal phase is characterized by the rise of progesterone (see Appendix A) (Hawkins & Matzuk, 2008). People with PMS seem to have an increased psychological sensitivity to these hormonal fluctuations (Cunningham et al., 2009). There is evidence for the role of hormonal fluctuations triggering depressive symptoms in some women via its effects on the serotonergic system (Payne, 2003). Past research has also shown an association between progesterone and amygdala-hippocampal complex -which plays a central role in anxiety responses to stressful situations- activation (Chung et al., 2016; Lisofsky et al., 2015). Anxiety proneness and progesterone levels have been shown to modulate menstrual cycle-related amygdala reactivity in PMDD patients, who already have a higher amygdala activity in general (Gingnell et al., 2012; Lin et al., 2013). However, patients with PMS cannot be distinguished by hormone levels alone (De Munck et al., 2008), so it might be that people with PMS have a certain (psychological) *sensitivity* to both anxiety and normal progesterone fluctuations, with the latter mediating these adverse effects on anxiety and mood (Nillni et al., 2011; van Wingen et al., 2008). Because of the earlier discussed findings that stress and rumination are mediators to anxiety and depressive symptoms and contributors to the onset of PMS, it seems that stress and rumination play into or are the result of an underlying vulnerability. Modulating stress and rumination, for example through mindfulness-based cognitive training, might be an effective approach for future PMS interventions, as they have already shown to be effective in the treatment of mood disorders such as depression (Kerr et al., 2013). In addition, cognitive bias modification could yield promising results, considering the shared vulnerability factors with depression and anxiety (Jones & Sharpe, 2017; Vrijsen et al, 2018). Therefore, we would advise checking for PMS symptoms in clinical practice, especially in sub-clinical settings, because it might help in the prevention of developing psychopathologies by better understanding the complex interplays at work. Moreover, future research should take childhood adversities into account whilst studying PMS. Recent research has shown that women who report childhood adversities (specifically childhood physical and emotional abuse) are 1.5 times more likely to experience PMS (Ito et al., 2021). In the context of the current study, a potential co-occurrence of childhood adversity and PMS could be

responsible for part of our observed effects on stress, rumination, and depressive symptoms (Kim et al., 2017). Moreover, in the context of our described trait measures, it should be noted that there could be an effect of 'state response consistency' on the observed effects (Bagby et al., 2004). Yet, if a certain state-specific effect is present, it would most probable diminish rather than increase any effects of level of PMS symptoms.

The question remains why we couldn't find higher levels of stress and rumination in the premenstrual/luteal phase compared to the follicular phase. These constructs might be stable throughout the cycle, or it might be due to the setup of this study. Both our test moments were conducted in the (estimated) middle of the corresponding menstrual phase. However, with regard to the premenstrual/luteal phase, PMS symptoms are typically at their worst right before menstruation (Cornforth, 2021), which is a few days later. In addition, both state questionnaires consider how participants felt *in the last seven days* rather than at that exact moment. Considering what the menstrual cycle looks like, these past seven days at the test moment would 1) generally not test the moment of the menstrual cycle when premenstrual symptoms would be most pronounced and 2) could include up to the ovulation as well, depending on the participant's luteal phase length, further inducing noise in this testing moment, which is reflected in the small effect sizes for the differences between the two phases (Cohen's d = < .15). For this reason, we should not exclude the possibility that stress and stress-related perseverative thinking might fluctuate in a systematic way throughout the cycle. Future research should try to reduce noise by measurement tools with a higher temporal resolution, to more accurately determine the phases of the cycle, such as symptom diaries (Labots-Vogelesang et al., 2021; Zendell, 2000).

Conclusion

Participants with increased premenstrual syndrome (PMS) symptoms scored higher on several measures of mood disorder vulnerability-related concepts such as stress, rumination, anxiety, and depressive symptoms. Our results further demonstrate the burden of PMS, which is in the same category as some major recognized disorders (Halbreich, 2003). This study found that the more severe PMS symptoms are, the higher the scores on trait measures of anxiety, depressive symptoms, stress,

and rumination as well as momentary stress and stress-related perseverative thinking. Stress and rumination seem to play a role in the vulnerability that people with PMS have to hormonal fluctuations, anxiety, and depressive symptoms. Because of the clear differences in trait measures between people with different levels of PMS symptom severity, future research should take into account the role of core psychological vulnerabilities when studying PMS interventions.

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