Associations between fluctuations in premenstrual symptoms and vagally mediated heart rate variability in daily assessments throughout the menstrual cycle: a feasibility study

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November 15, 2023

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Running head: Heart Rate Variability and premenstrual symptoms

Keywords: heart rate variability, vagal tone, premenstrual syndrome, premenstrual symptoms, menstrual cycle, ambulatory assessment

Abstract

Introduction

Premenstrual syndrome (PMS) affects up to 90% of individuals with an active menstrual cycle. Several studies have observed reduced vagally mediated heart rate variability in a single assessment during the luteal phase compared to an assessment during the follicular phase, especially in participants experiencing strong PMS symptoms. The aim of this investigation was to initially assess the relationship between premenstrual symptoms and vagally mediated heart rate variability throughout the menstrual cycle, as well as to examine the feasibility of conducting a large-scale study to verify this association.

Methods

Three participants completed daily ambulatory assessments of resting vagally mediated heart rate variability using mobile electrocardiographs and typical PMS symptoms. We calculated correlations between these measurements for each participant.

Results

PMS symptoms and vagally mediated heart rate variability showed medium to high correlations in each of the participants throughout the cycle. These associations were primarily driven by the relationship between vagally mediated heart rate variability and psychological symptoms rather than physiological symptoms. Visual inspection of the fluctuations confirmed the concurrent occurrence of a phasic reduction in vagally mediated heart rate variability parallel to the increases in PMS symptoms experienced during the mid to late luteal phase in each participant.

Discussion

The results support the notion of an association between PMS symptoms and vagally mediated heart rate variability. An ambulatory daily assessment paradigm proves to be feasible. Studies with larger samples are necessary to provide deeper insights into inter- and intra-individual differences as well as stronger knowledge on the mechanistic pathways of PMS.

1 Introduction

Premenstrual syndrome (PMS) encompasses a heterogeneous collection of symptoms that typically manifest in the week preceding menstruation, during the luteal phase of the menstrual cycle, and dissipate within a few days after menstruation begins. These symptoms can be of a physiological nature, such as bloating and water retention, or psychological, including feelings of stress, anxiety, or irritability. It is noteworthy that as many as 90% of menstruating individuals regularly experience at least one symptom associated with PMS (Tschudin et al., 2010).

The etiology of PMS remains unclear. A common hypothesis is that varying sensitivities to fluctuations in gonadal hormones throughout the menstrual cycle play a role (Rapkin & Akopians, 2012). This differential sensitivity may involve several systems, including the Gamma-Aminobutyric Acid (GABA) and serotonin systems (Nappi et al., 2022; Rapkin & Akopians, 2012). Vagally mediated heart rate variability (vmHRV) serves as a potential physiological marker that could contribute to our understanding of PMS. VmHRV is regarded as a marker for cardiac vagal control (Laborde et al., 2023), and research has linked it to a wide range of psychopathological states (Heiss et al., 2021) and cognitive outcomes (Holzman & Bridgett, 2017; Zahn et al., 2016). The associations are so consistent, that Beauchaine and Thayer (2015) have proposed vmHRV as a transdiagnostic biomarker for psychopathology.

In a meta-analysis conducted by Schmalenberger et al. (2019), consistent reductions in vmHRV of medium effect size were identified during the luteal phase when compared to measurements during the follicular phase. A limited number of studies, however, have explored the relationship between this vmHRV reduction and PMS.

The fluctuations in vmHRV are found to be moderated by the extend of premenstrual symptomatology (Schmalenberger et al., 2023) . The observed effect indicates that high PMS groups experience more substantial reductions in vmHRV during the luteal phase, whereas control groups show either smaller fluctuations (Zambotti et al., 2013) or no discernible difference (Baker et al., 2008; Matsumoto et al., 2007) in vmHRV between the follicular and luteal phases.

The consistent direction of the association between vmHRV and PMS is noteworthy, but it is important to acknowledge that all previous studies on this topic have involved only a single measurement during each cycle phase. Consequently, it is challenging to ascertain whether symptoms and vmHRV fluctuate in parallel

throughout the menstrual cycle. In an effort to shed more light on the relationship between vmHRV and PMS and to assess feasibility, we therefore initiated a pilot diary study involving three participants. This study aimed to gather daily assessments of premenstrual symptoms alongside measurements of resting vmHRV to follow the course of their association.

2 Methods and Materials

2.1 Participants

We tested three participants of different ages ($age_{participant\ 1} = 44$, $age_{participant\ 2} = 27$, $age_{participant\ 3} = 20$) who were recruited within our department. These participants provided informed consent and received either course credit or no compensation for their participation. In line with the guidelines suggested by Laborde et al. (2017), the participants did not take medication that could affect vmHRV, had no chronic diseases, and were not pregnant.

2.2 Testing protocol

Each participant received an introduction on how to use the mobile electrocardiography (ECG) device and a document with written instructions outlining the procedure. Measurements were taken each day at the same time, between 7 and 8 pm. The participants began by completing an online questionnaire assessing premenstrual symptoms, recording their last menstrual period, and responding to a number of control variables. Following the questionnaire, the ECG measurement was conducted. Participants attached the ECG device to their chest, set a timer for 6 minutes, initiated the ECG recording, and closed their eyes while the resting vmHRV measurement was taken. This measurement was performed with participants in a sitting position.

Participants were requested to complete the assessments daily over 1.5 menstrual cycles to ensure the inclusion of one complete cycle. We employed the backward- and forward-counting method to assess the cycle phase (Schmalenberger et al., 2021). We included two weeks before a reported menstruation onset (luteal phase) and two to three weeks (depending on reported average cycle length) after a reported menstruation onset (follicular phase) for the analysis.

2.3 Heart rate variability

Vagally mediated heart rate variability was assessed using a mobile 1-channel ECG device, the Bittium Faros 180. The device electrodes were attached to the chest, and data were collected at a sampling rate of 1000 Hz. Data preprocessing was performed using the Faros Software, which generated R-R interval and R peak timestamp series. The first and last 30 seconds of each measurement were removed, resulting in a 5-minute interval, to avoid artifacts caused by participant movement, as participants initiated and concluded the measurement themselves.

The root mean square of successive differences (RMSSD) was derived from the time series as measurement of vmHRV. The time series were analyzed in R (version 4.2.2) using the RHRV package (https://rhrv.r-forge.r-project.org/), following the package documentation. We chose this measurement over the high-frequency component of power spectral analysis due to its robustness to breathing rate and its clearer indication of parasympathetic activity (Chapleau & Sabharwal, 2011).

2.4 Premenstrual symptoms

Premenstrual symptoms were assessed with the German version of the shortened Premenstrual Assessment Form (PAF20) (Allen et al., 1991; Blaser et al., 2023). The questionnaire comprises the 20 most endorsed items from the long form PAF, which includes nearly 100 items in total. Each item represents a specific symptom, and participants are asked to rate how strongly they experienced each symptom during the last premenstrual phase using a 6-point Likert scale, ranging from "not at all/no change from normal" to "extreme change from normal". The German version of this questionnaire has demonstrated good validity and reliability and loads onto two distinct factors, creating psychological and physiological symptom scales. For this study, we adapted the questionnaire to a diary format, where participants reported how strongly they experienced each symptom in the previous 24 hours.

2.5 Control variables

The daily online questionnaire included several control variables that are known to influence vmHRV or PMS. Participants were asked to provide retrospective assessments of these variables for the last 24 hours. The control variables encompassed substance intake (alcohol, caffeine, nicotine), a one-item rating of the level of stress experienced that day on a Likert scale ranging from 1 to 9, a one-item rating of sleep quality on a 1-9 Likert scale, and reports of any physical health symptoms related to acute diseases, such as respiratory symptoms.

2.6 Analysis

All statistical analyses were conducted with R (version 4.2.2). To assess the association between premenstrual symptoms and RMSSD over the menstrual cycle, we conducted Pearson correlations between the two measurements for each participant individually. Furthermore, separate correlations were calculated for the physiological and the psychological subscale of the PAF20 with the RMSSD.

To test the association between PAF20 and RMSSD for all three participants, independently of the control variables, we conducted a linear mixed model predicting PAF20 sum scores. Participant intercepts were modeled as random effects to account for nesting of the data. The RMSSD and control variables were introduced as fixed effects.

3 Results

The RMSSD values were subjected to a log transformation to approximate a normal distribution, aligning with the conventions of other vmHRV research (Laborde et al., 2017). A visual representation of the symptom course and RMSSD for each of the three participants is presented in Figure 1. Pearson correlations between log-transformed RMSSD and daily symptom scores were moderate to high, $r_{participant1}(25) = -.41$, $p < .05$, $r_{participant\ 2}(35) = -.48$, $p < .01$, $r_{participant\ 3}(29) = -.43$, $p < .05$. The correlations were consistently higher in the psychological subscale than the physiological subscale (see Table 1). The associations between RMSSD and physiological symptoms were not significant in all three participants.

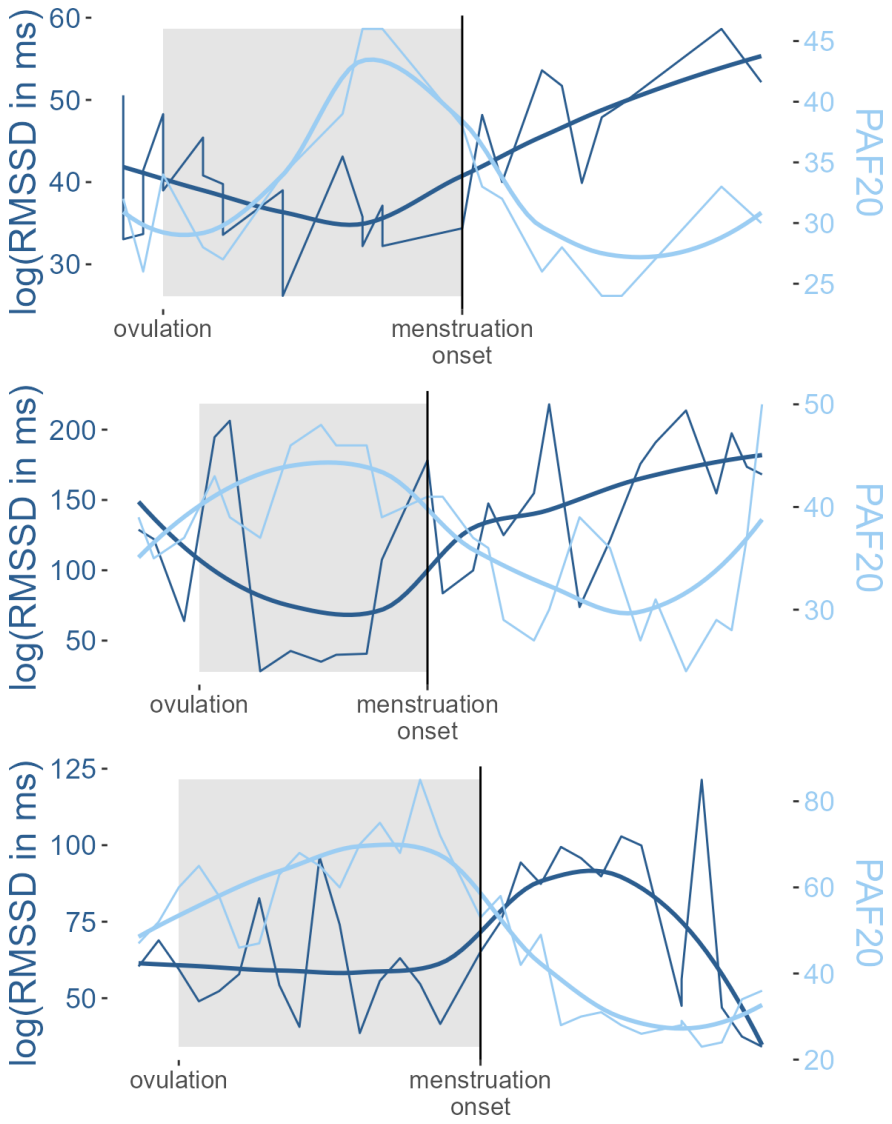
Table 1. Pearson correlations of vagally mediated heart rate variability and premenstrual symptom scores

	Psychological	*symptoms*		*Physiological*	*symptoms*	
	r	**df**	**p**	**r**	**df**	**p**
Participant 1	-.50	25	**.008**	-.25	25	.21

log(RMSSD)	Participant 2	-.57	35	**<.001**	-.07	35	.68
	Participant 3	-.46	29	**.010**	-.31	29	.093

Notes. The symptom scores are the sum scores of the psychological and physiological subscale of the daily ratings of the short form of the premenstrual assessment form (PAF20). RMSSD – root mean square of successive differences; df – degrees of freedom.

Figure 1. Course of vagally mediated heart rate variability and premenstrual symptoms over a menstrual cycle



Note. The plots show the covarying vagally mediated heart rate variability and premenstrual symptom scores over one cycle for participants 1-3 (top to bottom). Grey shaded area indicates the luteal phase, which is marked by increases in symptoms and decreases in vagally mediated heart rate variability. The thin lines show the raw values, while the thicker lines indicate trend lines using the LOESS (locally estimated

scatterplot smoothing) method. RMSSD – root mean square of successive differences, PAF20 – sum score of short form of the premenstrual assessment form.

For the control variables, stress ratings were log-transformed to approximate a normal distribution. Nicotine usage was not included due to the absence of variance. Sport and alcohol consumption were both recategorized as factors with three levels (sport: no sport, <60 min, >60 min; alcohol: no consumption, one drink, >one drink).

The results of the linear mixed model predicting PAF sum scores are presented in Table 2. After introducing all control variables, RMSSD remained a significant predictor of premenstrual symptoms with a standardized regression weight of -0.28.

Table 2. Results of linear mixed model predicating premenstrual symptoms.

	PAF sum score
Predictors	*β*
(Intercept)	0.05
sleep	0.10
stress	0.46
caffein	0.13
alcohol [one drink]	-0.35
alcohol [more drinks]	-0.77
sport [1-60min]	0.38
sport [<60min]	-0.40
log(RMSSD)	-0.28
Random Effects	
σ^2	0.47
$\tau_{00\ vpn}$	0.61
ICC	0.57
$N_{\ vpn}$	3
Observations	95
Marginal R^2 / Conditional R^2	0.288 / 0.693

Note. Participant intercepts were introduced as random effects. Bold p-values indicate significant predictors. PAF – premenstrual assessment form short version; RMSSD – root mean square of successive differences.

4 Discussion

In this pilot study, our aim was to gain a better understanding of the co-occurrence of premenstrual symptoms and vmHRV reductions during the luteal phase of the menstrual cycle and to assess feasibility of daily ambulant assessments. Through daily measurements of vmHRV and premenstrual symptoms in three participants, we discovered parallel fluctuations of PMS symptoms and vmHRV over one menstrual cycle. The PMS symptoms and vmHRV were negatively correlated, with medium to high associations, indicating that the characteristic peak of premenstrual symptoms a few days before menstruation onset is accompanied by a dip in vmHRV.

These findings highlight and support the notion of vmHRV being involved in PMS, which is consistent with

previous research (Baker et al., 2008; Matsumoto et al., 2007; Schmalenberger et al., 2023; Zambotti et al., 2013) . Importantly, the association between vmHRV and PMS was primarily driven by the psychological symptoms in the PMS questionnaire. The sum score of the physiological symptom scale did not show significant associations with vmHRV in any of the participants. This finding aligns with previous research that consistently associates vmHRV with psychopathological outcomes (Beauchaine & Thayer, 2015). VmHRV has, therefore, been suggested as a peripheral indicator for top-down regulation responsible for flexible attention allocation and inhibiting stress responses to internal and external stimuli (Thayer & Lane, 2000). Decreases in vmHRV, indicative of decreases in this capacity, may have a mediating role by increasing negative affect and stress in response to physiological changes during the luteal phase.

The association between vmHRV and PMS symptoms remains consistent when controlling for variables known to influence PMS. The results also confirm the established association between PMS symptomatology and stress (e.g., Lee & Im, 2016).

The results provide a first exploration of the cyclic changes of vmHRV and symptoms faced during a menstrual cycle in every-day life using daily ambulatory assessment. The findings suggest that conducting an extensive study on this relationship could yield crucial insights into the mechanisms underlying the course of premenstrual symptoms. Such a study appears not only feasible with the current technical resources but also has the potential to open up new approaches for PMS treatment through the regulation of vmHRV.

Acknowledgements

The first author was partly supported by a PhD scholarship from the University of Potsdam (Potsdam Graduate School) with fundings from the Graduate Fund of the State of Brandenburg (Germany).

During the preparation of this work, the first author utilized ChatGPT 3.5 to enhance the text's readability. Prompts used were aimed at tasks such as "check grammar and spelling in this paragraph." After employing this tool/service, the author reviewed and edited the content as necessary and assumes full responsibility for the publication's content.

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