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Does Premenstrual Syndrome induce changes in the Autonomic Nervous System?

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Abstract

Premenstrual syndrome (PMS) is a collection of physical and emotional symptoms related to a woman's menstrual cycle. This study aims to see if PMS influences ANS (Autonomic Nervous System) function, central integrative mechanisms (cognitive and motor), and mental functioning strongly enough to provide a reliable evaluation of the presence and severity of PMS, along with the extent of the body changes that correlate with PMS symptoms. Vital signs of thirty female students were measured during both follicular and luteal phases, and results are documented. Premenstrual symptoms are sometimes experienced in females, showing physical, behavioral, and emotional signs. Although no pathological changes were found, physical, behavioral, and emotional changes were found. Most women of childbearing age experience a regular recurrence of various symptoms in the late luteal phase of their menstrual cycle. Regardless of the presence of the PMS, subjects had changes in the ANS before and after their menstruation cycle. Therefore, the study proves that the association between PMS and alterations to the ANS is weak.

Keywords: Premenstrual syndrome; luteal phase; follicular phase; etc

Abbreviations

PMS = Premenstrual Syndrome.
ANS: Autonomic Nervous System.
DBP = Diastolic Blood Pressure.
SBP = Systolic Blood Pressure.
HR: Heart Rate.
BPM: Beats per Minute.
BP = Blood Pressure.
EKG: Electrocardiogram.
ANOVA: Analysis of Variance.
SPSS 11: Statistical Package for the Social Sciences.

Supportive Tools Used

Premenstrual calendar.
Daily Rating Scale.
Zung Anxiety Scale.
Beck Depression Scale.

Introduction

Premenstrual syndrome (PMS) is a collection of physical and emotional symptoms related to a woman's menstrual cycle. While most women of childbearing age (up to 85%) report having experienced more than 200 physical, behavioral, and emotional symptoms related to normal ovulatory function, PMS is defined as a consistent pattern of emotional and physical symptoms. These symptoms usually occur only during the Luteal Phase of the menstrual cycle (5-11 days before their menstruation) and are of "sufficient severity to interfere with some aspects of life," happening in only about 5-10% of women [1]. Therefore, some level of discomfort is expected during this "vulnerable period," but only a few women will have symptoms that reach the level of PMS (12.6% to 31%) [2]. For this research purpose, PMS will be defined according to the Diagnostic Criteria for Premenstrual syndrome outlined by the American College of Obstetricians and Gynecologists and the International Classification of Diseases, Tenth Revision (ICD-10). Almost all symptoms are associated with ovulatory body changes, for example, temperature, weight, and edema. The studies so far are not conclusive about whether premenstrual syndrome is a psychological or a hormonal condition. The authors claim that PMS manifests similarly to mental disorders in some subsets of women with particularly severe PMS symptoms (verbal abuse, violence, extreme irritability, anxiety, and depression) because the woman lacks coping and communication skills. Previous research raised the possibility that the integration between motor and mental (cognition) processing differs during young healthy females' follicular and luteal phases of the menstrual cycle. Cognition refers to mental processes known as attention, remembering, producing and understanding language, solving problems, or making decisions. During mental arithmetic tasks, some changes in cognitive processing were recorded. Motor integrative mechanisms were also recorded on handgrip tests comparing the follicular and luteal phases of the menstrual cycle. This study aims to see if PMS influences ANS function, central integrative mechanisms (cognitive and motor), and mental functioning strongly enough to provide a reliable evaluation of the presence and severity of PMS, along with the extent of the body changes that correlate with PMS symptoms.

Study Design

Case Control Study (Participants act as their own controls).

Study Setting

The study was conducted between June 2019 and December 2019 in two Caribbean Islands, Bonaire and Curacao.

Materials and Methods

The study was carried out per the Declaration of Bonaire and Curacao principles. Verbal consent from the participants was taken. Data was collected from 20 women living in Bonaire and 15 women in Curacao. Participants were all in the pre-menopausal ages. All females who participated were said to have good mental and physical health. Five participants were excluded from the study because they disclosed their health problems after data collection. They had to be excluded because of their health problems, such as cardiac defects.

Participants were requested to avoid strenuous exercise in the 24 hours preceding the tests and to avoid consuming coffee, alcohol, smoking, and heavy meals at least 2 hours before tests. Participants volunteered and did not receive any course credits for their participation in the study.

Experimental Procedure

Tests were conducted at room temperature controlled at 27°C in the labs in Bonaire and Curacao. All tests were performed on the same subject between 11 am - 12 pm or 3 pm - 5 pm. Participants were asked to complete various activities where their comfort level was tested. Participants were asked to come in and be examined on two separate occasions:

1. During the second half of the menstrual cycle, the luteal phase: 14 days or more after the first day of the last menstrual period, when symptoms are worse and
2. The second visit is 4 - 7 days after the menstrual period ends, during the first half of the menstrual cycle: the follicular phase, when subjects are symptom-free.

Test Procedure

Devices used include MARQUETTE VU ®, an EKG, a Standard mercury sphygmomanometer to measure blood pressure (BP), measuring tape to measure ankle circumference, waist, and height, and a scale used to measure an individual's weight.

Participants were given sufficient supine rest before the orthostatic test. EKG electrodes using standard limb leads were then applied to the participants and were recorded. This test was for the cardiovascular function that consists of three reflecting cardiac parasympathetic (PANS) functions and three tests of reflecting cardiovascular sympathetic (SANS) responses using the original Ewing autonomic test battery. The test included the following:

1. The blood pressure response to the mental arithmetic challenge, handgrip, and standing.
2. The heart rate response to forced breathing, handgrip, and standing up.

The entire test consisted of five autonomic function sub-tests conducted after each participant rested in a supine position. Tests were performed in the following order:

1. Blood Pressure (BP) and heart rate (HR) at rest.
2. BP and HR response to mental arithmetic challenge.
3. BP and HR response on handgrip for strength.
4. BP and HR response to standing (measured in the lying position followed by the standing position).

Resting Heart Rate & Blood Pressure

Reduced parasympathetic activity causes resting tachycardia, and this test is therefore associated with cardiovascular autonomic failure. An EKG recorded the resting heart rate (HR) for two minutes (4-6 QRS complexes). The current upper range for average HR is 100 bpm, and normal BP is 120/80 mm of Hg.

Mental Arithmetic Test

In this exercise, participants were instructed to count backward, starting from 200, subtracting seven numbers each time, while the examiners distracted participants. Distracting the participant drew their attention away from the task at hand, which is expected to produce a mild increase in blood pressure and heart rate, suggesting efferent sympathetic pathways functioning.

Handgrip Exercise

Participants were asked to squeeze the lock to the labs as hard as possible to test their strength, which is expected to produce a mild increase in blood pressure and heart rate. An EKG recording was taken to show changes in heart rate and blood pressure. An increase in less than 10 mm of Hg in blood pressure was found to be abnormal.

Postural changes in systolic and diastolic BP

In this test, each participant rested in a supine position to perform and to be recorded for three different blood pressure and heart rate data. Resting HR is determined by the vagal tone that decreases once a subject stands with consequent changes in the heart rate of 11-29 beats per minute. Standing up HR and BP were recorded once participants were done with the supine position task.

Questionnaire

Participants were asked to complete three standardized questionnaires about physical, behavioral, and emotional symptoms. The questionnaires include the Daily Rating, Anxiety Index, and Depression Scale. Each questionnaire contains questions regarding participants' moods and effects on the testing day. Participants were instructed to rate each item for how they felt at their worst today on a scale of 0-10 for the Daily Resting Scale, with "zero" being the least and ten being extreme. However, the Anxiety Index and Depression Scale were from 0-100 with a similar scaling system, with zero being "least" and 100 being "extreme." Later, scores were summed up for each questionnaire, and each participant was given a final score. These recordings were done during their luteal phase (seven days before the next menstruation) and their follicular phase (within seven days after the completion of menstrual bleeding). The difference between both trials was then computed.

Statistical Analysis

SPSS 11.0 program is used for data analysis. All data were expressed as mean ± Standard Error, and P-values < 0.05 were considered statistically significant. Regarding the parameters of symptoms with menstrual cycles and other clinical features, the ANOVA (Analysis of Variance) test using post hoc Tukey's test was used for comparisons between groups and paired t-test for within-group comparisons.

Results

Since our independent variables were dichotomous, we used the ANOVA test to analyze the data. The measured variables were heart rate and blood pressure (systolic and diastolic). Of the variables being tested, we did not find much statistical significance for differences in heart rate. The mean resting heart rate, heart rate one, in the luteal phase was 74.57 beats per minute (BPM), with a standard deviation of 10.71. In the follicular phase, the resting heart rate, heart rate five, was 75.00 BPM, with a standard deviation of 10.43 (Table 1). The mean heart rate for the mental arithmetic test, heart rate two, in the luteal phase was measured to be 93.57 with a standard deviation of 15.59, and for the follicular phase, heart rate six, the mean was 95.27 BPM with a standard deviation of 14.31 (Table 1). The mean heart rate for the strength test, heart rate three, was 95.60, with a standard deviation of 14.80 for the luteal phase. For the follicular phase, the resting heart rate, heart rate seven, was 93.23, with a standard deviation of 16.26 (Table 1). The mean heart rate while the participants were standing at rest, heart rate four, was 83.47 BPM with a standard deviation of 12.90 for the luteal phase, and for the follicular phase, heart rate eight, the mean heart rate was 87.80 BPM with a standard deviation of 15.64 (Table 1).

Again, using ANOVA (Analysis of Variance), the following variable being measured was systolic blood pressure. The mean systolic blood pressure (SBP) at rest, SBP one, was 113.13 mm of Hg with a standard deviation of 7.54 mmHg for the luteal phase, and for the follicular phase, SBP five, was 110.07 mm of Hg with a standard deviation of 6.76 (Table 1). The mean SBP for the cognitive exercise, SBP 2, was 120.47 mm of Hg with a standard deviation of 7.55 for the luteal phase, and the follicular phase SBP mean, SBP 6, was found to be 117.13 mm of Hg with a standard deviation of 8.48 (Table 1). For the strength exercise, the mean SBP, SBP 3, was found to be 123.07 mm of Hg with a standard deviation of 8.28 in the luteal phase, and for the follicular phase, the mean SBP, SBP 7, was found to be 117.53 mm of Hg with a standard deviation of 11.03. The mean SBP while the participants were standing at rest, SBP 4, was 113.20 mm of Hg with a standard deviation of 6.50 for the luteal phase. For the follicular phase, the mean SBP, SBP 8, was said to be 107.13 mm of Hg with a standard deviation of 8.16 (Table 1).

Still using the ANOVA test, the following variable being measured was diastolic blood pressure. The mean diastolic blood pressure (DBP), DBP 1, was said to be 68.73 mm of Hg with a standard deviation of 6.06 DBP for the luteal phase. For the follicular phase, the mean resting DBP, DBP 5, was 68.77 mm of Hg with a standard deviation of 5.62 (Table 1). For the cognitive exercise during the luteal phase, the mean DBP, DBP 2, was said to be 74.80 mm of Hg with a standard deviation of 5.93. In the follicular phase, the mean DBP, DBP 6, was considered 73.93 mm of Hg with a standard deviation of 7.15 (Table 1). For the strength exercise during the luteal phase, the mean DBP, DBP 3, was 79.00 mm of Hg with a standard deviation of 6.35. For the follicular phase, the mean DBP, DBP 7, was found to be 75.87 mm of Hg with a standard deviation of 6.80 (Table 1). The mean DBP during the luteal phase while participants were standing at rest, DBP 4, was found to be 68.45 mmHg with a standard deviation of 4.11. For the follicular phase, the mean DBP, DBP 8, was 68.97 mm of Hg with a standard deviation of 7.12 (Table 1).

ANOVA Test

AVONA Test	*N*	*Mean*	*Std. Deviation*	*Std. Error Mean*
Heart Rate				
1.00	30	74.5667	10.70509	1.95447
2.00	30	93.5667	15.59329	2.84693
3.00	30	95.6000	14.80354	2.70274
4.00	30	83.4667	12.89943	2.35510
5.00	30	75.0000	10.43205	1.90462
6.00	30	95.2667	14.31164	2.61294
7.00	30	93.2333	16.26013	2.96868
8.00	30	87.8000	15.64124	2.85569
Total	240	87.3125	16.03729	1.03520
Systolic Blood Pressure				
1.00	30	113.1333	7.53719	1.37610
2.00	30	120.4667	7.54633	1.37777
3.00	30	123.0667	8.27515	1.51083
4.00	30	113.2000	6.50411	1.18748
5.00	30	110.0667	6.75652	1.23357
6.00	30	117.1333	8.47606	1.54751
7.00	30	117.5333	11.02578	2.01302
8.00	30	107.1333	8.16102	1.48999
Total	240	115.2167	9.44722	0.60982
Diastolic Blood Pressure				
1.00	30	68.7333	6.06251	1.10686
2.00	30	74.8000	5.93296	1.08321
3.00	30	79.0000	6.34633	1.15868
4.00	30	68.4667	4.10830	0.75007
5.00	30	68.7667	5.62435	1.02686
6.00	30	73.9333	7.14835	1.30510
7.00	30	75.8667	6.80128	1.24174
8.00	30	68.9667	7.12201	1.30029
Total	240	72.3167	7.22673	0.46648

Table 1: One-way ANOVA Test was done for Heart rate and blood pressure (Systolic (SBP) and Diastolic Blood pressure (DBP)). Numbers 1, 2, 3, and 4 correspond to resting, mental arithmetic testing, strength test, and resting standing up in the luteal phase, respectively. Numbers 5, 6, 7, and 8 correspond to resting, mental arithmetic testing, strength test, and resting standing up in the follicular phase, respectively.

The mean Pre-Daily Rating Scale was calculated to be 24.77 with a standard deviation of 13.95, whereas the mean Post-Daily Rating Scale was 12.80 with a standard deviation 10.45 (Table 2.1). The mean Pre Anxiety Index was 48.23 with a standard deviation of 12.01, whereas the mean Post Anxiety Index was 39.13 with a standard deviation 10.79 (Table 2.1). The mean Pre Depression scale was 9.70 with a standard deviation of 7.66, and the mean Post Depression scale was 7.43 with a standard deviation of 11.25 (Table 2.1). The mean pre-waist measurement was 90.00 cm with a standard deviation of 10.73 cm, whereas the mean post-waist measurement was 88.73 cm with a standard deviation of 10.19 cm (Table 2.1). The mean pre-ankle measurement was 22.67 cm with a standard deviation of 1.34 cm, whereas the mean post-ankle measurement was 22.57 cm with a standard deviation 1.22 (Table 2.1). The mean pre-weight measurement was 60.13 cm with a standard deviation of 11.42, whereas the mean post-weight measurement was 59.87 cm with a standard deviation of 11.26 (Table 2.1). The mean Pre Height and mean Post Height measurements were 161.67 cm with standard deviations of 6.26 cm (Table 2.1).

Pair 1 – Pre-Daily Rating Scale	30	24.7667	13.95234	2.54734
Post-Daily Rating Scale	30	12.8000	10.44658	1.90728
Pair 2 – Pre-Anxiety Index	30	48.2333	12.01345	2.19335
Post-Anxiety Index	30	39.1333	10.79187	1.97032
Pair 3 – Pre-Depression Scale	30	9.7000	7.66159	1.39881
Post-Depression Scale	30	7.4333	11.24548	2.05314
Pair 4 – Pre-Waist	30	90.0000	10.73184	1.95936
Post-Waist	30	88.7333	10.19443	1.86124
Pair 5 – Pre-Ankle	30	22.6667	1.34762	0.24604
Post-Ankle	30	22.5667	1.22287	0.22326
Pair 6 – Pre-Weight	30	60.1333	11.42210	2.08538
Post-Weight	30	59.8667	11.26402	2.05652
Pair 7 – Pre-Height	30	161.6667[a]	6.25511	1.14202
Post-Height	30	161.6667[a]	6.25511	1.14202

Table 2.1: T-test. a. The correlation and t cannot be computed because the standard error of the difference is 0.

Paired Sample Correlations

According to the 95% Confidence Interval of the Difference, the P value for pair 1, Pre and Post Daily Rating scale, was 0.089 (Table 2.2). Similarly, the P value for pair 2, Pre and Post Anxiety Index, was 0.042 (Table 2.2), and the P value for pair 3, Pre and Post Depression Scale, was 0.007. The P values for pairs 4, 5, and 6 Pre and Post Waist measurement, Pre and Post Ankle, and Pre and Post Weight measurement were all 0.000 (Table 2.2).

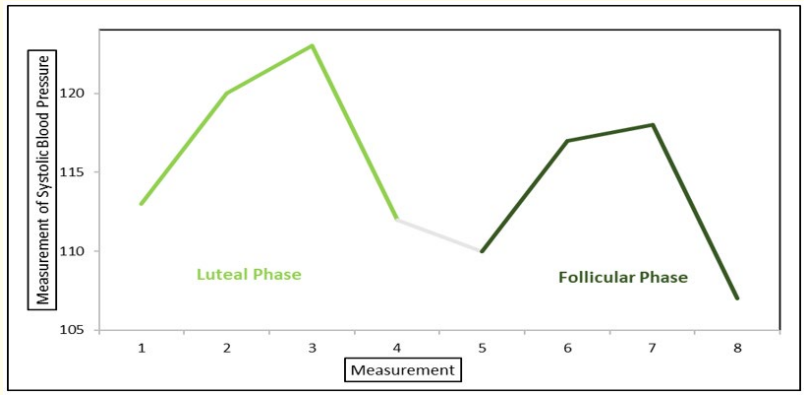
Discussion

This study observed statistically significant changes in the mean of SBP measurements between the luteal phase, measurements 1-4, and the follicular phase measurements 5-8 (Graph 1). Likewise, DBP measurements showed significant changes between both phases (Graph 2). The changes in these measurements proved our hypothesis that participants showed an increase in their SBP and DBP during their luteal phase compared to results recorded during their follicular phase. This rise indicates that these participants were experiencing premenstrual symptoms during their luteal phase. Except for heart rate, the overall data showed that participants were experiencing increased physiological symptoms during their luteal phase; the same is analyzed in the discussion section. So, the comprehensive data indicated that participants were experiencing increased physiological symptoms during their luteal phase while height remained constant for all the participants. The mean waist size between pre-and post showed a difference of 1.27 cm. To go into detail, the mean waist measurement of the 30 participants during the luteal phase was 90.00 cm, while during the follicular phase, it decreased to 88.73 cm (Table 2.1). The same was shown for ankle measurement, with a 0.1 cm increase during the luteal phase. This

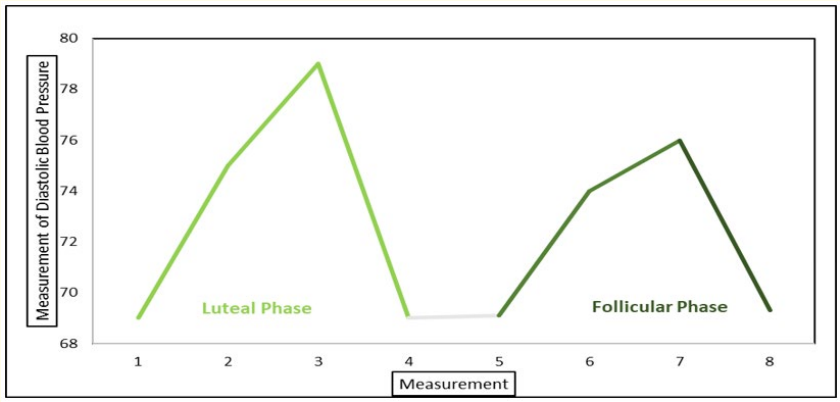
change in the waist and ankle measurement indicates that during the luteal phase, participants were experiencing an increase in fluid retention, leading to an increase in waist and ankle size [3]. Thus, participants' weights were also increased during the luteal phase. The mean difference in weight was 0.26 kg higher during the luteal phase (Table 2.1).

Paired Samples Correlations	*N*	*Correlation*	*Significance*
Pair 1 – Pre-Daily Rating Scale Post-Daily Rating Scale	30	0.316	0.089
Pair 2 – Pre-Anxiety Index Post-Anxiety Index	30	0.373	0.042
Pair 3 – Pre-Depression Scale Post-Depression Scale	30	0.480	0.007
Pair 4 – Pre-Waist Post-Waist	30	0.995	0.000
Pair 5 – Pre-Ankle Post-Ankle	30	0.956	0.000
Pair 6 – Pre-Weight Post-Weight	30	0.996	0.000

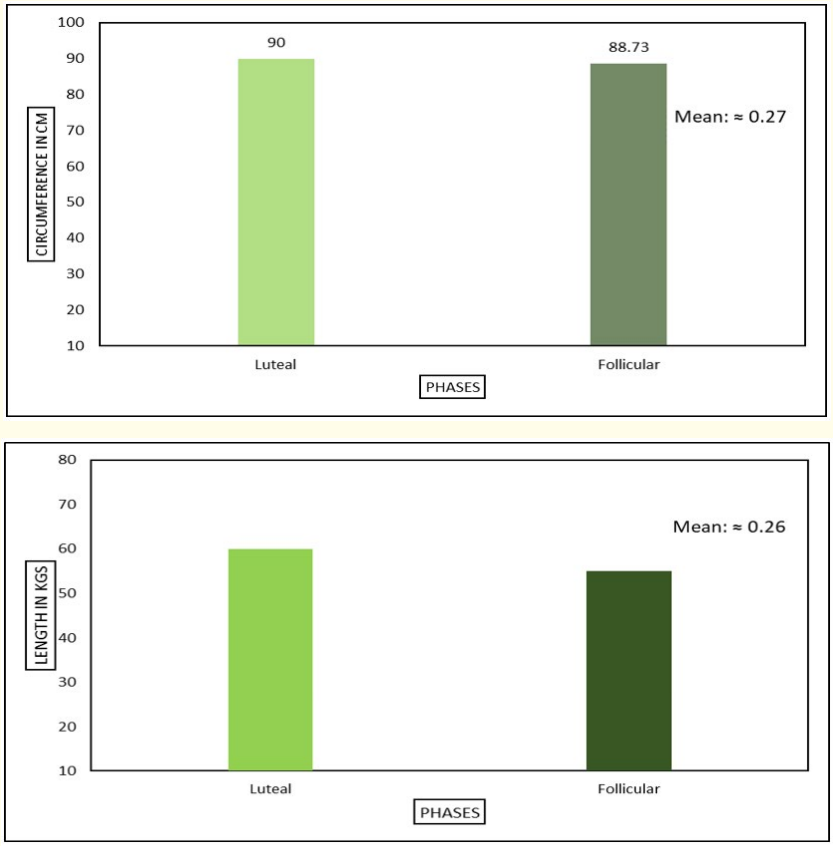
Table 2.2: Paired T Samples Test shown highly significant difference between mean for Pre Daily Rating Scale Post Daily Rating Scale (p = .000); Pre Anxiety Index - Post Anxiety Index (p = .001); Pre Waist - Post Waist (p= .000).



Graph 1: On the x-axis, numbers 1-4 represent the patient at rest, the patient during the cognitive exercise, during the strength exercise, and the participant resting standing up, respectfully, during the luteal phase, while numbers 5-8 represent during the follicular phase.



Graph 2: On the x-axis, numbers 1-4 represent the patient at rest, the patient during the cognitive exercise, during the strength exercise, and the participant resting standing up, respectfully, during the luteal phase, while numbers 5-8 represent during the follicular phase.



Graph 3: On the x-axis, two clustered column charts represent the patient at rest, the patient during the cognitive exercise, during the strength exercise, and the participant resting standing up, respectfully, during the luteal and the follicular phases.

Similarly, the same was seen in the questionnaires that each participant completed during the luteal and follicular phases. On average, increased behavioral and emotional symptoms were experienced by each participant during the luteal phase. The mean value in the Pre Daily Rating Scale was 24.77, an 11.97 increase from the Post Daily Rating Scale of 12.80 (Table 2.1). During the luteal phase, participants showed higher anxiety; the mean Pre Anxiety Index was 48.23, a 9.1 increase from the mean Post Anxiety Index of 39.13. The same was seen in the participant's levels of depression. The mean Pre Depression Scale showed a 2.27 increase during the luteal phase with a value of 9.70 (Table 2.1).

Previous studies have documented similar results on autonomic nervous system involvement in the menstrual cycle. Previous research has shown that women with PMS have significantly reduced ANS activity in the late luteal phase compared to the follicular phase and that people with the most severe symptoms may have permanent depression of this critical regulatory system [4].

He also suggested that among women with very severe symptoms (i.e., women with premenstrual dysphoric disorder), decreased ANS activity is permanent, regardless of the menstrual cycle phase. Furthermore, in the late-luteal phase, altered ANS function (more precisely, decreased sympathovagal function) has been linked to premenstrual psychosomatic and behavioral symptoms [6].

A possible explanation for the observed results could be attributed to a single common cause: the hypothalamus. The hypothalamus is the primary regulator of homeostasis, controlling hormones, behavior, and ANS. Hypothalamic control of endocrine glands during the menstrual cycle influences progesterone, estrogen, ovulation, and endometrial shedding (Kirschbaum, 1999). Further, hypothalamic control of ANS may be evident in symptoms such as bloating, nausea, and appetite changes. Furthermore, hypothalamic control of behavior may manifest as irritability, nervousness, mood changes, or sleep disturbances. These changes are accomplished by hypothalamic orchestration of hormone release and function.

Interestingly, previous studies on the hypothalamic release of hormones measured participants' hormonal levels during their follicular phase and found that estrogen tends to increase dramatically during this period [7]. Estrogen, as a hormone, has a vasodilatory effect [8], which could explain the decrease in systolic blood pressure observed in the follicular phase (during the mental exercise task). Further research on the importance of those subtle changes we registered for cognitive performance, and the standing task is necessary to make conclusions regarding observed changes in the menstrual cycle.

There were several aspects of our research that we could have improved. When analyzing the heart rate graph, the data we collected did not match our hypothesis. The mean heart rate for all four test measurements during the luteal phase was expected to be higher than during the follicular phase. In our results, the mean heart rate during the resting heart rate 1 was 74.57, lower than the Resting Heart rate 5, which was 75.00. We expected Heart Rate 1 to be higher because this was taken during the participant's Luteal phase. According to other research studies, results varied for heart rate when comparing the luteal phase with the follicular phase. Our results indicated the same. Although heart rate varies from woman to woman, an increased heart rate during the luteal phase was expected due to decreased estrogen. Our results contradicted that decreased estrogen during the luteal phase should increase heart rate. This consistency could be due to diet. While we checked with each participant about what they ate and drank before coming in and reminded them to have the same meal or caffeinated beverages before their next visit, we did not set any diet restrictions for this study. Therefore, our results could be varied due to our inability to keep track of our participants' diets.

Further Improvements of This Study

Future research studies could have each participant eat the same meal and drink as a constant variable. Another influence on heart rate could have been due to temperature. According to a study, body temperature causes an increase of approximately ten bpm per degree centigrade. Our variability in heart rate could have been due to us not keeping track of the room temperature and keeping it constant [9].

Financial limitations also impacted several variables of our study. One way we could have better assessed each participant would have been to measure participants' hormonal levels during the menstrual cycle to objectify hypothalamic control's role better. This hormonal measurement would have also allowed us to check each participant at a certain hormonal level during the luteal and follicular phases, which was impossible in our study due to financial limits. Many students who wanted to volunteer for our study could not participate because they had no ride to the respective labs. We could not provide rides because we could not access a vehicle or any other accessible mode of transportation.

We also had a limited number of participants due to the requirement that the participant could not be on birth control. This exclusion prevented many women from participating. We also could not use any women who had heart problems or arrhythmias. A few women were unaware that they had any cardiovascular problems until we performed the EKG. For this reason, data from five participants had to be disregarded. In addition, the only females allowed to participate were students available on the Islands. Due to this restriction, this study could not be done on a larger scale to obtain more precise results.

Conclusion

Regular menstrual cycles signify that essential parts of the female body are usually working. Premenstrual symptoms (PMS) are sometimes experienced in females, showing physical, behavioral, and emotional signs. Most women of childbearing age undergo a regular recurrence of various symptoms in the late luteal phase of their menstrual cycle. This study was done on 35 participants; five were excluded due to health reasons. Although no pathological changes were seen, physical, behavioral, and emotional changes were found. During the participants' luteal and follicular phases, the changes in the autonomic nervous system were also observed using a wide variety of tests. Regardless of the presence or absence of the PMS, participants had autonomic nervous system changes before and after their menses. Future research could measure participants' hormonal levels during the menstrual cycle to better objectify the role of hypothalamic control.

Conflict of Interest Statement

The authors have no conflict of interest to declare including commercial relationships as well.

Acknowledgments

Thanks to Dr. Branka for guiding us throughout the research study, to Dr. Mirjana & Dr. Davidson for always providing us access to the Lab, to Dr. Dusic for helping us with the statistical tests, and most of all to the participants, without whom, this study would be impossible.

Participant's Consent

We took verbal consent from the participants and told them that they had the right to leave the study at any time.

Consent to Publish

No personal information, as well as copyrighted images, were not used in this study.

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