

# The Influence of Different Phases of Menstrual Cycle on Autonomic Reactivity to a Cognitive and Emotional Stressor- A Cross Sectional Study

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## ABSTRACT

To study the impact of different phases of menstrual cycle on certain select parameters affecting autonomic reactivity and cognitive and emotional status.

**Materials & Methods:** 62 eumenorrhic females aged 18–20 years were recruited after obtaining ethical clearance. Cognitive and emotional stressors in the form of PASAT and emotional stroop test and were conducted on 10<sup>th</sup> (follicular) and 20<sup>th</sup> (luteal) day of menstrual cycle after phase determination using basal body temperature and prism calendar. Hr, sbp and dbp were measured at baseline and following stressors.

**Statistical Analysis:** was done using SPSS version 20. Students paired t test was used to compare the results between the two phases. P < 0.05 was considered as statistically significant.

**Results:** Baseline: hr, sbp and dbp were more in the luteal phase as compared to the follicular phase.

*PASAT:* hr recovery was (3 minutes and 30 seconds) follicular and (4 minutes and 10 seconds) luteal phase, sbp recovery was (2 minutes and 20 seconds) follicular and (2 minutes and 50 seconds) luteal phase, dbp recovery was (1-minute and 40 seconds) follicular and (2 minutes and 10 seconds) luteal phase.

*Emotional Stroop Test:* positive word latency (1256.437 ms) follicular and (1034.54 ms) luteal phase. Negative word latency (1145.786 ms) follicular and (1335.304 ms) luteal phase.

**Conclusion:** the luteal phase was characterized with greater sns reactivity and hence cognitive and emotional stressors gathered more sympathetic activity and finally a definite interaction was sought between the gonadal hormones, ans and higher cognitive centres of a female.

**Keywords:** Blood pressure, Cognition, Emotional stroop.

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## INTRODUCTION

Every female has a unique kaleidoscope of changing sex hormonal profile which fluctuates in accordance with the phases of menstrual cycle. The menstrual cycle is defined as a natural repetitive phenomenon occurring in the female throughout the reproductive years of her life. The steroid hormones, mainly estrogen and progesterone and the rhythmic fluctuation in their secretion correspond to the physiological psychological and emotional responses in the female.<sup>1</sup> Ovarian steroids do not follow a linear trend and interact with the hypothalamo-hypophyseal axis as well as all the organ systems. The first half of the cycle, namely the follicular phase is constituted by an increase in the estrogen levels whereas the latter half of the cycle or the luteal phase experiences a peak in progesterone levels.<sup>2,3</sup> The hormonal alterations occurring during the different phases of menstrual cycle not only have a function in reproduction but have a profound interaction with the ans.<sup>4,5</sup> Experimental animal studies have shown that endogenous estrogen functions by increasing the vagal response and decreasing the sympathetic activity<sup>6</sup> whereas on the other hand progesterone functions in an opposite manner thereby increasing the sympathetic response.<sup>7</sup> These hormonal alterations are associated with significant neurohumoral changes which regulate the

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working of the cardiovascular system therefore changing the blood pressure, heart rate and rhythm.<sup>8,9</sup>

Stress is one of the major causes for increasing the mortality rate among females.<sup>10</sup> The nature of the cycle, in addition to being associated with future reproductive outcomes like fertility and timing of menopause, are also related to many other health-related outcomes.<sup>11</sup> Stress involves the activation of the sympathetic system, releasing catecholamines, namely adrenaline and noradrenaline into the bloodstream giving rise to cardiovascular changes in the form of raised blood pressure and heart rate. We have seen a rising trend of ischemic heart disease in post-menopausal

women which give strong evidence to the nature of the cycle to the cardiovascular system.<sup>12</sup>

Our brain processes new information, creates new memories and helps in recalling necessary information. We therefore have short term and long-term memory. Short term memory, also known as working memory is the kind of memory we receive, use quickly and discard. It stays active for a brief period of time.

Studies linking menstrual cycle phases to cognition suggest that the early follicular phase is associated with cognitive abilities such as spatial abilities and the luteal phase of the cycle associated with cognitive abilities like verbal fluency and verbal memory.<sup>13</sup>

The paced auditory serial addition test (PASAT) test involves a visual stimulus used to measure and assess this working memory and attention capacity<sup>14</sup> and how the hormones in our menstrual cycle interfere with this working memory and affect it.

The luteal phase, is usually one wherein the female experiences varying degrees of pre menstrual syndrome (pms)<sup>15</sup> and factors such as stress, age, body mass index and marital status contribute to this syndrome and its problems.<sup>16</sup> These emotionally disturbing symptoms occurring during the luteal phase have the potential to affect the normal working life of a female.<sup>17</sup> It is important to record the nature, timing, and severity of menstrual cycle-related symptomatology, and a prism (prospective record of the impact and severity of menstrual symptoms) calendar is used for the same. We will use this tool to assess the psychosomatic status of females during the month and how they fluctuate with the hormonal status.<sup>18</sup>

During this cycle, different emotions are experienced by a female. These are known to fluctuate with the changing hormonal status. An emotional stroop test will be used by us to grade the type of emotions and how these varied emotions can affect the degree of cognition within them.<sup>17</sup> there have not been many studies which have correlated this emotion affecting cognition phenomena with a females menstrual cycle.

We used PASAT and emotional stroop as cognitive and emotional stressors respectively to study the interactions of these different phases of menstrual cycle on executive and emotional and psychosomatic functioning.<sup>18</sup>

It is imperative to study these cardiovascular, cognitive, and emotional changes occurring within the female and correlate these with cyclical changes. These responses to cognitive and emotional stressors show the need for an everyday alteration and importance of the homeostatic mechanism in a female. Therefore, we put forward a hypothesis that the variation in cardiovascular, executive as well as emotional functioning occurring throughout the menstrual cycle may be due to the fluctuating gonadal hormones.

## MATERIALS AND METHODS

### Source of Data

75 non-obese females within the age of 17–19 years of MBBS phase 1 of Jawaharlal Nehru Medical College and Hospital,

Belgaum were enrolled for data collection according to a predetermined inclusion-exclusion criteria after which 13 students were excluded and all the tests were performed on these 62 subjects.

### Inclusion Criteria

- Females with history of at least 2 regular menstrual cycles (26–32 days)
- Age group 17–19 years

### Exclusion Criteria

- Females with history of irregular menstrual cycle for at least previous two cycles
- History of regular cigarette smoking, oc pill and alcohol consumption
- Students who practice regular exercise regime (3 times/week)
- History of cardiac, respiratory, and hormonal disorders

### Procedure

62 students were selected and briefed about the nature of the study and written, voluntary, informed consent was obtained from them. Prior ethical clearance letter no. Mdc/dome/84 was taken from the institute and all the procedures were conducted according to Declaration of Helsinki. All the participants reported to the research lab at the same time (8:30 am) to avoid bias due to circadian rhythms.

A prism (prospective record of the impact and severity of menstrual symptoms) calendar had to be filled for at least 2 consecutive cycles (complete cycles to be filled).

A prism calendar covers physical and emotional changes in the cycle under the following headings:

- Weight change
- Symptoms
- Lifestyle impact
- Life events
- Medications

And thus provides an overall state of physical and mental well-being of a female and helps identify psychosomatic symptoms and mood changes occurring throughout the cycle.

The subjects were examined on two separate occasions (based on basal body temperature)

1. Once during the follicular phase (10<sup>th</sup> day; with day 1 as the first day of bleeding)
2. Once during the luteal phase (20<sup>th</sup> day from the first day of bleeding)

Prior instructions were given to subjects to avoid coffee, nicotine, alcohol 24 hours prior to, heavy food 2 hours before the test. Drugs affecting cardiac autonomic functions like anti- cholinergic, sympathetic, and parasympathetic drugs were contraindicated 2 days before the test.

These tests conducted were non-invasive.

- Tests performed:
- The patient was introduced to 4 testing procedures:
- Baseline blood pressure and hr
- PASAT practice.

- PASAT 2.4, 2.0, 1.6, 1.2
- Emotional stroop test

A baseline rest of 20 minutes in supine position was given to all the participants so that all parameters are within the baseline.

### Baseline Blood Pressure

The blood pressure was recorded for each subject in a sitting posture using the omron m6 semi-automated sphygmomanometer model 11 em- 403c, Tokyo, Japan. The arm was initially relaxed and supported at the level of the heart.

The mean blood pressure is taken for 3 consecutive readings.

### Paced Auditory Serial Addition Test (PASAT)

PASAT, also known as paced auditory serial addition test, is used to assess the role of immediate memory and attention capacity where the stimuli is of a visual nature.<sup>14</sup>

PASAT involved presentation of a series of single digit numbers wherein the two most recently seen digits need to be added. For example, if the digits '2', '4' and '5' were presented, the participant would respond with the correct sums, which are '6' and then '9'. The speed of processing information was altered, and a similar sequence of digits were shown at different rates. 2.4 s, 2.0 s, 1.6 s, 1.2 s were used as rates of presentation of digits. A practice trial was used prior to beginning the first trial. The score reported was usually in the form of number of correct responses.

In our experiment, PASAT was used as a cognitive stressor. PASAT test contained 2 phases, namely PASAT practice and PASAT 2.4.

Following the measurement of baseline blood pressure, the subjects were introduced to the standard computer administered PASAT practice session.

Once the practice session was over, the subjects performed the PASAT trials and simultaneously, their blood pressure and hr was recorded.

It has been observed that when the PASAT test is administered on a subject, the subject is under a sympathetic nervous system stimulation, which normally raises the blood pressure and heart rate.

The PASAT has demonstrated high split-half reliability and evidence for convergent and divergent validity with good sensitivity for deficits in the areas of auditory information processing speed and flexibility.<sup>19</sup> It is a reliable test that is legitimate, highly sensitive and can be administered to assess immediate memory.

### Emotional Stroop Test

This test is based on the principle of how emotional disturbances within a person can affect their cognitive thinking and modulate their capacity and capability to take decisions under these stressful conditions.<sup>20</sup>

Words in different color were presented on the screen and the subject was required to name the color in which the word was presented accurately and quickly.

The words are from 4 categories:

category 1: aggressive words like 'death', 'bomb', 'ghost'

category 2: neutral words like 'box', 'chair', 'door'

category 3: positive words like 'warm', 'calm', 'cheerful'

category 4: color words like 'cyan' 'bronze' 'orange'

It was usually observed that the participants take a longer time (increased latency) to identify the

Color of negative words as compared to the neutral and positive words. Studies have shown that

Subjects show a slower response to identify the color of a word if it is associated to their emotional state.<sup>21</sup>

The emotional stroop test has been used as an experimental measure to assess the bias in attention with emotion laden information.

Results of some studies that have used emotional stroop have indicated that retest reliabilities for reaction times derived across interval were very high.<sup>22</sup>

This test was employed during the follicular and the luteal phase, and the latency to negative words is compared with positive words and again compared within the 2 phases of the cycle.

The results will reflect how the emotional status of a female is mainly due to the hormonal imbalance throughout the cycle.

## RESULTS

### A. Demographic Information

The 30 healthy females were included for the above study and the demographic data was plotted. Mean age group was 20 years (s.d. = 0.66), average weight was 54.7 kg (s.d.= 5.55), average height was considered to be 1.60 metres (s.d.= 0.04). Table 1 shows the demographic statistics of the study.

### B. Physiological Recording

Autonomic function tests for the testing of sympathetic activity were recorded and compared in follicular and luteal phase. The difference in the blood pressures was recorded. Table 2 shows the difference in the baseline blood pressure in the follicular and the luteal phase of the subjects. Figure 1 shows how the variables of heart rate, systolic and diastolic blood pressure increase in the luteal phase suggestive of increase in the sympathetic activity in the phase.

**Table 1:** Average demographic characters of participants

Age (yrs)	20.3 ± 0.66 (16-21)		
Weight (kg)	54.7 ± 5.55 (44-67)		
Height (m)	1.60 ± 0.04 (1.55-1.65)		
Body mass index (kg/m <sup>2</sup> )	21.4 ± 3.46 (20.44-36.38)		

**Table 2:** Baseline heart rate and blood pressure of participants

Variables	Follicular	Luteal	P value
Hr (rest)	80.5 ± 7.6	88 ± 5.44	0.03*
Sbp (rest)	110.9 ± 5.45	122.8 ± 5.3	0.05*
Dbp (rest)	71.3 ± 2.2	74.5 ± 8.1	0.03*

**C. PASAT Test**

Table 3 shows the time taken for the variables of heart rate, and blood pressure to come back to normal when a cognitive test is administered on the subjects.

It is observed that the mean blood pressure and the variation of the blood pressure with the administration of the PASAT test (cognitive stressor), was statistically significantly higher ( $p > 0.005$ ) in the luteal phase as compared to the follicular phase (Figure 2).

**D. Emotional Stroop Task**

Table 4 shows the latency (in milliseconds) for the identification of positive and negative words in the follicular and luteal phase respectively.

It is observed that there is increased latency of positive words in the follicular phase, where as in the luteal phase, increased latency is observed to negative words (Figure 3).

**DISCUSSION**

The current study was conducted with an intention to assess autonomic reactivity and cognitive and emotional status across different phases of menstrual cycle. The results show an increased sympathetic reactivity in the form of raised hr() bpm , sbp() mmhg and dbp () mmhg during luteal phase of menstrual cycle.

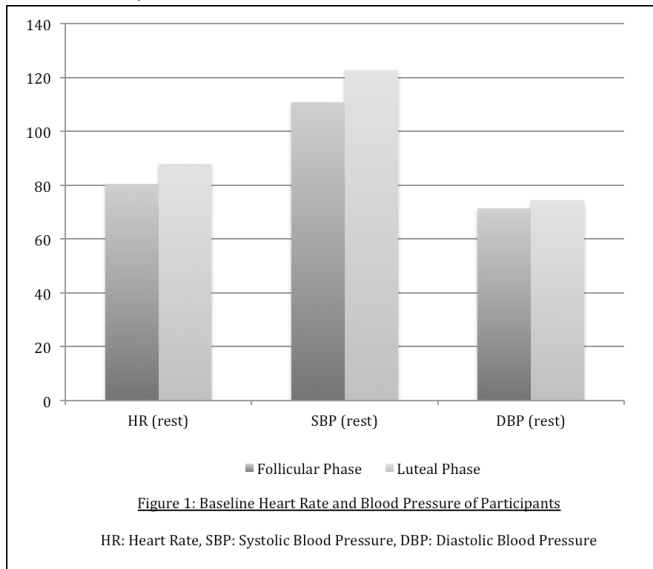


Figure 1: Baseline Heart Rate and Blood Pressure of Participants

Table 3: Recovery time on application of cognitive stressor

Variables	Follicular phase	Luteal phase	P value
Hr recovery	3 mins 30 secs	4 mins 10 secs	0.01*
Sbp recovery	2 mins 20 secs	2 mins 50 secs	0.02*
Dbp recovery	1 min 40 secs	2 mins 10 secs	0.05*

Table 4: Response after application of emotional stroop task

Variables	Follicular phase	Luteal phase
Positive word latency	1256.437 ms	1034.54 ms
Negative word latency	1145.786 ms	1335.304 ms

Cardiovascular system functions in an oscillatory manner to adjust with the variations in the external and internal environment throughout the day, also the blood pressure which shows diurnal variation. Variation in bp during the 2 phases of the cycle can also be accredited to the effect of ovarian hormones on cardiovascular function. There is significant vagal activity in the follicular phase as compared to a high rate of sympathetic response in the luteal phase. (4)the increased vagal activity at ovulation has shown to be influenced by the presence of estrogen while the greater sympathetic activity during the 2<sup>nd</sup> phase of the cycle has been contributed to the increased endogenous progesterone levels<sup>23</sup> estrogens exert their actions through two receptor

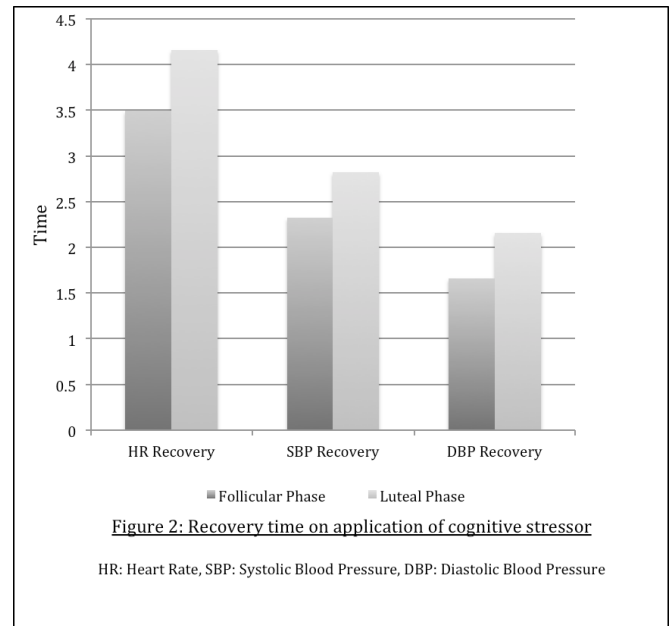


Figure 2: Recovery time on application of cognitive stressor

HR: Heart Rate, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure

Figure 2: Recovery time on application of cognitive stressor

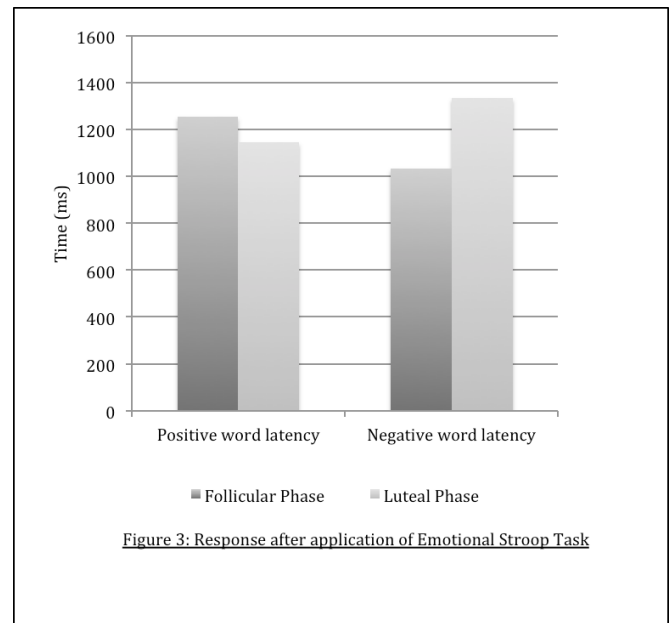


Figure 3: Response after application of Emotional Stroop Task

Figure 3: Response after application of Emotional Stroop Task



subtypes (era and erβ).<sup>24</sup> It was seen that sex hormones can influence the level of substances such as endothelin (et), most commonly et 1 and therefore cause its fluctuation.<sup>25</sup> Progesterone is known to counter this action.<sup>26</sup> A study has demonstrated an increase in nitrate/ nitrite levels in the follicle developing phases<sup>27</sup> estrogen regulates the production of these mediators by many mechanisms; it increases the responsiveness of endothelium dependent, bradykinin mediated vasoconstriction. It increases the levels of no synthase and thereby mediates vasodilation. Progesterone plays the opposite role.<sup>28</sup> As progesterone levels increase during luteal phase, they cause decrease in nitric oxide mediated vasodilation and therefore a predominance of sympathetic vasoconstrictor activity and a greater rise in the blood pressure and heart rate by acting directly on the sa node and increasing the automaticity.<sup>29</sup>

Measurement of urinary catecholamine during the ovulatory cycles of females have revealed a relative increase in the levels of norepinephrine in the 2<sup>nd</sup> half of the menstrual cycle (30) there has also been observed an increase in the incidence of hypertension and a greater heart rate variability in females who indulge in the administration of progesterone containing oral contraceptives as a documentary proof.<sup>31</sup> The vagal preponderance during the follicular phase has been demonstrated using hrv in young menstruating females.<sup>6</sup> heart rate and blood pressure have shown an increase due to the withdrawal of parasympathetic influence of estrogen due to antagonism by progesterone.<sup>32</sup>

With regards to a cognitive stressor in the form of PASAT it was observed that our participants showed an increase in the sympathetic response to stressor reactivity during their luteal phase as compared to the follicular phase. Hr recovery was (3 minutes and 30 seconds) follicular phase and (4 minutes and 10 seconds) luteal phase, sbp recovery was (2 minutes and 20 seconds) follicular phase and (2 minutes and 50 seconds) luteal phase, dbp recovery was (1-minute and 40 seconds) follicular phase and (2 minutes and 10 seconds) luteal phase this can be attributed to the predominance of progesterone in the luteal phase.<sup>19</sup> These changes can be concluded with a finding that cognitive stressors induce a greater sympathetic response in the luteal phase of the cycle which means that females perceive the second half of the cycle as being mentally and physically tasking.

To link the cycle phase to emotional responses we employed the emotional stroop test in our participants and we observed an reduced latency to negative words during the second half of menstrual cycle whereas reduced latency to positive words was seen during the follicular phase.

With the above said results we derived a conclusion that the luteal phase of a female is a 'negative emotional' driven phase. There have been many studies to show that a female shows a slower response to identify the color of a word which depicts her current emotional state of being<sup>21</sup> and our study came to the same conclusions. Positive word latency was (1256.437 ms) follicular phase and (1034.54 ms) luteal phase.

Negative word latency was (1145.786 ms) follicular phase and (1335.304 ms) in luteal phase.

Our findings indicate a higher sympathetic activity to cognitive and emotional stressors in the luteal phase due to increased progesterone levels as compared to follicular phase. Hence gender-based cyclical training & moderation is advocated for optimum results.

## CONCLUSION

Hormones throughout the menstrual cycle follow a rhythmic trend and have an unpredictable effect on the cardiovascular system. Luteal phase is predominated due to the hormone progesterone, which causes a higher sympathetic activity when cognitive and emotional stressors are applied, whereas the follicular phase which is dominated by estrogen does not lead to this relative increase in sympathetic activity.

## IMPLICATIONS

Modulation of these receptors by therapeutic agents is currently being considered for prevention and treatment of a wide variety of pathological conditions.<sup>24</sup>

Using these findings, modifications can be made in ones lifestyle and work understanding their cognitive capacities during different times of the month.

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