

ASSESSMENT OF STRESS AND COGNITION DURING DIFFERENT PHASES OF MENSTRUAL CYCLE AMONG YOUNG HEALTHY FEMALES

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ABSTRACT

INTRODUCTION: Mental stress refers to change in psycho-physiological state that people experience during demanding cognitive activity. The Hypothalamo-Pituitary Adrenal axis reactivity shifts during the adolescent period resulting in stress induced hormonal responses. Stress and cognitive function varies during different phases of menstrual cycle. Hence this study was chosen to find the relation between stress and cognition during different phases of menstrual cycle among adolescent females. **AIM:** To compare the stress and cognition during different phases of menstrual cycle among adolescent females. **METHODOLOGY:** After getting institutional ethical committee clearance the tests were carried out in the department of Physiology, SVMCH&RC, Pondicherry. Stress level with perceived stress scale and cognitive functions like Digit symbol substitution test, Letter digit substitution test, Mini mental status examination, Wechsler memory scale revised, reaction time and critical flicker fusion frequency were determined during the two phases of menstrual cycle among the female volunteers with regular menstrual cycle (n=30). **RESULTS :** Stress was decreased (p=0.29) in the proliferative phase compared to the premenstrual phase. Cognition was decreased in the premenstrual phase compared to proliferative phase but was not statistically significant. Simple reaction time (p=0.29), choice reaction time (p=0.25) were decreased and CFFF (p=0.24) increased in the proliferative phase compared to premenstrual phase. **CONCLUSION :** Increase in stress in the premenstrual period is associated with decrease in the cognition among the female adolescents. Thus apart from scholastic activities extra-curricular activities like music, YOGA, dance and physical training can be encouraged to decrease their stress level.

Key words: cognition, premenstrual phase, proliferative phase, stress

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Introduction:

Mental stress refers to change in psycho-physiological state that people experience during the period of demanding cognitive activity that requires sustained mental efficiency for a longer duration.¹ There is a distinction between eustress (stress which is more beneficial to the organism) and distress (stress with a negative bias), however, in this paper we deal about distress. It has become common among the students to stretch their limits to squeeze more time for reading.² Even quite mild acute uncontrollable stress can cause a rapid and dramatic loss of prefrontal cognitive functions.³ Excessive stress can cause: anxiety, reduced concentration, poor judgement, depression, insomnia. Stress happens throughout the life but the type of stress we experience and how we respond differs from person to person and is found

to be more in females when compared to males.⁴ Stress induced alteration in adolescent brain were associated with compromised emotional function and cognitive skills⁵.

In females, adolescence is a period during which many psychological and physiological changes occur. The menstrual cycle remains an intriguing, natural experiment of relevance for the study of ovarian steroid influence on emotion, behavior, and cognition.⁶ The biological activity of the menstrual cycle is created by the coordination among hypothalamic, hypophyseal and ovarian hormones.⁷ The psychosocial stress may impact the severity of premenstrual symptoms through activation of the Hypothalamic Pituitary-ovarian (HPO) axis, thus altering ovarian hormone levels, leading to change in their cognitive functions.⁸ Cognitive functions are known to vary during

different phases of menstrual cycle but in 1973 Barbara Sommer had concluded that no menstrual-cycle related changes in cognitive and perceptual motor performance was evident.⁶

Cognition can be tested and scored among the students using mini mental status examination (MMSE), Wechsler memory scale (WMS), letter digit substitution test (LDST), digit symbol substitution tests (DSST).⁹ Along with these questionnaire, simple non-invasive cognitive function tests like simple reaction time, choice reaction time, and critical flicker fusion frequency was also done.^{10,11}

Reaction time (RT) is an index of sensory motor performance. It is the time interval between the application of stimulus and appearance of voluntary response³. Since stress can be distracting, it may affect a person's ability to react as quickly to stimuli as those who are not experiencing significant stress.¹² RT is a simple tool to measure attention, concentration, execution and psychomotor speed. Critical flicker fusion frequency (CFFF) is an indicator of cortical arousal. It is used a tool to measure physical human fatigue, mental workload and cognitive function¹¹.

Though number of studies were done on stress related psychological dysfunctions like anxiety, depression and drug abuse on maturing adolescent brain very few studies were done to know the effect of stress on cognitive function during different phases of menstrual cycle in females and hence this study was undertaken.

OBJECTIVES

1. To compare stress level and cognition among the adolescent females during follicular and luteal phases of menstrual cycle.
2. To correlate the stress level with cognitive function test scoring and CFFF
3. To correlate the stress level with simple and choice reaction time

Material and Methods:

This observational study was conducted in the Department of Physiology, Sri Venkateshwaraa Medical College Hospital and Research Center, Ariyur, Pondicherry. 30 healthy female volunteers of age between 18-20 years with normal BMI (18-24 kg/m²) and regular menstrual cycle without any menstrual disorders were selected randomly and

the study was conducted from May to July of 2017. Females with history of color blindness and regular practice of Yoga/exercise were excluded.

After getting Institutional ethical committee clearance, informed & written consent was obtained from all the participants. Stress level was assessed using perceived stress scale (PSS). The following tests were used to measure the cognitive function. All the parameters were recorded during follicular phase (6th – 7th day) and luteal phase (25th & 26th day) of menstrual cycle for the female volunteers.

Digit symbol substitution test (DSST)⁹

The test will be done to assess neuropsychological activity of the brain. It consists of (eg. Symbol pair 1/-, 7/^) one digit and one symbol in pairs followed by a list of digits. Under each digit the subject should write down corresponding symbol as fast as possible within 90 seconds. The number of correct symbols within the time allowed is measured and scores are awarded.

Letter digit substitution tests (LDST)⁹

The test sheet will be given, the key gives the number 1-9, each paired with the different letter; the test items are printed beneath the key. Examinee will be asked to replace the randomized letters with appropriate digit indicated by the key. The first 10 items are used as a practice items eg. digit pairs (w/1, b/2, t/3.....j/9) followed by list of alphabets. Under each alphabet, the subject must be instructed to write down the corresponding digit within 60 seconds of time period. The correct digit was considered as a score.

Mini mental status examination (MMSE)⁹

It was done by asking a set of 11 questions under the following sections like orientation, registration, attention, calculation, recall and language. The questions are very basic like name of the year, season, month, date etc. the total score was assessed. The maximum score was 30. The score ≤ 23 is considered as cognitive impairment.

Wechsler memory scale revised (WMS-R)⁹

It includes two types of tests

Spatial addition sub test: It assess visuospatial storage and manipulation in working memory. The examinee will be shown 4×4 grid with blue and red dots on it for 5 seconds. They are asked to remember the location of the blue dots and ignore

the location of red dots on that page. The examinee will be shown a second page with blue and red dots for 5 seconds, the examinee have to add the two visual images together. The examinee is given 4x4 puzzle grid and red, blue and yellow cards. The examinee must place the blue dot in the grid in location where they see blue dots on either page and yellow dot where blue dot appear in common.

Design sub test: The examinee will be shown a page with designs placed in the grid. There are 4 times having 4,6,6,8 designs for examinee to remember respectively. The examinee will be asked to remember the design and its location. After seeing the stimulus page for 10 seconds, the examinee will be given puzzle grid and cards with designs on them. The examinee must select the cards with correct designs and place them in puzzle grid in correct position. After 20-30 mins of delay, the examinee will be given the cards to place in the grid again. Following the delay recall task, a delayed recognition is administered and scores are calculated for total, immediate, immediate content, immediate spatial, total delayed, delayed content and delayed spatial.

Reaction time

RT measurement includes the latency in the sensory neural code traversing the peripheral and central pathways along with perceptive, cognitive and volitional processing⁸. In Simple reaction time, there is only one stimulus and one response. 'X' at a known location, the subject has to press the button once the X is seen by him on the screen. In choice reaction time, the user must give a response that corresponds to the stimulus, such as pressing a key corresponding to a letter if the letter appears on the screen using Deary- Liewald Reaction time tester.²

CFFF

CFFF measuring instrument is a Portable device, in-house built LED based instrument. Monochromatic red LED light of wave length 630nm, fixed on white back ground is used as Flickering light source. Frequency adjustment done by software based variable frequency square wave oscillator (10-50 Hz). Frequency measured from the recorded data using audacity software. Subjects were tested in a minimally illuminated room, with the CFFF

measuring device kept at a distance of 30cm. Subjects will be properly instructed, asked to respond by lifting the hand and will be tested by increasing and decreasing the frequencies. When the frequency is increased, at one point the flickering stops and light is perceived as a steady source. If the frequency is decreased from higher levels at one point flickering appears. Both ascending and descending frequencies were recorded and the mean of the two is taken as CFFF.

Result:

Data are expressed as Mean± SD. Paired student's t test was used to compare the stress level, cognitive function scores, CFFF, SRT and CRT between both the phases of menstrual cycle. Pearson's correlation was used to correlate stress level and cognitive function parameters (cognitive function scoring, CFFF, SRT, CRT) in both the phases of menstrual cycle.

Table: 1 Comparison of stress, critical flicker fusion frequency and reaction time during both the phases of menstrual cycle

	PSS	CFFF (HZ)	SRT (msec)	CRT (msec)
LUTEAL	20.77±6.63	30.13±3.19	308±66.58	513±132
FOLLICULAR	19.43±5.44	30.80±3.45	297.2±4.66	474±88
P value	0.29	0.24	0.29	0.25

PSS- perceived stress scale, CFFF- critical flicker fusion frequency, SRT- simple reaction time, CRT- choice reaction time

Table: 1 shows that stress level increased in the luteal phase compared to follicular phase. CFFF increased in the follicular phase. Both the reaction time increased in the luteal phase compared to the other phase but none of them showed statistical significance

Table: 2 Comparison of cognitive function test scores during both the phases of menstrual cycle

Phases of menstrual cycle	MMS E	DSST	LDST	WMS - spatial addition	WM S- design

LUTEAL	27.27 ±2.13 2	25.63 ±4.42	41.57 ±6.27	3.06± 1.36	2.93 ±1.5 5
FOLLICULAR	27.90 ±2.07	26.70 ±5.61	42.30 ±7.42	3.83± 1.315	3.43 ±1.2 7
P value	0.22	0.33	0.50	0.01*	0.06

MMSE- mini mental status examination, DSST- digit symbol substitution test, LDST- letter digit substitution test, WMS- Wechsler memory scale * P< 0.05- statistically significant

Table: 2 shows that all the cognitive function test scores shows a trend of increase in the follicular phase compared to the luteal phase but not statistically significant. Spatial addition sub-test was significantly increased in the follicular phase.

Table: 3 Correlation between stress score and critical flicker fusion frequency and reaction time during both the phases of menstrual cycle

PSS	CFFF		SRT		CRT	
	r	p	r	p	r	p
LUTEAL	- 0.08	0.6 5	0.25	0.17	0.03	0.98
FOLLICULAR	- 0.35	0.0 5	0.07	0.68	0.08	0.67

Table: 3 indicates that CFFF is negatively correlated with stress in both the phases of menstrual cycle and SRT, CRT is positively correlated with stress in both the phases of menstrual cycle. None of the parameters shows significant correlation.

Table: 4 Correlation of stress score and cognitive function test scores during both the phases of menstrual cycle

PSS	WMS-spatial addition		WMS-design	
	r	p	r	p
LUTEAL	0.20	0.26	0.14	0.45
FOLLICULAR	-0.17	0.36	0.10	0.58

Table: 5 Correlation of stress score and cognitive function test scores during both the phases of menstrual cycle

PSS	MMSE		DSST		LDST	
	r	p	r	p	r	p
LUTEAL	0.0 8	0.6 6	- 0.15	0.4 1	0.1 6	0.3 7
FOLLICULAR	- 0.0 8	0.6 4	- 0.01	0.9 5	0.2 1	0.2 5

Table:4,5 MMSE, DSST and WMS-spatial addition sub test showed negative correlation with stress in follicular phase whereas only DSST showed negative correlation with stress in luteal phase of menstrual cycle.

Discussion:

Increased stress in the luteal phase as indicated by our PSS scoring in table: I might be due to ovarian hormones acting on the HPO axis, alters the stimulation of sympathetic nervous system leading to altered neurotransmitters and other brain functions.¹³ In our study during luteal phase among the 30 subjects 4 females had low stress scoring of 0-13, 21 females showed moderate stress level of 14 -36, 4 females had high stress score of 27- 40. Whereas in follicular phase 4 females showed low stress level and 26 showed moderate stress level and only 1 showed high stress scoring. Thus during luteal phase females in moderate stress score were jumped in to high stress level in our study which showed that female sex hormones have some effect on stress level along the different phases of menstrual cycle.

According to Robin et al. the effect of female sex hormones on HPO axis and its activation of stress hormones like cortisol, epinephrine and nor-epinephrine was more pronounced in females with premenstrual syndrome than with normal menstruating females.¹⁴ This might be the reason for insignificant increase in the stress level in luteal phase compared to follicular phase in our study which constitutes normal menstruating females without any premenstrual syndrome. Lavello et al. reported that exogenously administered nor-adrenergic

antagonist reduce the stress related neural responsiveness and interconnectivity, further emphasizes that stress hormones like epinephrine and cortisol plays an important role, and its level gets modified by the ovarian hormonal level especially estrogen and progesterone.¹⁵

Stress can modify cognition via epinephrine and slowly via glucocorticoids. Thus stress has inverse relation with cognition. This is similar to our result as shown in table:III. According to Taylor and Raskind et al. cognitive emotion related to prefrontal cortex gets improved by administration of prazosin which blocks alpha 1 adrenergic receptors.¹⁶ This is similar to our study as shown by table: I & II which showed that cognition was increased in the follicular phase compared to luteal phase which showed increased stress level. Our results were similar to the results got by Smith et al., who reported increase in cognitive performance in the early and late follicular phase compared to other days of the menstrual cycle.¹⁷

According to Latha et al. increase in cognition in the follicular phase might be due to the positive effect of estrogen on learning and memory.⁹ Walder et al. reported that increase in estrogen and concomitant decrease in cortisol during early follicular phase and cortisol level increase in the luteal phase further support our findings.¹⁸ Estrogen can easily pass through BBB and modulate the neuronal activity. The limbic system and prefrontal cortex which controls cognition and emotion, have high density of estrogen receptors.¹⁹ Estrogen was known to improve the memory and performance. Increased level of brain derived neurotrophic factor in the luteal phase showed that BDNF is inversely correlated with cognition. Increase in performance in the follicular phase might be due to kindling effect of estrogen. It also affects circadian rhythm activity and central functioning between hypothalamus and cerebral cortex. Women with PMDD showed pronounced impairment in cognitive performance and mood changes.²⁰ Studies on postmenopausal women showed that cognitive performance increases with hormonal replacement therapy. Effect of estrogen on cognition is more pronounced in menopause with treatment than with eumenorrhoeic females.²¹ Stroop test performance and its relation to estrogen

level showed that attention level decreases with decrease in estrogen level.²² Estrogen was known to have a protective role in Alzheimers disease.²³ Reaction time being a sensitive indicator of cognitive dysfunction increased in luteal phase but was not statistically significant. Increased SRT and CRT (as shown by table I) might be due to estrogen and progesterone causing salt water retention affecting axonal conduction and the neurotransmitter availability.⁷ According to Vijetha et al. CFFF indicates cortical arousal and cognition.¹¹ Being the indicator of cognition CFFF was found to decrease when stressors of different kind increase.²⁴

Conclusion:

Thus decreased stress level and increased cognition during follicular phase might be due to estrogen and decreased cognition and increased stress might be due to progesterone antagonizing the effect of estrogen in luteal phase of menstrual cycle in young healthy females

IMPLICATION

This study helps in early detection of stress induced cognitive decline among the adolescent females and its influence by the menstrual cycle. Thus tasks requiring fast reaction like emergencies during driving, training in sports has to be done with extra caution during the luteal phase.

Health education can be given to the students and general public to decrease the stress level and to increase the cognition, using stress management strategies like music therapy and regular practice of YOGA.

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