

Research Article

Menstrual Cycle Phase Influences on Neurocognitive Functions: A Computerised Psychometric Assessment

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Abstract

Female menstrual cycle phases have a significant impact on the nervous system. Sex differences in cognitive abilities have been related to sex hormones, but it is more controversial. The present study we investigated the influence of the menstrual cycle and sex differences on high brain functions by measuring them with computerised psychometric tests.

Our study was conducted on 25 healthy, naturally cycling females and 30 healthy males between the ages of 18 and 25 who participated voluntarily. The female participants completed three test sessions (early follicular phase, the late follicular phase, and the luteal phase). We measured sex hormone concentrations in blood samples collected three times from female and one time from male. Cognitive and motor skill tests were performed, which consisted of reaction time, decision making in stress, reasoning ability, and visual memory. In addition, the Beck Depression Inventory, State-Trait Anxiety Inventory-1 (STAI-1), and State-Trait Anxiety Inventory-2 (STAI-2) were applied to determine participants' moods as well as their short- and long-term anxiety symptoms. Decision making in stress and visual memory were significantly increased during the luteal phase compared to the early, the late follicular phases and male. The reaction times were significantly decreased male compared to the follicular phase.

The findings suggested that sex steroid hormone levels, fluctuating according to menstrual cycle phases, might have neuromodulatory effects on high brain functions.

INTRODUCTION

Neurocognitive and motor skills are differences depending on sex hormones in males and females. The menstrual cycle is a physiological phenomenon that occurs during the reproductive lifetimes of women [1]. The menstrual cycle is generally divided into the follicular (early and late) and luteal (early and middle) phases. The follicular phase is the time from menstruation to ovulation (typically on the 14th day), while the luteal phase occurs between ovulation and the beginning of the next menstrual cycle. During the menstrual cycle, considerable changes have been observed in levels of estrogen and progesterone hormones, both of which are sex steroids. Estrogen and progesterone hormone levels are low during the early follicular phase, while the estrogen hormone level increases significantly during the late follicular phase and peaks 24–36 hours before ovulation. The progesterone hormone level increases during the early and middle luteal phase, while the estrogen hormone level reaches a second peak level parallel to the progesterone level [2].

Despite years of research into the influence on emotions of the menstrual cycle and sex steroid hormones and their effects on behavior, cognition, and neuroprotection, their effects on the brain and peripheral nervous system remain unclear [3,4]. Many studies have been conducted to demonstrate that estrogen influences the electrical activity of neurons both centrally and peripherally. The effects of estrogen on neuronal growth, neuronal differentiation, and the formation of synaptic connections have also been observed [5,6]. Sex-related differences in cognitive abilities may depend on sex-hormones and their serum concentrations [7]. However, the effects of sex hormone and menstrual cycle on cognitive strategies have yielded inconsistent results. Most studies focus on changes behavioral performance measures. Some researchers have proposed that there is a difference in cognitive skills between the sexes, and the cognitive performance findings in females have been associated with the hormone level changes that occur during the menstrual cycle [8]. It has been thought that differences in various motor and cognitive skills in males and females result from the effects of sex

hormones. For example, males tend to perform better in terms of spatial abilities and gross motor skills than females, whereas females tend to perform better than males in terms of verbal abilities, perceptual speed-accuracy, and fine motor skills [6]. The sex-specific cognitive ability difference was observed during spatial navigation, by relative hormone increases during the luteal phase of the menstrual cycle [9]. While some researchers have proposed that menstrual cycle-dependent rather than cognitive changes emotion-related changes high progesterone levels are associated with increased amygdala reactivity and increased emotional memory [10]. However, functional imaging studies suggest that not all reflected at the menstrual phase-related changes performance level [11]. Recent studies conclude that the changes in brain activation patterns on spatial navigation and verbal fluency are similar during both tasks [12]. We argue that in human studies there are inconsistent results regarding cognitive changes along the menstrual cycle and further methodological improvements are needed in this regard.

We aimed to investigate the relationship between healthy female that during the phases of the menstrual cycle, and males decision-making ability in stress, visual memory, reasoning ability, reaction time by psychometric method, which is a computer-assisted method.

METHODS

Participants

In this study, participants consisted of 25 healthy young female (mean age: 21.00 years, SD =2.08 years) and 30 healthy young male (mean age: 21.26 years, SD =1.82 years). The participants had free of any medication and no history of psychological, neurological or endocrinological disorders. Female participants did not take hormonal contraceptives and they had a regular menstrual cycle with a mean duration of 29.72 days (SD = 2.23 days, range: 28–33 days). All participants were volunteer students who had achieved a general qualification for university entrance, i.e. male and female did not differ in educational status. Age also did not differ in male and female. All participants gave the informed written consent to participate in the study. The study was carried out in compliance with the Declaration of Helsinki.

Procedure

The women were tested in three different cycle phases. The early follicular phases were scheduled of menstruation from the onset of menses up to ninth days, i.e. before the estradiol peak (mean cycle day: 3.20, SD = 0.86). The late follicular phases were scheduled two days before ovulation the onset of next menses (mean cycle day: 13.40, SD =1.83). The luteal phases were among seven days after ovulation onset of next menses (mean cycle day: 22.12, SD =2.08). According to their early follicular, late follicular and luteal phase, each female was tested three times to realize the changes in estradiol and progesterone hormone levels. Each male was once tested. Daily blood samples were taken after applying psychometric tests between 10:00 a.m and 12:00 p.m. Male and for one complete menstrual cycle in female, and estradiol (E2) hormone level, progesterone hormone level, total serum testosterone hormone level, sex hormone binding

globulin (SHBG) level, free testosterone hormone level (men only) were measured to determine gonadal hormones (Tables 1,2). We applied the Beck Depression Inventory, STAI 1 (state anxiety) scale, STAI 2 (trait anxiety) scale for the evaluation of the psychological status and depressive symptoms (Tables 1,2). These scales used to measure psychological status are grouped as paper-pen tests. The STAI 1-State anxiety scale consists of asking people to describe how they feel at a 'particular moment in time'. This scale evaluates involve the intensity of a person's feelings of tension, nervousness, worry, and apprehension. STAI 2 trait anxiety scale, measures the general tendency to worry, especially in social situations that pose some threat to selfesteem [13]. STAI 1 and 2, which contain questions about how an individual feels, are scales of 20 items. Beck Depression Inventory includes 21 questions in total. It is a scale that evaluates individuals physically, mentally and cognitively [14]. Beck Depression Inventory is a 21-item self-report measure that assesses depressive symptoms and their severity in adolescents and adults. The marked items are added together to determine the total score, and higher scores indicate higher depression levels. Beck Depression Inventory is widely applied both in research and clinical practice [15].

Tasks

Cognitive and motor skill tests were performed in a computerised Vienna Test System [16], usually in the "Standardized Isolated Test Chamber" (illuminated, well-ventilated, etc.) between 10:00 a.m and 12:00 p.m. On each occasion of testing, a broad battery of cognitive and motor tasks was individually administered to each participant. All the tests were recorded by the computer. Then the obtained data were statistically assessed and analyzed.

Psychometric tests applied: Determination Test (DT); This test measures reaction accuracy, reactive stress tolerance, decision making in stress. In this test prepared in response mode, 20 stimuli for trial on a computer screen and 540 stimuli for the actual test are 834, 948, and 1078 ms. presented with speed. The number of correct answers from the determination test was recorded as the number of stimuli (DT accuracy score) that responded correctly from 540 stimuli. Determination reaction time (DT sec.), velocity median value of the correct responses to stimuli was recorded in seconds. Reaction Test Time (RT msec.); The presentation of an optical and/or acoustic stimulus for one second is such a simple reaction to that stimulus occurs. Raven's Standard Progressive Matrices (SPM score); This test measures reasoning and nonverbal intelligence. In the test consisting of 32 questions on the computer, it was asked to understand and evaluate the relationships between abstract visual shapes in accordance with observation and logic. Tachistoscopic Traffic Perception Test (TAVT accuracy score); In this test visual memory ability by briefly presenting pictures of traffic situations. Assessment of visual memory ability and skill in obtaining an overview [16].

Statistical Analysis

Power of the sample was estimated using g* Power 3.1.9.4. The minimum sample size was calculated as 28 for 0.25 effect size, 5% margin of error, 80% confidence interval, two groups, and 3 measurements. In our study, the nonparametric triple

related samples Friedman test was used to statistically compared the cognitive, motor functions of the early follicular, late follicular, and luteal phase in the menstrual cycle of females. Triple related samples Friedman test significance values of women's menstrual phases were adjusted with Bonferroni correction for post-hoc. Significant parameters according to the triple related samples comparison Wilcoxon test was used for pairwise related samples (early follicular-late follicular, early follicular-luteal, late follicular-luteal) comparisons and $p < 0.05$ values were considered significant. Mann-Whitney U test was applied to the pairwise groups that were divided into male-female. All statistical analyses were calculated by using SPSS version 15.0 (SPSS Inc, USA).

RESULTS

The median, minimum, maximum, p values of cognitive skills, motor skills are shown in the figures below including groups: women's menstrual phases group and women's menstrual phase-men group.

Table 1 have shown estradiol, progesterone, total testosterone, SHBG, Beck Depression score, STAI 1 score, STAI 2 score levels in women's menstrual phase. According to Table 1, hormone levels in the menstrual phases significantly changed ($p < 0, 05$). Depression and anxiety values are to evaluate the change in the psychological state according to cycle phases. There is no significant change in the psychological state according to cycle phases ($p > 0, 05$).

Table 2 have shown total testosterone, free testosterone, SHBG, Beck Depression score, STAI 1 score, STAI 2 score levels in men. According to Table 2, total testosterone and SHBG in the early and late follicular phases and men significantly changed ($p = 0,000$, $p = 0,000$ respectively). STAI 2 scores was significantly increased during the luteal phase compared to men ($p = 0,013$). Beck Depression and STAI 1 scores was significantly decreased during the late follicular ($p = 0,025$, $p = 0,047$ respectively) and luteal phase (STAI 1 scores $p = 0,046$) compared to men.

Table 1: Median, Min, max values of Hormones and Emotional Status in Women's Menstrual Phase

Hormones and emotional status median parameter values for each of the analyses are shown for the early follicular phase ($n = 25$), late follicular phase ($n = 25$) and luteal phase ($n = 25$), as well as the results of Chi-Square (assuming nonparametric) comparing the parameter estimates between the three menstrual phase.

Parameters	Early Follicular			Late Follicular			Luteal			X ² (2)	p
	Median	Min.	Max.	Median	Min.	max	Median	Min.	Max.		
Estradiol (pg/mL)	40,00	20,00	79,00	134,00	48,00	550,00	121,00	62,00	419,00	46,345	,000
Progesterone (ng/mL)	0,50	0,16	1,80	0,69	0,10	3,74	6,95	0,77	18,80	46,565	,000
Total Testosterone (ng/mL)	0,38	0,12	0,79	0,57	0,29	1,03	0,42	0,24	0,85	7,095	,029
SHBG (nmol/L)	63,80	18,40	105,00	61,40	17,70	150,00	62,60	23,50	162,00	,859	,651
Beck Depression score	10,00	2,00	21,00	5,00	0,00	22,00	6,00	0,00	29,00	5,286	,071
STAI 1 score	42,00	28,00	59,00	41,00	33,00	53,00	40,00	31,00	58,00	,420	,811
STAI 2 score	47,00	36,00	60,00	47,00	31,00	55,00	47,00	34,00	60,00	1,844	,398

Abbreviations: Min: Minimum; Max: Maximum; SHBG: Sex Hormone Binding Globulin; STAI: State-Trait Anxiety Inventory; X² (2): Chi-Square (differences)

p value was calculated using the Kruskal Wallis Test. $p < 0,05$ values were considered significant.

According to Table 3, the median DT accuracy during the luteal phase in all women ($n = 25$) was significantly higher than their early follicular phase ($p = 0,000$), the median DT (sec.) during the luteal phase was significantly shorter than their early follicular phase ($p = 0,002$), the median TAVT accuracy during the luteal phase was significantly higher than their early follicular phase ($p = 0,049$), the median SPM score during the luteal phase was higher than their early follicular phase but it was statistically non-significant ($p = 0,085$) and the median RT (msec.) during the luteal phase was shorter than their follicular phases but it was statistically non-significant ($p = 0,307$).

According to Table 4, the median DT accuracy during the luteal phase in women was significantly higher than men ($p = 0,029$). The median DT (sec.) in men was significantly shorter than women's early follicular phase ($p = 0,019$). The median RT (msec.) in men was significantly shorter than women's early follicular phase and late follicular phase ($p = 0,006$, $p = 0,026$ respectively). The median TAVT accuracy in men was significantly higher than women's early follicular phase ($p = 0,023$).

According to Figure 1 the median DT accuracy (score) was significantly increased during the luteal phase compared to the early follicular phase ($p = 0,000$), the median DT accuracy (score) was significantly increased during the luteal phase compared to men ($p = 0,029$).

According to Figure 2 the median DT (sec.) was significantly decreased during the luteal phase compared to the early follicular phase ($p = 0,002$), the median DT (sec.) was significantly decreased men compared to the early follicular phase ($p = 0,019$).

According to Figure 3 the median RT (msec.) was significantly decreased men compared to the early follicular phase and the late follicular phase ($p = 0,006$, $p = 0,026$ respectively) and the median RT (msec.) was decreased during the luteal phase compared to the follicular phases but it was statistically non-significant ($p = 0,307$). According to Figure 4 the median TAVT accuracy (score) was significantly increased during the luteal phase compared to the early follicular phase ($p = 0,049$), the median TAVT accuracy was significantly increased men compared to the early follicular phase ($p = 0,023$).

Table 2. General Distribution of Hormones and Emotional Status in Men

Hormones and emotional status median parameter values for each of the analyses are shown for the early follicular phase (n = 25), late follicular phase (n = 25), luteal phase (n=25) and men (n=30) as well as the results of Mann-Wdhitney U Test (assuming nonparametric) comparing the parameter estimates between the three menstrual phase and men.

Parameters	Early Follicular			Late Follicular			Luteal			Men		
	median	min	max	median	min	max	median	min	max	median	min	max
d	0,38 ^a	0,12	0,79 ^d	0,57 ^a	0,29	1,03	0,42	0,24	0,85	4,06 ^b	2,50	6,11
SHBG (nmol/L)	63,80 ^a	18,40	105,00	61,40 ^a	17,70	150,00	62,60	23,50	162,00	23,30 ^b	4,21	39,40
Beck Depression score	10,00	2,00	21,00	5,00 ^a	0,00	22,00	6,00	0,00	29,00	9,00 ^b	2,00	24,00
STAI 1 Score	42,00	28,00	59,00	41,00 ^a	33,00	53,00	40,00 ^a	31,00	58,00	44,50 ^b	33,00	51,00
STAI 2 score	47,00	36,00	60,00	47,00	31,00	55,00	47,00 ^a	34,00	60,00	45,00 ^b	30,00	65,00

Abbreviations: Min: Minimum; Max: Maximum; SHBG: Sex Hormone Binding Globulin; STAI: State-Trait Anxiety Inventory

p value was calculated using the Mann-Whitney U Test. **a,b** the top icons show differences between the groups. There are significance between the different icons (p<0,05).

Table 3: Median, Minimum and Maximum Values of Cognitive and Motor Skills in Women's Menstrual Cycle Phases

Cognitive and motor skills median parameter values for each of the analyses are shown for the early follicular phase (n = 25), late follicular phase (n = 25) and luteal phase (n=25), as well as the results of Chi-Square (assuming nonparametric) comparing the parameter estimates between the three menstrual phase.

Tests	Early Follicular			Late Follicular			Luteal			X ² (2)	p
	Median	Min.	Max.	Median	Min.	Max.	Median	Min.	Max.		
DTaccuracy	254,00 ^a	189,00	320,00	282,00	185,00	348,00	291,00 ^b	196,00	329,00	14,73	0,000
DT(sec.)	0,76 ^a	0,62	0,90	0,72	0,61	0,86	0,68 ^b	0,60	0,85	12,90	0,002
SPMscore	105,00 ^{n.s}	84,00	132,00	109,00 ^{n.s}	91,00	132,00	109,00 ^{n.s}	97,00	123,00	6,64	0,085
TAVTaccuracy	47,00 ^a	43,00	51,00	49,00	43,00	54,00	49,00 ^b	45,00	53,00	6,28	0,049
RT(msec.)	552,00 ^{n.s}	413,00	710,00	535,00 ^{n.s}	442,00	803,00	524,00 ^{n.s}	442,00	686,00	2,36	0,307

Abbreviations: Min: Minimum; Max: Maximum; X² (2): Chi-Square (differences)

p value was calculated using the Friedman test. ^{a,b}p<0,05 Significance values have been adjusted by the Bonferroni correction for post-hoc. ^{n.s}p>0,05

Table 4: Comparison of Median, Minimum and Maximum Values of Cognitive and Motor Skills in Women and Men

Cognitive and motor skills median parameter values for each of the analyses are shown for the early follicular phase (n = 25), late follicular phase (n = 25), luteal phase (n=25) and men (n=30) as well as the results of Mann-Whitney U Test (assuming nonparametric) comparing the parameter estimates between the three menstrual phase and men.

Tests	Early Follicular			Late Follicular			Luteal			Men		
	Media n	Min.	Max.	Median	Min.	Max.	Median	Min.	Max.	Median	Min.	Max.
DT accuracy	254,00 ^a	189,00	320,00	282,00	185,00	348,00	291,00 ^b	196,00	329,00	258,00 ^c	196,00	379,00
DT(sec.)	0,76 ^a	0,62	0,90	0,72	0,61	0,86	0,68	0,60	0,85	0,69 ^b	0,50	0,85
SPM score	105,00	84,00	132,00	109,00	91,00	132,00	109,00	97,00	123,00	109,00	84,00	132,00
TAVT accuracy	47,00 ^a	43,00	51,00	49,00	43,00	54,00	49,00	45,00	53,00	49,50 ^b	38,00	55,00
RT (msec.)	552,00 ^a	413,00	710,00	535,00 ^a	442,00	803,00	524,00	442,00	686,00	505,50 ^b	407,00	804,00

p value was calculated using the Mann-Whitney U Test for each group. ^{a,b,c}p<0,05

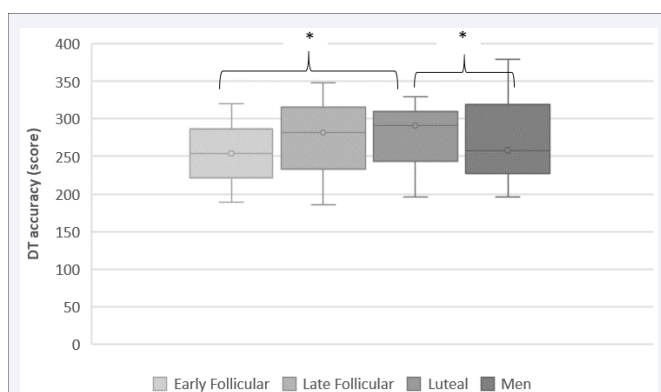


Figure 1 Comparison of Median, Minimum and Maximum Values of DT Accuracy (score) in Women's Menstrual Phase and Men. *p < 0.05.

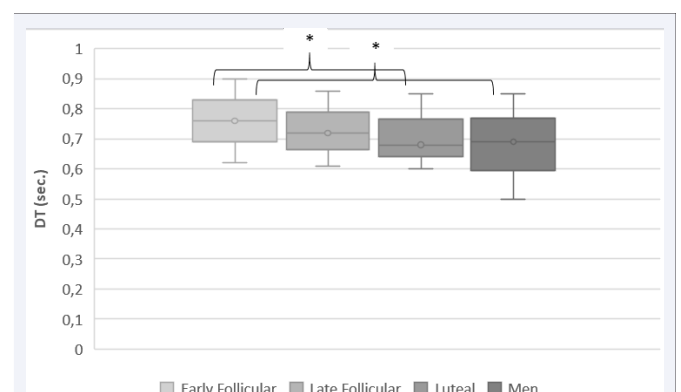


Figure 2 Comparison of Median, Minimum and Maximum Values of DT (sec.) in Women's Menstrual Phase and Men. *p < 0.05.

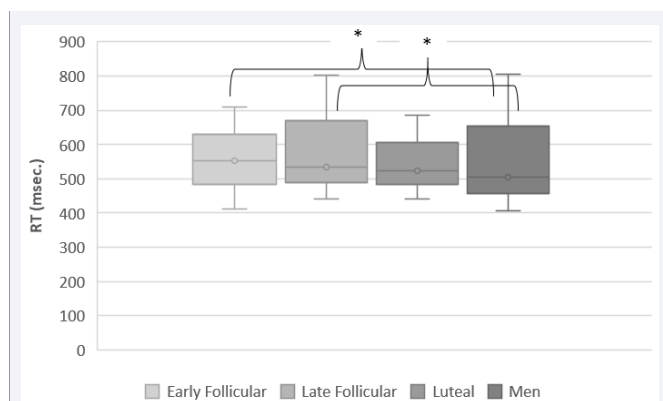


Figure 3 Comparison of Median, Minimum and Maximum Values of RT (msec.) in Women's Menstrual Phase and Men. * $p < 0.05$.

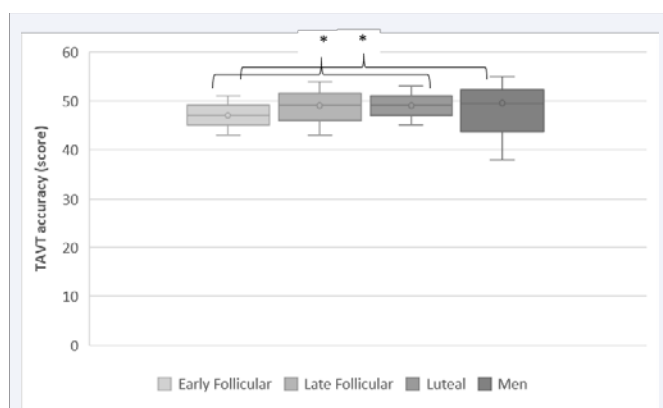


Figure 4 Comparison of Median, Minimum and Maximum Values of TAVT Accuracy (score) in Women's Menstrual Phase and Men. * $p < 0.05$.

DISCUSSION

The present study has been designed to investigate sex, menstrual cycle on the neurocognitive and motor skill using computerised test methods. We observed that the reactive stress tolerance, reaction accuracy, reaction speed and visual memory were increased during the luteal phase (high progesterone) compared to the early follicular and the late follicular phase (low progesterone), furthermore the reaction time was decreased male compared to female menstrual cycle phases, but the reaction accuracy was increased during the luteal phase compared to male (Figures 1-4). It can be observed that there are effects of sexual dimorphism in cognitive-motor skills. There are significant differences in emotional state between men and women. Depression and state anxiety was decreased during the late follicular and luteal phase compared to male but trait anxiety was increased during the luteal phase compared to male (Table 2). The effects of hormones fluctuating in the menstrual cycle phases are thought to cause sexual dimorphism. The findings of our study support many previous menstrual cycle studies, but the most striking feature of the present study is that these findings were determined methodologically by computerised and quantitative data. In the study measured the simple reaction time in female with normal cycles, it was found that the reaction

time gradually increased in all phases except the menstruation phase [17]. Consistent with the literature, we found that the reaction accuracy and speed of decision making in stress and the simple reaction time decreased during the early and late follicular phase and increased during the luteal phase. We can say that the increased levels of estrogen and progesterone hormones during the luteal phase affect decision-making and speed. The relationship between hormone levels and cognitive skills should be investigated with more people in the future. The luteal phase, which is the stage of preparation for pregnancy, positively influences the sensory and motor coordination of female. Researchers who compared the spatial and motor performances during the mid-luteal and menstrual phases in female, claimed that the mid-luteal phase performance was higher than the performance during the menstrual phase [18]. Consistent with this study, we found that female had higher cognitive and motor skills at the time of progesterone and estrogen elevation (mid luteal phase) than the follicular phase (menstrual phase) (Figure 1,2,4) (Table 3). Mental rotation test was performed during menstruation and ovulation phase in female and in male. Compared to all phases of female, it was observed that the reaction time of male was faster and the number of errors was lower [19]. In our study, consistent with this literature, it was found that male's reaction time was faster than all menstrual phases of female. In our study, although it was found that female's reaction accuracy during the luteal phase was higher than male's, the reaction time of male was faster than all menstrual phases of female (Figure 1-3) (Table 4). This finding is consistent with the literature. In one study, it was found that female in non-menstrual phases had a better working memory than male [20]. Consistent with this study, we observed that visual memory of female during the early follicular phase was lower than that of male. The visual memory performance increased during the late follicular and luteal phase in female (Figure 4). According to the study, the cognitive ability of female was similar during the preovulatory phase compared to male, and the visual reaction time of male was higher than that of female during the postovulatory phase. Stroop test was used as an other cognitive test and female's reading color interferences were found better than male. Reseachers asserted that the difference in cognitive skills in different tasks may be due to the changes in sex hormones [21]. Our study supports Chandrakala's assertion that there was a difference in cognitive skills between male and female. Contrary to their findings, while the reactive stress tolerance and reaction accuracy of female was higher during the luteal phase (postovulatory) in our study, it was found that male's reaction time and visual memory performance were higher than the early follicular phase (preovulatory) of female. In another study, in which visual memory performance of female in the menstrual cycle was measured, visual memory scores during the menstrual phase were lower than during the luteal phase [22]. In a recent study, it has been indicating that task performance for the working memory function is good in the premenstrual stage [23]. Like the studies, the luteal phase was the phase with the highest visual memory in our study. It can be said that estrogen hormone, which is high, and progesterone hormone, which is dominant, have a positive effect on cognitive and motor skills during the luteal phase. We think that cognitive skills increase during the luteal phase known as preparing for physiology of pregnancy. To sum up, the present study shows

the menstrual cycle effects differences in the brain functions by a computerised psychometric method. We observed that the female's brain functions were increased during the luteal phase compared to the other phases. High levels of estrogen and progesterone during the luteal phase, which is the process of preparation for pregnancy, have an effect on female's cognition and further studies are needed with more people including pregnant female. As a limitation of our study, although hormone levels and cognitive relationships were investigated with a small number of women, methodologically based on reliable measurement with computer may contribute to future studies. In conclusion, high brain functions measured by the psychometric method vary according to the stages of the menstrual cycle. Sex steroid hormones that fluctuate throughout the menstrual cycle can have neuromodulatory effects on higher brain functions.

DATA AVAILABILITY

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

ETHICAL STATEMENT & INFORMED CONSENT

The authors declare that they have no conflict of interest. All procedures performed in research involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors. Informed consent was obtained from all individual participants included in the research.

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