

Menstrual Cycle Phase Effects on Memory and Stroop Task Performance

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Abstract The present study examined differences in Stroop and memory task performances modulated by gonadal steroid hormones during the menstrual cycle in women. Thirty women with regular menstrual cycles performed a logical memory task (Wechsler Memory Scale) and the Stroop task. The results showed a significant difference in Stroop task performance between low and high levels of estradiol and progesterone during the menstrual cycle, but there was no significant difference in memory performance between the two phases, nor was there any significant mood change that might have influenced cognitive performance. These findings suggest that sex-related hormone modulation selectively affects cognitive functions depending on the type of task and low level secretion of estradiol appears to contribute to reducing the level of attention that relates to the prefrontal cortex.

Keywords Sex hormones · Menstrual cycle · Attention · Memory · Stroop test · Prefrontal cortex

Introduction

In an extensive review of studies concerning sex differences in human cognitive abilities, Kimura (1996) agreed with the

previous claims that women perform consistently better than men on tasks of verbal-related ability (e.g., memory recall and fluency) whereas men perform better than women on spatial ability-related tasks (Maccoby, 1966). Kimura proposed a model that explains why there is a sex difference in cognitive abilities. Kimura's model is sometimes called the "sex-related hormone theory" and the main points are that most of the sexually differentiated functions are strongly influenced by the amount of hormonal secretion, while the role of estrogen is critical in verbal ability and perceptual speed.

Many researchers who are interested in cerebral functional asymmetry have reported findings that cognitive performance in women appears to be modulated by the fluctuation of sex related hormone levels over the menstrual cycle (e.g., Hausmann & Gruturkun, 2000; Heister, Landis, Regard, & Schroeder-Heister, 1989; Hollander, Hausmann, Hamm, & Corballis, 2005; Purdon, Klein, & Flor-Henry, 2001), although there is no consistency among findings. For example, some studies have reported robust asymmetries in spatial bisection (McCourt, Mark, Randonovich, Willson, & Freeman, 1997) and figure recognition (Bibawi, Cherry, & Hellige, 1995) during the high steroid phase, mostly in the midluteal phase. Other studies have shown the most pronounced hemisphere asymmetry pattern in face recognition (Heister et al., 1989) and figural comparisons (Rode, Wagner, & Gunturkun, 1995) during menses, when steroid concentrations are low.

One of the possible reasons for these inconsistencies is that researchers have estimated the position in the cycle by counting the days backwards from the predicted starting date of the next menstruation, instead of measuring the serum concentrations of steroidal hormones directly from the blood samples of the participants. The levels of hormone secretion cannot be identified by only day counting since there are substantial individual differences in hormone secretion

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levels so that measuring from blood sample is crucially important to examine possible effects of hormonal influence on cognitive performances. Also, the reliability of hormonal concentration measurement by saliva assays is less than that of blood sample (Hampson, Finestone, & Levy, 2005).

Apart from the studies on the relation between sex-related hormones and functional cerebral asymmetry, we examined sex-related developmental changes in cognitive abilities that relate to prefrontal cortex function in middle-aged and elderly people (Hatta, Nagaya, & Onishi, 2005b). We hypothesized that, if sex-related hormones affect cognitive performance, then well documented sex differences, such as women's superior verbal abilities, as suggested by Kimura, must disappear after menopause in women.

Our previous study, which is part of the Nagoya University Cohort Study at Y-Town, found supportive data for this hypothesis (Hatta et al., 2005b). In that study, 512 participants in a rural town, ranging from 39 to 89 years of age, were given attention (digit cancellation test), verbal memory, and letter fluency tasks. Different developmental patterns were shown in attentional perceptual speed, logical memory, and letter fluency. That is, on the attention task, a significant sex difference (female advantage) was shown only among the 40-year-olds, and the female advantage was diminished after the 50s. On the logical memory task, a significant sex difference was shown only among the 40-year-olds, whereas it was not significant in the over 50 age groups. On the letter fluency task, a significant sex difference was not shown in the 40s but it was apparent in the 60- and 70-year-old age groups.

The findings showed that the sex difference in cognitive abilities does not remain stable throughout human life, especially in women, and strongly suggest that biological factors, such as sex-related hormones that contribute to prefrontal cortex function, seem to be related to age-related sex differences (Taketani & Maehara, 2001). The findings also indicate that sex-related hormones might have differential effects depending on the type of cognitive abilities, such as attention, memory, and verbal fluency.

These findings motivated us to devise a more precise examination of the influence of sex-related hormones on cognitive abilities, especially those related to prefrontal cortex function. Many previous studies have suggested that attention-related function is governed by the prefrontal cortex and that memory is governed by the medial temporal lobe (e.g., Baddeley, 2000; Lawrence, Ross, & Stein, 2002; Posner & DiGirolamo, 2000; Squire & Knowlton, 2002). Then, the present study was designed to assess two types of cognitive abilities, attention-related and memory factors, at different phases of the menstrual cycle in women as a preliminary trial. Blood assays of gonadal steroid hormones for all participants during each session can ensure a validation of the cycle phase and made it possible to test the relationship between the cortical area and the type of cognitive

performance. It was our primary concern to clarify whether sex-related hormonal modulation had a diffuse type of effect on cognitive function generally or sex-related hormones affected specialized areas, such as the prefrontal cortex (attention-related function), but not to the medial temporal lobe (memory-related function).

Method

Participants

Thirty healthy women (M age, 25.6 years; SD = 3.3; range, 20–34), with regular menstrual cycles (26–30 days), volunteered to participate in this experiment. All participants were nurses and naïve as to the hypothesis and were not given any compensation for their participation in the study. Of these, data from three women were excluded based on their hormonal assays (see below). None used oral contraceptives, hormonal replacement, or any other medication that could influence the central nervous system.

Procedure

All participants were tested twice, once during the menses and once during the midluteal phase, in a counterbalanced order. The order of memory and attention tasks was counterbalanced across participants. Both test sessions were conducted at nearly the same time of the day so as to reduce potential effects of circadian rhythms.

At the beginning of Session 1, the participants were given the instructions for the two cognitive tests and then the data on the menstrual cycle were collected. Additionally, participants' mood status was assessed by J-SACL (Stress-Arousal Check List, Japanese version; Hatta, 1995), in order to control for the possibility of potential premenstrual changes caused by gonadal hormones that might affect cognitive task performance (Boyle, 2002; Erez & Isen, 2002; George & Zhou, 2002; Hollander et al., 2005).

Following the study by Hollander et al. (2005) that examined sex hormone influences on the attention task, the women in this study were tested during the low steroid menses (cycle day 2–3) and the high steroid midluteal phase (cycle day 21–22), in order to yield the largest differences in progesterone and estradiol levels. Directly after every session, a blood sample was collected. Serum levels of estradiol and progesterone were analyzed by the an independent blood analysis laboratory (Medic Lab. Inc., Gifu city, Japan). The assessment of serum gonadal sex hormone level of each participant provided validation of individual cycle phases. To prepare the testing schedule of the experiment, the participants were required to confirm the onset of menses for the first or the second session.

The ethical committee of Nagoya University Graduate School of Environmental Studies approved this study and each participant provided written informed consent.

Measures

Each participant was evaluated for memory and attention function at two phases: Session 1 (menstrual phase) and Session 2 (midluteal phase) by the same examiner.

Memory Function

Memory function was evaluated by the logical memory task from the Japanese version of the Wechsler Memory Scale-Revised (WMS-R). On this task, the examiner read through a sentence that consisted of 25 segments twice, and the participants recalled the sentence orally. Two different sentences were employed across participants. On this test, the scores ranged from 0 to 25 points. In the original test manual, two indices of immediate recall and delayed recall conditions were prepared. However, the score of immediate recall condition was used for the analysis, because the Pearson's correlation coefficients between immediate and delayed recall condition was $r = .92$ (Hatta, Nagahara, Iwahara, & Ito, 2005a).

Stroop Test

The Stroop test was employed to evaluate attention and information processing speed (e.g., MacLeod, 1991; MacLeod & MacDonald, 2000). In this test, participants were required to name the color of words (red, yellow, blue, and green) that were printed in colors incongruent to the name of the color. The names of the colors were arranged randomly in an 8×5 matrix (Stroop condition) on an A4 size sheet (Hatta, Ito, & Yoshizaki, 2001). Participants were asked to perform tasks as fast and as accurately as possible. The time (s) required to complete the tasks and the errors were measured. However, the mean error response was 0.07% and therefore only time data were examined.

Mood Status

Participant's mood was evaluated twice at the beginning of Session 1 and 2 by the Japanese version of the Stress Arousal Checklist (J-SACL). The J-SACL (Hatta, 1995) was originally developed by Cox and Mackey (1985). This checklist consisted of two factors: stress (feeling of unpleasantness/pleasantness or hedonic tone) and arousal (wakefulness/drowsiness or vigor tone). On this checklist, participants selected the extent of a personal mood among four alternatives of exactly fits, largely fits, don't know, or does not fit for

each of 30 adjectives, such as irritable or calm. Both scores ranged from -15 to 30 . The normal standard of stress score ranges from 2 to 8 and arousal score from 1 to 6 .

The validity and applicability (repetitive application) were demonstrated in a study of teachers' stress by Hatta and Nishiide (1991), for nurses' stress by Hirose, Hatta, and Yoneda (1998), and for computer workers by Hatta, Yoshida, Kawakami, and Okamoto (2002), as well as for mood and cognitive function variations in long-term hospitalized patients with spine and hip fracture diseases (Hatta, Hasegawa, & Matsuyama, 2006).

Results

The main concern of this study was to examine the interaction of two types of cognitive tasks and two time phases (hormonal level change). However, it is crucially important to confirm that hormonal level differences existed between the two phases and mood changes did not affect cognitive performances. Thus, we first examined for validation of cycle phase and mood levels.

Validation of Cycle Phase

We followed Hollander et al.'s (2005) criterion of at least twice as high hormonal secretion level in the midluteal phase as in the menstrual phase. Based on this criterion, the data of three participants were not included in the following analyses. According to Rode et al. (1995), the level of estrogen is expected to be between 370 and 920 nmol/l during the midluteal phase and 35 – 185 nmol/l during the menses, and the level of progesterone between 10 and 100 nmol/l during the midluteal phase and 0 – 10 nmol/l during the menses.

Table 1 shows the levels of estradiol and progesterone in midluteal and menstrual phases of our participants. Both progesterone and estrogen levels in the midluteal phase of our participants were more than twice those in the menstrual phase. Paired t -tests showed significant differences between phases of progesterone, $t(26) = 7.49$, $p < .01$, and estradiol levels, $t(26) = 7.23$, $p < .01$. Thus, validation of the cycle phases of the participants was confirmed for our data; that is, the progesterone levels were significantly higher in the midluteal phase than in the menstrual phase.

Table 1 Hormonal modulation at the low steroid menses (cycle day 2–3) and the high steroid midluteal phases (cycle day 21–22)

| | Low level phase | | High level phase | |
|--------------------|-----------------|-------|------------------|-------|
| | M | SD | M | SD |
| Estradiol (nmol/l) | 25.67 | 19.52 | 97.10 | 51.38 |
| Progesterone | 0.91 | 0.30 | 9.99 | 6.47 |

Cognitive Performance

Memory Task

Table 2 shows the mean score of the logical memory task (number of words correctly recalled) as a function of hormonal modulation phases, i.e., in midluteal and menstrual phases. Paired *t*-tests were conducted for the score on the logical memory task. The result showed that there was no significant difference between two phases, $t(26) = 1.29$. The correlation between hormone level and memory task performance at midluteal and menstrual phases were not significant ($r = .15$ and $.11$, respectively).

Attention Task

Table 2 also shows the mean required time (s) for color names (Stroop condition) as a function of hormonal modulation phases. The analysis showed that the score of the Stroop condition in the menstrual phase was significantly higher than in the midluteal phase, $t(26) = 4.49$, $p < .01$. The correlation between hormone level and attention task performance at midluteal and menstrual phases were not significant ($r = .18$ and $.14$, respectively).

Mood Evaluation

Table 3 shows mean scores of Stress and Arousal factors on the J-SACL. To examine whether the mood status differed between the menstrual and the midluteal phase, paired *t*-tests were conducted for the Stress and Arousal factors. There

Table 2 Cognitive task performance at the low steroid menses (cycle day 2–3) and the high steroid midluteal phases (cycle day 21–22)

| | Low level phase | | High level phase | |
|----------------------------------|-----------------|-----|------------------|-----|
| | M | SD | M | SD |
| Stroop test (s) | 24.6 | 3.9 | 28.2 | 5.9 |
| Logical memory task ^a | 20.5 | 2.5 | 19.8 | 3.5 |

^a Absolute range, 0–25

Table 3 Stress and Arousal factor scores in J-SACL at the low steroid menses and the high steroid midluteal phases

| | Low level phase | | High level phase | |
|-----------------------------|-----------------|-------|------------------|-------|
| | M | SD | M | SD |
| Stress factor ^a | −4.04 | 10.75 | 0.00 | 10.31 |
| Arousal factor ^b | −7.19 | 7.74 | 1.37 | 7.06 |

^a Absolute range, −16 to 20

^b Absolute range, −10 to 14

were no significant differences for the Stress factor, $t(26) = 1.46$, or for the Arousal factor, $t(26) < 1.00$.

Discussion

In this study, we examined the hypothesis that sex-related hormone modulation affected on cognitive performance, by using blood assays of gonadal steroid hormones for all the participating women during each session, in order to ensure a validation of the cycle phase. Since most previous studies relied upon the usual method that estimates the position in the cycle by counting the days backwards from the predicted start date of the next menstruation, the validity of the findings for the effects of hormonal modulation on cognitive performances is not necessarily strong compared with blood assay confirmation. Therefore, although many studies have examined the relationship between cognitive performances and sex-related hormones, as shown in Kimura's (1996) review, we aimed to conduct more reliable examination of the relationship between sex-related hormone modulation and cognitive performance.

Hampson et al. (2005) reported the effect of menstrual cycle of healthy women on an implicit memory task. They reported that women at the menstrual phase could identify primed and unprimed stimuli at a more degraded level of fragmented objects compared to that of midluteal phase. However, they measured ovarian hormones by saliva assays, not blood assays.

Our primary concern was whether sex-related hormonal modulation, as measured by blood assay, was related to types of cognitive function. To this end, a memory task (evaluated by the logical memory task) and an attention-related task (evaluated by the Stroop test) were employed. According to MacLeod and MacDonald (2000), the Stroop test can be classified as a cognitive task that reflects attention. Based on the researchers who hypothesized hierarchical structures, such as target detection, sustaining, and filtering allocation in attention mechanisms, the Stroop test performance is believed to relate strongly to the sustaining and filtering allocation stages (Banich, 1997; Sohlberg & Mateer, 1989). Brain imaging studies have also identified the functional activation areas on Stroop test performance. Most studies have revealed that the frontal area, such as the supplemental motor area (BA 6), the frontal cingulate gyrus (BA 26), and the inferior parietal area (BA 44), affected Stroop test performance (Bench et al., 1993; Cater, Mintun, & Cohen, 1995; Leung, Skudlarski, Gatenby, Peterson, & Gore, 2000; Peterson et al., 1999, 2002).

A recent report by Swick and Jovanovic (2002) suggests a crucial role of the frontal cingulate gyrus (BA 26) on target selection in the attention allocation situation, such as a Stroop test task. On the other hand, it has been thought that a logical

memory task strongly reflects on the function of medial temporal lobes. Since the report of a patient who showed persistent amnesia despite preserved cognitive function other than declarative or episodic memory after resection of bilateral medial temporal lobes (Scoville, 1968), the crucial role of medial temporal lobes on memory function has been stressed. The results of recent studies to examine the neural substrates of the performance of various verbal memory tests using fMRI and PET studies are not necessarily consistent. Schacter and Wagner (1999) claimed that activation of anterior and posterior medial temporal lobes could be observed in a PET study whereas predominantly posterior medial temporal lobe activation only was shown in an fMRI study during encoding. However, recent fMRI studies have reported minimal medial temporal lobe activation during retrieval, and one fMRI study suggested that retrieval of verbal stimuli activated the middle and posterior hippocampus (Ino, Doi, Kimura, Ito, & Fukuyama, 2004). Johnson, Saykin, Flashman, McAllister, and Sparling (2001) reported that in addition to the left medial temporal lobe regions that are engaged during word processing, the right hippocampus and right frontal lobe are also involved in successful memory ability. Differential fMRI activation in medial temporal lobe structures depending on successful and unsuccessful recognition memory was also reported (Casasanto et al., 2002). As seen from these findings, neural substrates of verbal memory, such as on a logical memory task, are still controversial. It has recently been suggested that these “separatistic” views concerning cognitive function and region in brain imaging data may be outdated (Desenbach et al., 2006). However, though we have no crucial evidence at present, it may be possible that neural substrates of the logical memory task and the Stroop task do not overlap.

To address our primary concern, that is, whether sex-related hormonal modulation affected cognitive performance as a function of task demand, we employed two types of cognitive tasks: one relates primarily to the prefrontal cortex (Stroop task) while the other relates mainly to the medial temporal lobes (logical memory task). The findings revealed that sex-related hormonal modulation affected the attention-related performance whereas it did not have a strong effect on memory performance. That is, our findings suggest that the sex-related hormonal modulation selectively effects cognitive performance. Our findings seem to be consistent with the following studies.

A study by McCourt et al. (1997) suggested that steroid hormones might influence attention. In their study, participants were asked to use a pushbutton laser pointer and point toward a vertical line on a wall that exactly coincided with the participants' midsagittal plane. Participants tended to err to the left of the line (implying right hemisphere activation). They found that this bias was increased during the midluteal phase compared to the menstrual phase. Another study by

Hollander et al. (2005) examined differences in an “attentional blink” task modulated by steroid hormones during the menstrual cycle. Participants were required to detect a target item, and then a probe item, each of which could appear in either stream. If the probe item appeared 200 ms after the target, detection of the probe was impaired. This phenomenon was the “attentional blink.” They found an increased “attentional blink” during the midluteal cycle phase, suggesting that attention-related performance is effected by gonadal steroid hormones, in particular estradiol.

Why does sex-related hormonal modulation affect only attention-related performance but not memory performance? The answer is not clear at present, but the neural network mainly within the right hemisphere, or interhemispheric interaction, seems to relate strongly to the difference in attention performances by sex-related hormonal modulation. Larisch et al. (1998) speculated, though without clear description of mechanisms, that hormonal modulation induces the selective right hemisphere biochemical system changing on striatal dopamine receptors. Mead and Hampson (1996) reported relative suppression of performance in face recognition and a rhyming words task during the phase of high estradiol levels.

We should note that several findings are not consistent with our results. Miles, Green, Sanders, and Hines (1998) reported the findings of an influence of estrogen on verbal memory tasks, but not on other cognitive tasks, such as mental rotation. Houseman, Becker, Gather, and Gunturkun (2002) reported that progesterone reduced cerebral hemispheric asymmetries, presumably due to its glutamatergic and GABAergic effects, which might diminish the cortico-cortical transmission via corpus callosum. Alexander, Altemus, Peterson, and Wexler (2002) also showed that progesterone decreased intrahemispheric communication, which means that high estrogen levels in the luteal phase will suppress right hemisphere function while enhancing left hemisphere function. Hao et al. (2007) reported that layer III pyramidal neurons in dorsal prefrontal cortex were sensitive to ovarian hormone in female rhesus monkeys and it relates to synaptic plasticity during the menstrual cycle.

These studies strongly suggest the importance of further examination to address the issue as to whether sex-related hormone modulation selectively affects attention-related performance, and also the mechanisms associated with the selective action by the accumulation of different kinds of attention and memory related cognitive performance.

Finally, we examined whether the possible differences in cognitive performance by sex-related hormonal modulation are caused by mood changes induced by certain psychological factors in menstrual circulation. Our results suggest that this is most unlikely. The evaluation by J-SACL showed that stress factors changed slightly between the two phases in our experiment, but it was not statistically significant.

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