

Cognitive performance across the menstrual cycle

Efrat Barel*, Maayan Krispil, Inbar Yaari

Department of Behavioral Sciences, The Max Stern Academic College of Emek Yezreel, Emek Yezreel 19300, Israel

Abstract

Previous studies have demonstrated that ovarian hormones, namely estrogen and progesterone, affect cognitive performance. Higher levels of ovarian hormones have been shown to be positively associated with better performance in tasks that typically show female superiority, whereas lower levels have been found to be associated with better performance on tasks usually showing male superiority. The aim of the present study was to analyze the modulation effect of the menstrual cycle on various cognitive abilities. Thirty women with a typical menstrual cycle completed a cognitive battery that consisted of four cognitive tasks: Mental Rotation, the Water-Level test, Verbal Fluency, and Digit Span. The battery was completed at two time points – during the early follicular phase and during the ovulatory cycle phase. Results showed a significant cycle effect for mental rotation scores, such that women's scores were higher during the early follicular phase (under lower levels of estrogen) and lower during the ovulatory cycle phase (under higher levels of estrogen). Furthermore, a significant cycle effect for verbal fluency was found, such that scores were higher during the ovulatory cycle phase (under higher levels of estrogen) and lower in the early follicular phase (under lower levels of estrogen). No significant cycle effects were found for the Water-Level test or for the Digit Span task. The findings suggest that sex hormones, as reflected by menstrual cycle phase, selectively modulate cognitive performance.

Keywords: Menstrual cycle, Visuospatial abilities, Verbal abilities.

Accepted on October 22, 2019

Introduction

Sex differences in cognitive abilities have been widely studied. Although men and women do not demonstrate differences in general intelligence [1,2], men tend to outperform women in visuospatial abilities, whereas women tend to outperform men in some verbal abilities [2,3]. More specifically, research has found that men outperform women on various visuospatial tasks, such as navigation strategies and geographic orientation [4-6]. However, the largest effect size has been found for mental rotation [7-12]. Women have been shown to outperform men in verbal abilities, especially verbal memory [13,14] and verbal fluency tasks [7,15]. In other areas, such as vocabulary, verbal reasoning, and line orientation [16], sex differences findings have been inconsistent.

The mechanisms underlying sex differences in cognitive abilities involve a complex interplay between biological and environmental variables. Environmental factors include play experiences and socio-cultural gender stereotypes, which have been associated with higher performance in related cognitive skills [17-19]. Among the biological variables, research has suggested that endocrine factors, such as sex hormones, play an important role in the sex differences found in cognitive abilities [3]. Sex hormones, including androgens, estrogens, and progestins, can affect a wide range of organs, including the brain. These hormones exert the greatest effect during two sensitive periods in development: the first is during the prenatal and/or neonatal period and the second is during the postnatal period [3,20]. It has been suggested that these sensitive periods for hormonal secretion are associated with sex differences in cognitive abilities [16,21,22]. Researchers have termed these

hormonal effects as organizational (formation of the developing brain) and activational (activation of neural events) [3].

Activational influences of sex hormones on cognitive performance have been widely studied in humans. Evidence of cognitive differences resulting from activational effects comes from three main research directions: (a) the effects of hormone replacement on cognitive abilities in men and women; (b) the relationship between individual differences in hormone levels and cognitive abilities; and (c) links between normal hormone fluctuations and differences in cognitive abilities [21]. Results of the last one have shown inconsistent results [23]. In the context of the menstrual cycle, the natural fluctuation of ovarian hormones enables an investigation of the role of estrogen and progesterone on cognitive performance.

In the visuospatial domain, some studies have reported that women scored higher on some visuospatial tasks during the menstrual phase (when estrogen is low) as compared to the midluteal phase (when there is a high concentration of both estrogen and progesterone) [24,25]. Studies have also demonstrated variation in women's performance on mental rotation tasks in association with estrogen levels across the menstrual cycle. Better performance was found during the menses, when estrogen levels were low, in comparison with other phases of the cycle when estrogen levels were high [26-29]. Furthermore, some studies have shown that the magnitude of sex differences in mental rotation performance were reduced if women were tested at menses [30]. In the few studies that included estrogen and progesterone measures to validate menstrual phase, researchers found that performance on mental rotation tasks was negatively correlated with estrogen levels [25-

27,31], but was not significantly correlated with progesterone levels [26]. Although many studies have found significant differences in mental rotation performance across the menstrual cycle, not all studies provide support for these findings [32-35], perhaps due to methodological differences [26]. Regarding other visuospatial tasks, mixed findings have been demonstrated. For example, Hampson and colleagues found that women in the low estrogen stage of the menstrual cycle scored higher on the closure test (which tests object recognition based on shape cues) than women in the high estrogen stage. In contrast, Pletzer et al. [36] did not find significant performance differences in spatial navigation across phases of the menstrual cycle.

In the verbal and memory domains, performance differences across the menstrual cycle are inconsistent. Among the verbal tasks, some studies have demonstrated an improvement in verbal fluency during the high-hormonal luteal phase compared to the early follicular phase [29,34]. However, other studies reported no relationship between verbal performance and menstrual cycle stage [35,36]. In relation to memory tasks, a few studies supported the notion that higher levels of estrogen are associated with better working memory performance; women tested during the time in the menstrual cycle when estrogen levels were high scored higher and with fewer errors than women who were tested when estrogen levels were low [37,38]. Other studies demonstrated a decrease in visual memory scores coupled with a significant decrease in estrogen levels [39]. However, not all studies documented this association between estrogen levels and memory performance. For example, Mordecai, Rubin, and Maki [40] showed that women taking oral contraceptives exhibited enhanced verbal memory performance during the active pill phase, whereas no changes in verbal memory were apparent across the cycle among naturally cycling women. In addition, Phillips and Sherwin [39] did not find significant differences in performance on a digit span task, paired-associate learning, immediate and delayed paragraph recall, and immediate recall of visual material among women who were in the menstrual or luteal phases of their cycles.

The objective of the present study was to examine changes in women's cognitive performance across the menstrual cycle, including visuospatial, verbal and memory abilities. Visuospatial cognition is not a unitary concept; rather it refers to three main categories: spatial perception, mental rotation, and spatial visualization [11]. In the present study, visuospatial abilities were addressed through the use of mental rotation and spatial perception tasks, which typically show male superiority. Furthermore, the present study assessed verbal fluency and memory tasks, which are typically associated with female superiority. Given the primary role of estrogen fluctuations in cognitive performance, the present study assessed cognitive performance in two menstrual phases, one characterized by high estrogen levels (ovulatory cycle phase) and the other by low estrogen levels (early follicular). We hypothesized that

visuospatial performance would increase in the early follicular phase of the menstrual cycle, and that verbal and memory performance would increase during the ovulation phase.

Research Methodology

Participants

Thirty healthy undergraduate female students (mean age = 25.93 ± 3.29 years) from a college in the north of Israel participated in the study. All participants self-reported to be right-handed. Participants were recruited from various departments (behavioral sciences, social sciences, economics, and management information systems) through advertisements, and did not receive monetary compensation for their participation. All participants reported that they were in good physical health, had no psychiatric or neurologic illnesses, were not taking any psychoactive or hormone medications or substances, and were heterosexual. None of the women were currently using oral contraceptives, and all reported having a typical menstrual cycle of 27-29 days. Participants were tested twice: on the first day and on the 14th day of their menses, as determined by self-report. We chose these two timepoints because they represent two different phases in the menstrual cycle, one in which estrogen levels are typically at their highest and one in which estrogen levels are typically at their lowest. As such, we based our predictions of cognitive ability differences on these two time periods.

Measures

Participants responded to demographic questions (sex, age) and participated in four cognitive tests. All measures were completed using pencil and paper.

Cognitive test battery

Four types of tasks were presented to the participants: two verbal and two visuospatial cognitive tasks.

Verbal cognitive tasks

Digit span: Digits between 0 and 9 were presented in sequences ranging from 2 to 9 digits. Immediately after each sequence of numbers, participants were instructed to list the digits in the same serial order [41].

Verbal fluency: Participants were asked to generate as many words as possible beginning with three specified letters of the Hebrew alphabet (corresponding with the English letters A, B and D). Proper names and different forms of the same word (e.g. plurals) were not allowed. One minute was allocated for each letter. Participants' scores were determined by calculated as the mean of words generated for all three letters [41].

Visuospatial cognitive tasks

Mental rotation task: This task, based on Shepard and Metzler [42], involved five models. Pairs of photographs of each model were produced, in which the models appeared nearly identical,

except that they were rotated in space with respect to each other. Participants were presented with five models at a time and were instructed to decide which two models were the same by mentally rotating them in their head. Participants completed six trials of this task and received a score of 1 (correct) or 0 (incorrect) in each trial. Scores were then summed to create a total score for each participant.

The water-level test: In this task, based on Piaget and Inhelder's [43] original test, participants were shown images of 8 bottles tilted at varying angles in different directions. Participants were instructed to draw a line indicating where the water level would be if the bottle was filled halfway with water. The correct answer was always a horizontal line. If the participant's response was within 5 degrees of a horizontal line, it was coded as correct.

Procedure

The study was approved by the Institutional Review Board (IRB) of the college in which study procedures took place. After providing informed consent, participants completed a brief demographic questionnaire. Subsequently, participants completed the cognitive tests at two different timepoints once during the first day of their menstrual cycle (early follicular phase) and once on the 14th day of their menstrual cycle (ovulatory cycle phase). The order in which participants completed the tasks was counterbalanced, such that half of the participants started in the follicular phase and half started during ovulation.

Results

Participant characteristics

Thirty female students (mean age 25.93 ± 3.29 years) from various departments in a college participated in the study. Participants completed the cognitive tests at two different timepoints once during the first day of their menstrual cycle (early follicular phase) and once on the 14th day of their menstrual cycle (ovulatory cycle phase).

Scoring

For the digit span task, the correct sequences scores were summed to create a total score for each participant. For the

verbal fluency task, the mean of words generated for all three letters was calculated. For the mental rotation as well as the water-level task, correct scores were summed to create a total score for each participant.

Correlations between cognitive tasks

Correlations between task performances in each phase of the menstrual cycle are shown in Table 1. A positive correlation was found between performance on the Verbal Fluency task and on the Digit Span task during the early follicular phase only; a higher score on the verbal fluency task was correlated with a higher score on the Digit Span task. Positive correlations were also found between performance on the Verbal Fluency task and on the Water-Level task, both in the early follicular and in the ovulatory cycle phases; higher scores on the Verbal Fluency task were correlated with higher scores on the Water-Level task.

Cognitive abilities during the menstrual cycle

Table 2 shows the means, standard deviations, effects sizes (Cohen's *d*), and *t* and *p* values for cognitive performance as a function of menstrual phase. As expected, there was a significant phase difference for scores on the mental rotation task, with participants scoring higher in the early follicular phase as compared to the ovulatory cycle phase. In other words, participants performed more accurately on the mental rotation task when estrogen levels were lower. Furthermore, there was a significant phase difference for scores on the verbal fluency task, such that participants scored higher during the ovulatory cycle phase as compared to the early follicular phase. Thus, participants' performance on the verbal fluency test was enhanced during the menstrual cycle phase in which estrogen levels were higher. There were no significant differences in performance on the Water-Level Test or the Digit Span Test by menstrual cycle phase.

Discussion

In the present study, we examined whether cognitive performance changes as a function of female menstrual cycle phase. The results of the present study support previous findings regarding menstrual cycle influences on mental rotation and verbal fluency abilities. Specifically, participants performed

Table 1. Correlations between cognitive tasks during two phases of the menstrual cycle. Note: * $P < 0.05$, ** $P < 0.01$.

Variables	Early follicular				Ovulation			
	1	2	3	4	1	2	3	4
1 Mental rotation	-				-			
2 Water-level test	0.14	-			0.24	-		
3 Verbal fluency	-0.07	0.48**	-		-0.09	0.53**	-	
4 Digit span	0.08	0.16	0.44*	-	0.2	0.17	0.36	-

Table 2. Means (SD), *t*, *p*-values, and Cohen's *d* for cognitive performance as a function of menstrual phase. Note: * $P < 0.05$.

Variables	Early follicular	Ovulation	<i>t</i>	<i>d</i>
Visuo-spatial tasks				
Mental rotation	2.37 (1.40)	1.93 (1.26)	2.15*	0.23
Water-level test	5.90 (2.96)	5.63 (2.80)	0.94	0.07
Verbal and Memory tasks				
Verbal fluency	11.73 (4.25)	12.67 (4.70)	2.41*	0.15
Digit span	9.50 (1.96)	9.70 (1.99)	0.74	0.07

more accurately in mental rotation tasks during the early follicular phase as compared to their performance during the ovulatory cycle phase. These findings are in accordance with previous studies, which show that women perform better on mental rotation tests during menstruation, when estrogen levels are low, as compared with other phases of the menstrual cycle in which estrogen levels are high [24-29].

Several studies have investigated cognitive performance in relation to estrogen and progesterone levels. Findings from those studies have shown that performance on mental rotation tasks was negatively correlated with estrogen levels [25-27,31], but not significantly correlated with progesterone levels [26]. In the last two decades, imaging techniques have provided opportunities to explore the neural networks underlying mental rotation processes. Results of several studies, which took into account menstrual cycle phase, have indicated that the phase of menstrual cycle plays an important role in the activation patterns of specific cerebral regions [44]. For example, Gizewski et al. [45] found that women in the ovulatory cycle phase showed a stronger activation in the frontal areas and left fusiform gyrus in comparison to men who showed activation in different frontal and parietal areas, which are regarded as the classic mental rotation areas. Furthermore, Schöning et al. [44] tested brain activation during a mental rotation task among men and women; women were tested in two phases of their menstrual cycle early follicular and midluteal. They showed that, among women, several cerebral regions exhibited enhanced activation during the midluteal phase. Moreover, estrogen levels were associated with brain activation in parietal and frontal areas among women in both cycle phases. These findings might be explained by the interaction of sex hormones with neurotransmitter systems [46]. For example, estrogen and progesterone have opposite effects on the GABAergic and on the dopaminergic neurotransmission systems [46]. This rationale has gained support from animal [47], as well as human studies [36,48].

On the other hand, we did not find a significant effect of menstrual cycle on another visuospatial ability, that of spatial perception, which was tested with the Water-Level task. Spatial perception refers to people's ability to evaluate spatial relationships with respect to the orientation of their own body, while ignoring distracting information [11]. It has been found that the Water-Level test is sensitive to sex differences, with males outperforming females [49]. In the search for an association between menstrual cycle phase and visuospatial performance, previous findings have demonstrated inconsistent results. For example, Hampson et al. [26] found that women in the low estrogen stage of their menstrual cycle scored higher on a closure test than women in the high estrogen stage. In contrast, other researchers did not find significant performance differences along the menstrual cycle when visuospatial abilities were tested with the hidden figures test [27] and the spatial navigation task [36]. Despite the inconsistent results across studies, our findings are in accordance with studies that show that mental rotation tasks produce the largest effect sizes when examining sex differences in cognitive abilities relative to other visuospatial abilities [8-10]. Perhaps other visuospatial measures are less sensitive and, therefore, produce mixed

results, both in studies that explore sex differences, as well as in studies that explore the role of menstrual cycle phase on visuospatial abilities.

In regard to verbal fluency across the menstrual cycle, our findings showed that verbal fluency was enhanced during the ovulatory cycle phase. Our findings are in accordance with previous studies that found that verbal ability was lowest during the early follicular phase, when estrogen levels were low [25,34]. However, other studies examining the relationship between estrogen levels and verbal fluency performance have found a positive correlation [50]. Studies on sex differences in language lateralization suggest that functional cerebral asymmetries (FCAs) are stable in men, whereas in women they change along the menstrual cycle [34,51]. Hausmann et al. [26] postulated that sex hormones reduce FCAs through their influence on glutamatergic and GABAergic effects on interhemispheric transmission. In a functional neuroimaging study, Weis and colleagues [15] examined the role of estrogen in cyclic changes of FCAs on verbal performance. They found that FCAs during the follicular phase were reduced due to elevated levels of estrogen. Therefore, they concluded that estrogen plays an important role in modulating functional brain organization across the menstrual cycle.

When we examined the role of menstrual phase on memory performance, we did not find performance differences across the menstrual cycle. This finding is consistent with other studies that also did not find an association between estrogen levels and memory performance [39,40]. However, other studies have demonstrated that women tested during phases of the menstrual cycle that are characterized by high levels of estrogen, had higher scores and made fewer errors on memory tests than women who were tested when estrogen levels were low [37,38]. Additionally, a few neuroimaging studies have shown that there is increased brain activation during phases of the menstrual cycle in which hormone levels are higher (i.e., midluteal and ovulatory phases). For example, researchers have found that during these phases, there was increased brain activation in the inferior frontal gyrus during verbal memory tasks [52,53] and increased activation in the hippocampus and striatum during working memory tasks [54,55]. As noted previously, the present study failed to demonstrate an association between menstrual cycle phase and memory performance. Perhaps the inconsistency, which characterizes the literature, is due to the fact that various memory tasks demand different encoding processes. In verbal memory tasks that involve semantic encoding (word lists, paired associations), women score higher than men [56]. However, in digit span tasks, which require serial encoding, the female advantage disappears [57].

The present study has some limitations. First, because of the small sample, caution should be taken in interpreting and generalizing the results. Second, the early follicular and the ovulatory phases of the menstrual cycle that were chosen for sampling are based on the assumption that estrogen levels are at their lowest and highest levels, respectively. Other studies, however, have sometimes chosen different phases; for example, the luteal phase, which is known to be characterized by high

progesterone levels. Because both estrogen and progesterone are relevant to the present study, the chosen phases, which focused on estrogen levels, allowed only a partial examination of the hormones that vary during a menstrual cycle. Third, to deepen our understanding of the role of sex hormones on cognitive performance, it is necessary to broaden the sampling method to include men and women, including women who are using oral contraceptives. Lastly, although utilization of the counting method (i.e., choosing particular days of the cycle) to measure menstrual cycle phase has been legitimately applied in previous studies [29], confirming actual hormone concentrations is necessary for validating menstrual phase [25].

Conclusion

In summary, the present findings suggest that sex hormones, as reflected by menstrual cycle phase, selectively modulate cognitive performance. Whereas participants' performance on mental rotation and verbal fluency tasks changed as a function of menstrual cycle phase, performance on spatial perception and digit span tasks did not change. These results are in accordance with neuroimaging studies, which shed light on the underlying brain organization mechanisms involved in the impact of sex hormones on cognitive performance. Further neuroimaging studies that incorporate the role of menstrual cycle phase with sex hormones measures are still needed to deepen our understanding of the differences (anatomically and functionally) between and within females and males.

References

- Collaer ML, Hines M. Human behavioral sex differences: A role for gonadal hormones during early development? *Psychological Bulletin*. 1995;118(1):55-107.
- Hines M. *Brain Gender*. Oxford, UK: Oxford University Press. 2004.
- Halpern DF. *Sex differences in cognitive abilities* (4th edn.), Psychology Press. New York, NY, USA. 2012.
- Driscoll I, Hamilton DA, Yeo RA, et al. Virtual navigation in humans: the impact of age, sex, and hormones on place learning. *Horm Behav*. 2005;47(3):326-235.
- Iachini T, Sergi I, Ruggiero G, et al. Gender differences in object location memory in a real three-dimensional environment. *Brain Cogn*. 59(1):52-59.
- Parsons TD, Larson P, Kratz K, et al. Sex differences in mental rotation and spatial rotation in a virtual environment. *Neuropsychologia*. 2004;42(4):555-562.
- Barel E, Tzischinsky O. The role of sex hormones and of 2D:4D ratio in individual differences in cognitive abilities. *Journal of Cognitive Psychology*. 2017;29(4):497-507.
- Burton LA, Henninger D. Sex differences in relationships between verbal fluency and personality. *Current Psychology*. 2013;32(2):168-174.
- Hines M, Fane BA, Pasterski VL, et al. Spatial abilities following prenatal androgen abnormality: Targeting and mental rotations performance in individuals with congenital adrenal hyperplasia. *Psychoneuroendocrinology*. 2003;28(8):1010-1026.
- Peters M, Manning J, Reimers S. The effects of sex, sexual orientation, and digit ratio (2D:4D) on mental rotation performance. *Arch Sex Behav*. 2007;36(2):251-260.
- Linn MC, Petersen AC. Emergence and characterization of sex differences in spatial ability: A meta-analysis. *Child Dev*. 1985;56(6):1479-1498.
- Voyer D, Voyer S, Bryden MP. Magnitude of sex differences in spatial abilities: A meta-analysis and consideration of critical variables. *Psychol Bull*. 1995;117(2):250-270.
- Bleecker ML, Bolla-Wilson K, Agnew J, et al. Age-related sex differences in verbal memory. *J Clin Psychol*. 1988;44(3):403-411.
- Kramer JH, Delis DC, Daniel M. Sex differences in verbal learning. *J Clin Psychol*. 1988;44(6):907-915.
- Weiss EM, Kemmler G, Deisenhammer EA, et al. Sex differences in cognitive functions. *Personality and Individual Differences*. 2003;35(4):863-875.
- Kimura D. Sex hormones influence human cognitive pattern. *Neuroendocrinology Letters Special Issue*. 2002;23(Suppl. 4):68-77.
- Caldera YM, Mc Culp A, O'Brien M, et al. Children's play preferences, construction play with blocks, and visual-spatial skills: are they related? *International Journal of Behavioral Development*. 1999;23(4):855-872.
- Caldera YM, Huston AC, O'Brien M. Social interactions and play patterns of parents and toddlers with feminine, masculine, and neutral toys. *Child Dev*. 1989;60(1):70-76.
- Quaiser-Pohl C, Lehmann W. Girls' spatial abilities: Charting the contributions of experiences and attitudes in different academic groups. *Br J Educ Psychol*. 2002;72(2):245-260.
- Collaer ML, Reimers S, Manning JT. Visuospatial performance on an internet line judgment task and potential hormonal markers: sex, sexual orientation, and 2D:4D. *Arch Sex Behav*. 2007;36(2):177-192.
- Halari R, Hines M, Kumari V, et al. Sex differences and individual differences in cognitive performance and their relationship to endogenous gonadal hormones and gonadotropins. *Behav Neurosci*. 2005;119(1):104-117.
- Hines M. Gender development and the human brain. *Annu Rev Neurosci*. 2011;34:69-88.
- Hausmann M, Schoofs D, Rosenthal HES, et al. Interactive effects of sex hormones and gender stereotypes on cognitive sex differences- A psychobiosocial approach. *Psychoneuroendocrinology*. 2009;34(3):389-401.
- Hausmann M, Güntürkün O. Steroid fluctuations modify functional cerebral asymmetries: the hypothesis of

- progesterone-mediated interhemispheric decoupling. *Neuropsychologia*. 2000;38(10):1362-1374]
25. Maki PM, Rich JB, Rosenbaum RS. Implicit memory varies across the menstrual cycle: estrogen effects in young women. *Neuropsychologia*. 2002;40(5):518-529]
26. Hampson E, Levy-Cooperman NA, Korman JM. Estradiol and mental rotation: relation to dimensionality, difficulty, or angular disparity?. *Horm Behav*. 2014;65(3):238-248]
27. Hausmann M, Slabbekoorn D, Van Goozen SHM, et al. Sex hormones affect spatial abilities during the menstrual cycle. *Behav Neurosci*. 2000;114(6):1245-1250.
28. Mäntylä T. Gender differences in multitasking reflect spatial ability. *Psychol Sci*. 2013;24(4):514-520.
29. Šimić N, Santini M. Verbal and spatial functions during different phases of the menstrual cycle. *Psychiatr Danub*. 2012;24(1):73-79.
30. McCormick CM, Teillon SM. Menstrual cycle variation in spatial ability: relation to salivary cortisol levels. *Horm Behav*. 2001;39(1):29-38.
31. Courvoisier DS, Renaud O, Geiser C, et al. Sex hormones and mental rotation: an intensive longitudinal investigation. *Horm Behav*. 2013;63(2):345-351]
32. Epting LK, Overman WH. Sex-sensitive tasks in men and women: a search for performance fluctuations across the menstrual cycle. *Behav Neurosci*. 1998;112(6):1304-1317]
33. Kozaki T, Yasukouchi A. Sex differences on components of mental rotation at different menstrual phases. *Int J Neurosci*. 2009;119(1):59-67.
34. Hampson E. Variations in sex-related cognitive abilities across the menstrual cycle. *Brain Cogn*. 1990;14(1):26-43]
35. Griksiene R, Rukenas O. Effects of hormonal contraceptives on mental rotation and verbal fluency. *Psychoneuroendocrinology*. 2011;36(8):1239-1248]
36. Pletzer B, Harris TA, Scheuringer A, et al. The cycling brain: Menstrual cycle related fluctuations in hippocampal and fronto-striatal activation and connectivity during cognitive tasks. *Neuropsychopharmacology*, 2019;44:1867-1875]
37. Hampson E, Morley EE. Estradiol concentrations and working memory performance in women of reproductive age. *Psychoneuroendocrinology*. 2013;38(12):2897-2904]
38. Rosenberg L, Park S. Verbal and spatial functions across the menstrual cycle in healthy young women. *Psychoneuroendocrinology*. 2002;27(7):835-841.
39. Phillips SM, Sherwin BB. Variations in memory function and sex steroid hormones across the menstrual cycle. *Psychoneuroendocrinology*. 1992;17(5):497-506.
40. Mordecai KL, Rubin LH, Maki PM. Effects of menstrual cycle phase and oral contraceptive use on verbal memory. *Horm Behav*. 2008;54(2):286-293]
41. Gordon HW, Harness BZ. A test battery for diagnosis and treatment of developmental dyslexia. *DASH Speech and Hearing Disorders*. 1977;8:1-7
42. Shepard RN, Metzler J. Mental rotation of three-dimensional objects. *Science*. 1971;171(3972):701-703.
43. Piaget J, Inhelder B. The child's conception of space (F. J. Langdon & J. L. Lunzer, Trans.). London. UK: Routledge & Kegan Paul. 1956.
44. Schöning S, Engelen A, Kugel H, et al. Functional anatomy of visuo-spatial working memory during mental rotation is influenced by sex, menstrual cycle, and sex steroid hormones. *Neuropsychologia*. 2007;45(14):3203-3214]
45. Gizewski ER, Krause E, Wanke I, et al. Gender-specific cerebral activation during cognitive tasks using functional MRI: comparison of women in mid-luteal phase and men. *Neuroradiology*. 2006;48(1):14-20]
46. Barth C, Villringer A, Sacher J. Sex hormones affect neurotransmitters and shape the adult female brain during hormonal transition periods. *Front Neurosci*. 2015;9:37.
47. Khan MM, Dhandapani KM, Zhang QG, et al. Estrogen regulation of spine density and excitatory synapses in rat prefrontal and somatosensory cerebral cortex. *Steroids*. 2013;78(6):614-623]
48. Protopopescu X, Butler T, Pan H, et al. Hippocampal structural changes across the menstrual cycle. *Hippocampus*. 2008;18(10):985-988]
49. Geer EA, Quinn JM, Ganley CM. Relations between spatial skills and math performance in elementary school children: A longitudinal investigation. *Dev Psychol*. 2019;55(3):637]
50. Maki PM, Zonderman AB, Resnick SM. Enhanced verbal memory in nondemented elderly women receiving hormone-replacement therapy. *Am J Psychiatry*. 2001;158(2):227-233.
51. Bibawi D, Cherry B, Hellige JB. Fluctuations of perceptual asymmetry across time in women and men: Effects related to the menstrual cycle. *Neuropsychologia*. 1995;33(1):131-138]
52. Craig MC, Fletcher PC, Daly EM, et al. Physiological variation in estradiol and brain function: a functional magnetic resonance imaging study of verbal memory across the follicular phase of the menstrual cycle. *Horm Behav*. 2008;53(4):503-508.
53. Dietrich T, Krings T, Neulen J, et al. Effects of blood estrogen level on cortical activation patterns during cognitive activation as measured by functional MRI. *Neuroimage*. 2001;13(3):425-432]
54. Jacobs E, D'Esposito M. Estrogen shapes dopamine-dependent cognitive processes: implications for women's health. *J Neurosci*. 2011;31(14):5286-5293]
55. Joseph JE, Swearingen JE, Corbly CR, et al. Influence of estradiol on functional brain organization for working memory. *Neuroimage*. 2012;59(3):2923-2931]
56. Berenbaum SA, Baxter L, Seidenberg M, et al. Role of the

hippocampus in sex differences in verbal memory: memory outcome following left anterior temporal lobectomy. *Neuropsychology*. 1997;11(4):585]

57. Otero Dadin C, Rodrigez Salgado D, Fernandez E. Natural sex hormone cycles and gender differences in memory. *Actas Esp Psiquiatr*. 2009;37(2):68-74.

***Correspondence to:**

Efrat Barel
Department of Behavioral Sciences
The Max Stern Academic College
of Emek Yezreel, Emek Yezreel
Israel
Tel: 972-50-2481549; Fax: 972-4-6765784
E-mail: efratb@yvc.ac.il