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Natural sex hormone cycles and gender differences in memory

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Objective. To analyze gender differences in memory and the influence of the natural sex hormone cycles on it.

Method. A total of 20 men and 19 women were assessed with memory tests two times coinciding with two hormonal phases of the diurnal cycle of testosterone in men or menstrual cycle in women.

Results. It was observed that women perform better than men in delayed verbal memory as well as in immediate and delayed object recall, and men in digit span. It was also found that there was a significant effect of the hormonal cycles on verbal working memory, immediate object recall and on the spatial component of visuoconstructive memory. Finally, hormonal cycles determine the existence and direction of gender differences in verbal working memory, delayed object recall and in the spatial component of visuoconstructive memory.

Conclusions. Natural sex hormone cycles seem to influence gender differences in some measurements of memory.

Key words:
Memory. Gender differences. Sex hormone cycles. Healthy young subjects.

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Ciclos naturales de las hormonas sexuales y diferencias entre sexos en memoria

Objetivo. Analizar las diferencias entre sexos y la influencia de los ciclos naturales de las hormonas sexuales en memoria.

Método. Se evaluó a 20 hombres y 19 mujeres con pruebas de memoria en dos ocasiones coincidentes con dos fases hormonales bien del ciclo diurno de la testosterona en los varones o bien del ciclo menstrual en las mujeres.

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Resultados. Se observó que las mujeres rinden mejor que los hombres en memoria verbal a largo plazo y en memoria visual de objetos a corto y largo plazo y que los hombres rinden mejor que las mujeres en la amplitud de memoria inmediata de dígitos. Se apreció que los ciclos hormonales influyen en el rendimiento en memoria de trabajo para material verbal, en memoria visual de objetos a corto plazo y en el componente espacial de la memoria visoconstructiva. Asimismo, los ciclos hormonales determinan la existencia y dirección de diferencias entre sexos en memoria de trabajo para material verbal, así como en memoria visual de objetos a largo plazo y en el componente espacial de la memoria visoconstructiva.

Conclusiones. Los ciclos naturales de las hormonas sexuales parecen influir sobre las diferencias entre sexos en algunas medidas de memoria.

Palabras clave:
Memoria. Diferencias entre sexos. Ciclos de hormonas sexuales. Jóvenes sanos.

INTRODUCTION

There are anatomical and functional differences between the male and female brain¹⁻⁴ that lead to the supposition that differences exist between genders in neuropsychological performance. However, the results in this regards have not been consistent since no differences between men and women appear in some studies⁵⁻⁷, while others establish typical neuropsychological performance patterns for each gender⁸.

The male neuropsychological pattern is characterized by better performance in the task of throwing objects where accuracy is assessed⁹, in mathematical problem solving and abstract reasoning^{10,11}, as well as in spatial skills, fundamentally in mental rotation^{12,13}. On its part, the female pattern is characterized by better performance in fine motor movements¹⁴, greater perceptive sensitivity¹⁵, better linguistic skills¹⁶ and better performance in both verbal¹⁷⁻²¹ and visual²²⁻²⁴ memory. The superiority of one gender over another in spatial memory will depend on the component studied. Thus, in recall of objects distributed in a space, women retain the com-

ponents of spatial distribution better while men are generally superior in the spatial locating of the objects²⁵⁻²⁸.

On the other hand, there are works that have shown variations in neuropsychological performance in relationship with natural sex hormone cycles. Variations in spatial performance based on testosterone levels have been studied in men, and have shown a positive linear relationship in some cases²⁹, while finding a curvilinear relationship in others³⁰. In the case of women, variations have been studied in performance during the menstrual cycle in spatial tasks³¹⁻³⁶, in verbal skills and fine motor movements³⁵, and in visual and spatial memory^{37,38}, as well as in working memory tasks with verbal material³⁹. In general, the results indicate that performance improves in tasks characteristics of the female pattern and worsens in tasks characteristics of the male one in the phases of the cycle with high ovarian hormone levels while the contrary occurs in those phases with low hormone levels.

These results show us that the typical neuropsychological performance patterns of each gender may vary in relationship with the natural sex hormone cycles. However, the influence of these hormone cycles has not been taken into account when analyzing the neuropsychological differences between genders⁴⁰. Furthermore, the study of their influence on memory is uncommon in young and healthy adults, since this is generally approached either in elderly persons or in those with hormone disorders or under treatment with hormones. Thus, in this work, we have established the objective of analyzing the differences between genders and the influence of the natural sex hormone cycles on performance in memory of healthy young subjects.

METHODS

Participants

The sample is made up of 39 young healthy subjects, 20 men and 19 women, all university students who voluntarily participated, giving their informed consent.

Exclusion criteria were background of neurological, psychological, psychiatric and hormonal type, existence of sensory and/or motor deficit, and prescription of hormone treatments or medications that could interfere in the central nervous system functioning. In the case of women, those who do not have a menstrual cycle with a regular duration of 28 to 30 days and those taking oral contraceptives were also excluded.

Instruments

All the subjects were given a semistructured interview in order to collect sociodemographic and clinical information. Furthermore, each participant underwent an evaluation of

laterality with the Edinburgh Laterality Inventory⁴¹ and a verbal and visual memory evaluation that consisted of the following tests: Rey Auditory Verbal Learning Test⁴², Digit Span and Letter-Number Sequencing subtest of the Wechsler Memory Scale⁴³, Copying and Reproduction of Complex Geometric Figures Memory Test⁴⁴, Benton Visual Retention Test, form C, administration A⁴⁵ and the Object Visual Memory and Spatial Location Test⁴⁶.

Procedure

All the subjects were evaluated on two occasions, establishing two times in the day, the first hour of the morning and last hour of the evening, coinciding with the two daytime cycle phases of testosterone in males. The menstrual cycle was taken into account in women. Two evaluations were made in two phases: the menstrual phase, between days 3 and 5 of the cycle and the luteal phase, between days 16 and 18. The establishment of the cycle phase was made by calculating the days from the last menstruation date reported by the participants, considering the first day of menstruation as day zero of the cycle. A counterbalance procedure was conducted to establish the order of the evaluations, so that half of the subjects were evaluated for the first time in the morning and the other half in the evening. In the case of women, half were evaluated for the first time during the menstrual phase and the other half during the luteal one. An interval of 15 days passed for all the subjects between the first and second evaluation since that is the period that separates the two phases of the menstrual cycles studied.

In the first evaluation the semistructured interview was performed, the Edinburgh Laterality Inventory was administered⁴¹ and then the memory neuropsychological tests were applied in a session of approximately one hour long. The data of the subjects obtained previously in the interview were confirmed in the second evaluation and then the memory tests were applied for another time.

Statistical analysis

The data were analyzed with the SPSS statistical program for Windows, version 14.0⁴⁷. A repeated measures analysis of variance was performed, using the hormone cycle phase as intrasubject factor with two levels, phase of high levels of hormones (men in the morning, women in the luteal phase) and low hormone level phase (men in the evening, women in menstrual phase), and also considering the gender as inter-subject factor.

RESULTS

In regards to the description of the sample, all the subjects were right-handed and the mean age of the men was 19.3

(SD=1.26) and of the women 18.5 (SD=1.31). Differences in age were not statistically significant: $t(37) = 1.998$; $p = 0.053$. On the other hand, menarche age of the women was 12.7 (SD=0.98) and mean duration of the cycle was 28.9 (SD=0.88) days.

Mean values and standard deviation for those memory measurements obtained by men and women according to the hormone cycle phase in which some of the factors or interaction between both have had a significant effect are shown in table 1. In addition, the statistics of contrast F and its associated probability are shown. The results of the ANOVA show a significant effect of the gender variable on the score of the delayed recall trial of the Rey Auditory Verbal Learning Test: $F(1, 37) = 4.232$; $p = 0.047$, and on immediate recall: $F(1, 37) = 4.363$; $p = 0.044$, and delayed recall: $F(1, 37) = 4.09$; $p = 0.05$, of the Object Visual Memory test, so that women obtained a higher score than men in these measurements. This same factor had a significant effect on the

total: $F(1, 37) = 7.071$; $p = 0.012$, and span scores: $F(1, 37) = 6.943$, $p = 0.012$, of the Forward Digital Span, and in the total: $F(1, 37) = 7.219$; $p = 0.011$, and span scores: $F(1, 37) = 5.617$; $p = 0.023$, of the Backward Digit Span, observing, in both cases, a higher score in men than in women.

On the other hand, a significant effect of the hormone cycle phase in the total score of the Letter-Number Sequencing subtest was observed: $F(1, 37) = 4.868$; $p = 0.034$, it being greater in the phase of low levels of hormones. A significant effect of the hormone phase on the immediate recall score of the Object Visual Memory Test was also observed: $F(1, 36) = 4.952$; $p = 0.032$, and in the rotation errors of the Benton Visual Retention Test: $F(1, 37) = 4.507$; $p = 0.041$, so that these scores are greater in the phase of high levels of hormones.

Finally, the interaction between gender and hormone cycle phase was significant in the total: $F(1, 37) = 4.868$; $p = 0.034$,

Table 1	Significant results by gender and hormone phase for measurements of memory					
	Men		Women		F	p
Hormone phase	High M (dt)	Low M (dt)	High M (dt)	Low M (dt)		
Rey Auditory Verbal Learning test						
Delayed trial	13.05 (1.88)	13.15 (1.8)	14.11 (1.2)	13.74 (1.37)	4.232	0.047 ^a
Forward Digit Span						
Total	11.2 (3.04)	11 (1.78)	9.58 (1.61)	9.32 (1.95)	7.071	0.012 ^a
Span	7 (1.38)	7.2 (0.95)	6.53 (0.84)	6.16 (1.02)	6.943	0.012 ^a
Backward Digit Span						
Total	8.15 (2.32)	8.5 (1.82)	6.84 (1.74)	6.79 (1.75)	7.219	0.011 ^a
Span	5.6 (1.27)	5.85 (1.09)	4.89 (1.05)	5.11 (1.1)	5.617	0.023 ^a
Letter-Number Sequencing						
Total	12.4 (2.23)	12.4 (2.89)	10.89 (1.94)	12.47 (1.95)	4.868	0.034 ^b
Span	6.05 (0.89)	5.9 (0.91)	5.37 (0.9)	6.11 (0.94)	8.282	0.007 ^c
Benton Visual Retention						
Rotations	0.3 (0.66)	0.4 (0.68)	0.74 (0.81)	0.21 (0.42)	4.507	0.041 ^b
					7.928	0.004 ^c
Object Visual Memory						
Immediate	18.5 (2.5)	17.3 (3.4)	19.58 (0.69)	19.11 (2.36)	4.363	0.044 ^a
					4.952	0.032 ^b
Delayed	18.6 (1.85)	17.45 (3.24)	19.16 (0.96)	19.26 (1.37)	4.09	0.05 ^a
					4.292	0.045 ^c

^a Significant differences between genders ^b Significant differences between hormone phase. ^c Significant differences between genders based on hormone phase.

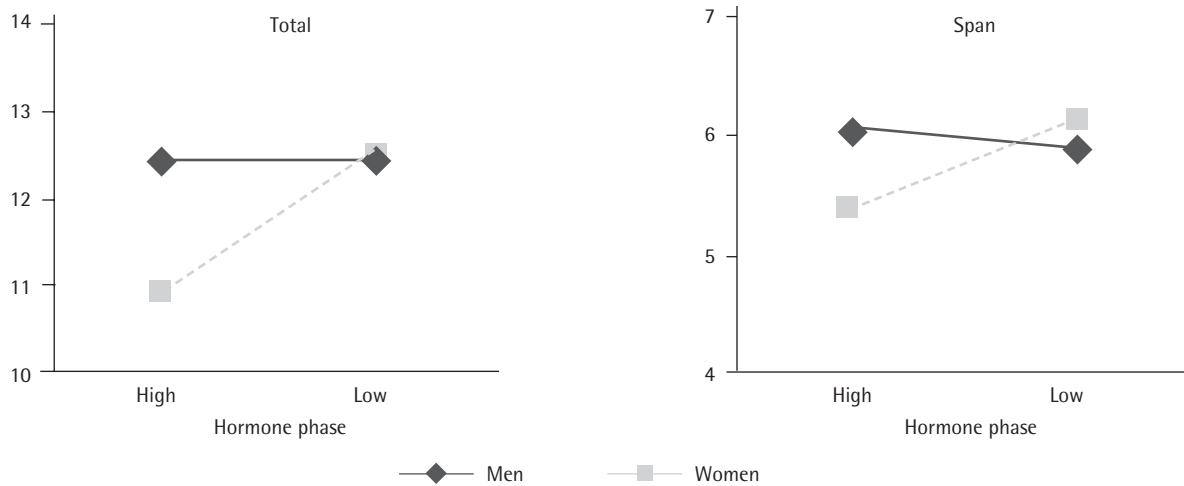


Figure 1 | Mean scores in Letters and Numbers obtained by men and women in the two hormone cycle phases

and span scores: $F(1, 37) = 8.282$; $p = 0.007$, of the Letter-Number Sequencing subtest, so that men obtained higher scores than women only in the phase of high levels of hormones (fig. 1). The interaction was also significant in the delayed recall score of the Object Visual Memory Test: $F(1, 37) = 4.292$; $p = 0.045$, so that women obtained a higher score than men during the phase of low levels of hormones (fig. 2). Finally, interaction was also significant in the score corresponding to the rotation errors of the Benton Visual Retention Test: $F(1, 37) = 9.728$; $p = 0.004$, it being observed that during the phase of high levels of hormones, women committed more errors of this type than men while in the phase of low levels of hormones, men committed more errors than women (fig. 3).

CONCLUSIONS

The results obtained show that there are differences between genders in some memory measurements and variations in the memory performance based on the hormone cycles. Some of the differences between men and women found have been independent of the hormone variations that are produced in each gender. However, in other measurements, the differences depend on the hormone cycle phase the subjects are in.

Regarding the differences between genders, independently of the hormone phase, a female advantage is obser-

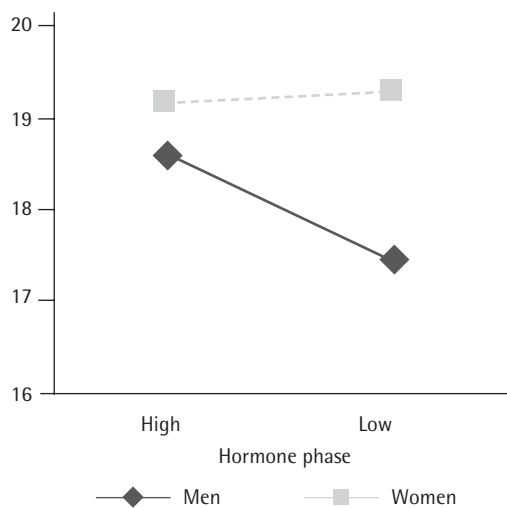


Figure 2 | Mean scores in the delayed recall in the Object Visual Memory Test obtained by men and women in the two hormone cycle phases.

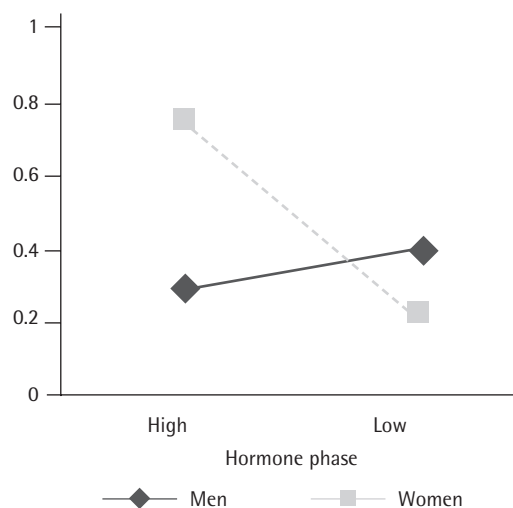


Figure 3 | Mean scores in the rotation errors of the Benton Visual Retention Test obtained by men and women in the two hormone cycle phases.

ved in long-term recall of words (Rey Auditory Verbal Learning Test) and in short and long-term object visual recall (Object Visual Memory and Spatial Location Test), and a masculine advantage in digit memory span (Digit Span subtest).

The male advantage for digit recall and female advantage for recall of word lists could be related with the fact that women generally use semantic type strategies for coding verbal material while men generally use serial type strategies^{48,49}. In relationship with this, women are favored in recall of information benefited by semantic coding, such as word lists, while men are favored in recall of information that requires serial coding, such as digit series. It has also been observed in previous works that there is a feminine advantage in long-term recall of words²¹, and a masculine one in the digit memory span⁵⁰.

On the other hand, the feminine advantage in visual recall of objects could be related with the hypothesis on the utilization of verbal labels for recall of visual stimuli^{22,51} and the consequent advantage in visual recall of daily objects found in previous studies⁴⁶. In addition, as in other works²⁴, we observe that this advantage does not occur when stimuli are less susceptible of verbal coding and they should be drawn.

Regarding the variations in memory performance based on the hormone cycle, we have found that the performance in working memory (Letter-Number Sequencing subtest), and in the spatial component of the visuoconstructive memory (rotation errors of the Benton Visual Retention Test), improve when there are low hormone levels. However, the short-term object visual recall improves during the high hormone levels phase. These results follow the line of those obtained in previous works in which it has been seen that neuropsychological performance may vary based on the natural cycles of sexual hormones^{30-32,37-39}.

Finally, our results indicate that an interaction effect is produced between gender and hormone cycle phase on the performance of some memory measurements. Thus, the differences between genders may be interpreted based on the hormone cycle phase in which the subjects are found.

In the verbal working memory, it is observed that there is a male advantage only in the phase of high levels of hormones since the female performance improves in the low hormone levels phase, that is, the menstrual phase, until become equal to that of the masculine one. These results are not consistent with those obtained by Rosenberg and Park³⁹ who indicated that there is better performance in verbal working memory tasks in women in the luteal phase of the cycle. However, given the fact that the mental rotation strategies facilitate manipulation of the verbal stimuli in these tasks⁵², these results would be coherent in works that find better performance of men in comparison with women in mental rotation tasks^{12,13}. Furthermore, this agrees with previous works in which it was observed that spatial performan-

ce in women is better in those cycle phases with low hormone levels^{31,34}, and suggests that there would be an inhibitor effect of estrogens on spatial performance.

In addition, the differences between men and women in the spatial component of visuoconstructive memory could be explained by the inhibitor effect of the estrogens on spatial performance, since it has been observed that when there are low hormone levels, feminine performance improves and even exceeds that of masculine performance while performance improves in the inverse sense in men when there are low levels of testosterone. These results are coherent with the works that find improvement in men in spatial performance when there are high levels of testosterone²⁹ and worsening in women with high levels of ovarian hormones^{31,34}.

Finally, in long-term object recall, an advantage in women is only observed in the low hormone levels phase since recall in this phase of men worsens while that of women remains constant. These results point to a positive effect of testosterone on visual memory performance⁵³. Although this effect is not sufficient in men to achieve the female performance in short-term object recall.

Finally, we can conclude that the natural cycles of the sexual hormones may condition the existence and direction of the differences between men and women in memory. Thus, we consider that the hormone cycle, both masculine and feminine, is an important factor that should be taken into account when the neuropsychological differences between genders are being studied, at least in memory and in subjects with characteristics that are similar to the sample used herein.

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