Review

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Gender differences in cognitive functions and influence of sex hormones

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Objective. To review scientific evidence on gender differences in cognitive functions and influence of sex hormones on cognitive performance.

Method. Systematical search of related studies identified in Medline.

Results. Women outperform men on verbal fluency, perceptual speed tasks, fine motor skills, verbal memory and verbal learning. Men outperform women on visuospatial ability, mathematical problem solving and visual memory. No gender differences on attention and working memory are found. Researchers distinguish four methods to investigate hormonal influence on cognitive performance: *a)* patient with hormonal disorders; *b)* neuroimaging in individuals during hormone administration; *c)* in women during different phases of menstrual cycle, and *d)* in patients receiving hormonal treatment (idiopathic hypogonadotropic hypogonadism, postmenopausal women and transsexuals). The findings mostly suggest an influence of sex hormones on some cognitive functions, but they are not conclusive because of limitations and scarcity of the studies.

Conclusions. There are gender differences on cognitive functions. Sex hormones seem to influence cognitive performance.

Key words:
Sex differences. Cognitive performance. Intelligence. Transsexualism. Sex hormones.

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Diferencias de género en las funciones cognitivas e influencia de las hormonas sexuales

Objetivo. Revisar las evidencias científicas sobre las diferencias cognitivas en función del género y la posible influencia de las hormonas sexuales en el rendimiento cognitivo.

Método. Se realizó una búsqueda sistemática de la bibliografía a través del sistema Medline sobre artículos relacionados con el tema.

Resultados. Las mujeres presentan un mayor rendimiento con respecto a los hombres en fluencia verbal, velocidad perceptiva, habilidad motora fina, tareas de memoria verbal y aprendizaje verbal. Los hombres superan a las mujeres en tareas visuoespaciales, resolución de problemas matemáticos y memoria visual. No se encuentran diferencias en función del género en atención y memoria de trabajo. Los estudios que evalúan la influencia de factores hormonales se han realizado en diversos grupos: *a)* pacientes con trastornos hormonales; *b)* pacientes sometidos a neuroimagen tras la administración hormonal; *c)* en mujeres sanas en función del ciclo menstrual, y *d)* en pacientes sometidos a tratamiento hormonales (hipogonadismo hipogonadotrófico, mujeres posmenopáusicas y trastorno de la identidad de género). Estos estudios en su mayoría encuentran una influencia de los niveles hormonales en diversas capacidades cognitivas, aunque los resultados no son del todo concluyentes por las limitaciones y escasez de estos estudios.

Conclusiones. Existen diferencias cognitivas en función del género y las hormonas sexuales parecen ejercer una influencia en estas funciones cognitivas.

Palabras clave:
Diferencias de género. Rendimiento cognitivo. Inteligencia. Transexualidad. Hormonas sexuales.

INTRODUCTION

Different studies have demonstrated gender differences in aspects such as personality[1], response to stress[2], vulnerability to develop certain psychiatric disorders[3] and cognitive functions. A review of the studies that have evaluated cognitive differences in gender function has been done in this article and the involvement of sex hormones in these differences has been reviewed parallelly.

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GENDER DIFFERENCES IN COGNITIVE FUNCTIONS

Cognitive performance areas in which gender differences have been most widely studied are intelligence and memory.

Gender differences in intelligence

Several studies that have evaluated the differences in general intelligence between men and women have not found statistically significant differences between men and women in relationship with the Total Intelligence Quotient (measured according to the WAIS scales)[4,5]. However, this finding is not surprising since the Intelligence Quotient obtained from most of the general intelligence scales, such as the WAIS or Stanford-Binet battery, were specifically constructed to avoid these differences between genders, as the tests —or items— forming the scales are balanced from one gender to the other. On the contrary, they do differ in the deviations of the distributions according to gender. Thus, greater dispersion in the distribution of intelligence in the case of men has been found[6,7]. Regarding specific skills[8], numeric aptitude (only the tasks of resolving mathematic problems) and spatial aptitude are better in men[9-14]. On the contrary, verbal fluency, fine motricity and perceptual speed have been found to be higher in women[12,15-17]. However, in recent years, studies indicate that the magnitude of the differences found in the verbal fluency or mathematical problem solving tasks is moderate to small while that found in the more complex tasks of spatial aptitude is elevated [13,18,19]. Regarding spatial aptitude, the meta-analysis conducted by Linn and Petersen (1985) found differences in all the types of tasks studied. These were ordered from lower to greater magnitude of the differences: visualization (skill to use analytic strategies to manipulate spatial information), spatial perception (orientation of a body in space) and mental rotation (speed and accuracy to rotate figures in two or three dimension spaces)[13].

Gender differences in memory

Memory is a wide concept that refers to coding processes and recall of information. The studies conducted with reference to gender differences in memory have basically focused on the distinction between verbal vs. visuospatial memory and on working memory.

Gender differences in memory

The findings on gender differences in verbal, visuospatial and working memory are detailed in the following.

- *Verbal memory.* Several studies have demonstrated greater performance in women in certain tasks that involve verbal memory -tasks of verbal learning, associated verbal pairs or logical memory[15,20-23].
- *Visuospatial memory.* Gender differences in favor of men in the retention of spatial information[23-25] and in the reproduction of previously presented stimuli have been found[20]. There is controversy regarding remembering the site of objects; some authors find no differences[25] while others find a greater performance in women[26,27].
- *Working memory.* No differences were found in the tasks that imply verbal working memory, such as the WAIS Digit subtest immediate repetition of a series of numbers in the same order in which they are presented (direct digits) or in inverse order (inverse digits) based on gender[28,29].

INFLUENCE OF HORMONE FACTORS IN GENDER DIFFERENCES FOUND IN COGNITIVE PERFORMANCE

Gender differences in cognitive performance have been demonstrated since childhood, however these differences are not stressed significantly until puberty[30]. This fact, together with the findings that relate the action of estrogens on central nervous system structures related with memory, suggest an influence of the hormone factors in the differential cognitive performance between men and women with high probability.

The influence of hormone factors on the cognitive functions has been studied both based on the organizing effects of the sex hormones on the CNS and on the activating effects. Organizing effects refer to the permanent structural and functional changes in the brain produced during the fetal development stage when the brain is exposed to the different sex hormone levels. Activating effects refer to the changes that these induce from the pubertal stage, in which there is a considerable increase of the hormone levels. These levels act on the brain structures organized by the sex hormones during the prenatal stage. The paradigms used for the study of the cognitive differences based on gender are presented in the following.

Cognitive performance study in women with congenital hormone disorders

Different authors have studied the influence of hormone factors in cognitive functions in individuals who were exposed to abnormal levels of sex hormones during the prenatal stage, such as women with congenital adrenal hyperplasia or women affected by Turner syndrome.

Congenital adrenal hyperplasia is a congenital disorder leading to excessive exposure and production of adrenal

Table 1 Cognitive differences found in different studies based on gender

Cognitive performance	Findings	Authors
Intelligence		
General intelligence	No differences are found	Weschler, 1958; Turner et al., 1977
Distribution of intelligence	Greater dispersion in men	Brody, 1992
Verbal fluency	Greater in women	Feingold, 1988; Halpern, 1992
Perceptual speed	Greater in women	Feingold, 1988; Mann et al., 1990
Fine motricity	Greater in women	Hall y Kimura, 1995
Mathematical aptitude	Greater in men	Gouchie et al., 1991;
Spatial aptitude	Greater in men	Voyer et al., 1995; Collins et al., 1997; Feingold, 1988; Mann et al., 1990 y Linn et al., 1985
	Greater gradient in mental rotation > spatial > visualization	
Memory		
Verbal memory	Greater in women	Mann et al., 1990; Ivison et al., 1977; Bleecker et al., 1988; Basso et al., 2000; Lewin et al., 2001
Visuospatial memory	In general, greater in men	Ivison et al., 1977; Lewin et al., 2001; Kail et al., 1977; Postma et al., 1998
Working memory	No differences have been found	Makarek et al., 1993; Makarek et al., 1995

androgens during prenatal development. Several studies that evaluated cognitive performance in women with adrenal hyperplasia in adult age have found superior performance in visuospatial[31,32] and inferior performance in verbal tasks[33] than in a control group of unaffected women. That is, these women have developed a pattern of cognitive performance that is more similar to that found in the masculine population. In a recent study, better performances have been found in these women in specific target-like visuospatial tasks, but not in those of mental rotation type[34]. This suggests that the visuospatial tasks of mental rotation are influenced by exposure to androgens in a moment subsequent to the prenatal development, perhaps in the first six months of post-natal life[34].

In women affected by Turner syndrome (45X0), ovarian development occurs normally until the 4th-5th month of pregnancy, after which this prematurely undergoes involution. In studies on cognitive performance in women with Turner syndrome, performance within normality has been found in verbal tasks and decreased performance in visuospatial tasks[35-40], a performance that does not improve with androgen administration in adolescence[41]. Furthermore, inferior performances in tasks that imply attention and working memory[38,40], susceptible to improvement with the administration of estrogens[42], numeric aptitude[35,39,40,43] and motor skills (both gross and fine motricity)[44] have been found. This performance profile has been explained by the lack of early exposure to androgens that is believed to be the development mechanism of visuospatial skills[45].

Cognitive performance studies and parallel assessment of neuroimagng after hormone administration

Greater activation has been found in neuroimaging studies during neuropsychological task performance in temporal and parietal cortical areas in young and post-menopausal women who receive estrogen treatment[46-48]. These findings are related with increased blood perfusion and glucose metabolism in certain brain regions related with estrogen administration[49]. They suggest a favorable effect of these due to their action on cerebral structures related with memory and other cognitive functions. Similar studies also find an increase in men who receive androgen treatment in the activation predominately of the frontal brain regions[50]. The results of these types of studies, however, are not conclusive due to the reduced number of studies and the differences in methods used. Furthermore, the clinical repercussion of these findings is doubtful.

Cognitive performance studies based on menstrual cycle

The objective of these studies is to evaluate the differences in cognitive performance based on variation of the estrogen and progesterone levels produced during the menstrual cycle. The starting hypothesis would be that during the phase having the greatest increase in estrogen levels, performance in verbal tasks would improve and, on the contrary, performance in visuospatial tasks would be-

Table 2 Results of studies that evaluate cognitive differences in individuals under hormone influence

Studies	Results	Authors
Studies in patients with congenital hormone disorders		
Women with congenital adrenal hyperplasia	Improvement of visuospatial tasks. Worsening of verbal tasks (performance pattern closest to that of the masculine population)	Perlman et al., 1973; Resnick et al., 1986; Helleday et al., 1994
Women with Turner syndrome	Improvement of target, but not mental rotation, task	Hines et al., 2003
	Worse performance in visuospatial and visuperceptive tasks	Downey et al., 1991; Bender, 1993; Reiss et al., 1993; Ross et al., 1995
	Worse performance in attention and working memory	Rovet et al., 1990; Rovet et al., 1993
	Worse performance in arithmetic	Bruandet et al., 2004
	Worse performance in motor skills	Salbenblatt et al., 1989
Studies on cognitive performance and parallel evaluation of neuroimaging after hormone administration		
Studies in young and post-menopausal women	Greater activation in temporal and parietal cortical areas in women who receive estrogen treatment	Shaywitz et al., 1999; Maki et al., 2000; Greene et al., 2000
Studies of blood perfusion in men with androgenic treatment	Greater activation of frontal brain regions	Azad et al., 2003
Cognitive performance studies based on menstrual cycle		
Elevated estrogen levels	Greater performance in verbal memory	Maki et al., 2002; Drake et al., 2000;
	Greater performance in verbal fluency	Rosenberg, 2002; Phillips, 1992
	Worse performance in visuospatial and visuoperceptive tasks	Maki et al., 2002; Drake et al., 2000
	Worse performance in visual memory	Drake et al., 2000
	Some studies do not find any relationship	Gordon et al., 1993
Cognitive performance studies in patients with hormone treatment		
Men with hypogonadotropic hypogonadism	No improvement of performance in spatial tasks after androgen administration	Hier, 1982
Post-menopausal women	Observational studies: improvement in verbal tasks and verbal memory after hormone replacement therapy administration	Hogervorst et al., 2000; Leblanc et al., 2001;
	Controlled studies: different results	Hogervorst et al., 2000; Leblanc, 2001
	Increased risk of cognitive deterioration	Shumaker et al., 2003; Rapp et al., 2003
Patients with gender identity disorders		
Man to woman transsexuals	Improvement in verbal memory	Miles et al., 1998
Woman to man transsexuals	Improvement in visuospatial tasks	Van Goozen et al., 1994; Van Goozen et al., 1995; Slabbekorn et al., 1999

come worse. As a whole, the results of these types of studies are contradictory. Several authors find better performance in implicit verbal memory[51], delayed verbal memory[52], verbal fluency[51], verbal working memory[53] and verbal learning[54] in the intermediate period of luteal phase (in which the estradiol and progesterone levels are higher) in regards to the menstrual phase (in which the lowest sex hormonal levels are found). On the contrary, in the menstrual phase and at the onset of the follicular phase (in which low sex hormone levels are found) perfor-

mance in specific perceptual tasks, of mental rotation, and in immediate and delayed visual memory improve[51,52]. Some studies have found no type of relationship[53,55]. There is a study that has also evaluated the influence of testosterone levels in verbal fluency, finding a positive relationship[52] and others conducted in our country that do not find alterations in cognitive performance in pregnant and puerperal women[56]. The criticism of most of these studies has been based on the fact that *a)* they do not consider progesterone levels; *b)* they do not adequately choose the most sensitive menstrual cycle phase to confirm the hypothesis or not; *c)* they include samples that are too small, or *d)* they lack protocolization of the neuropsychological tests chosen.

Cognitive performance studies in patients under hormone treatment

Studies in men with hypogonadotropic hypogonadism

Lower performance has been found in studies in men with hypogonadotropic hypogonadism in visuospatial tasks regarding control subjects or males with post-pubertal acquired hypogonadism[57]. Administration of androgen replacement therapy in these patients did not improve performance in these spatial tasks. This suggests the role of the organizing effects of the androgens on the cerebral regions involved in spatial functions.

Studies in postmenopausal women using estrogen replacement therapy

There is an extensive number of studies that evaluate the effects of estrogen replacement therapy on cognitive performance and, more specifically, on the prevention of cognitive deterioration in the woman. The most recent meta-analyses have found a selective improvement after the administration of hormone replacement therapy in abstract reasoning, data processing, verbal memory, attention and motor speed in healthy[58] and symptomatic[59] post-menopausal patients and in patients who are menopausic due to surgery[60]. In general, a greater association has been found in the observational studies[58-60]. However, in a controlled and randomized study, Shumaker et al. (2003) found surprising results that contrast with the previous ones[61]. The results suggest that the risk of dementia was two times greater in the group of women who used hormone replacement therapy in comparison with the group of women who used placebo, although the absolute risk was very small. In the same way, replacement therapy with estrogens plus progestins did not prevent mild cognitive deterioration[61], and no beneficial effect of the administration of estrogens plus progestins was found on cognitive performance (measured according to the Mini-Mental State Examination) regarding the placebo[62].

In summary, although the observational studies have found a relationship between hormone replacement treatment and prevention of cognitive performance, controlled and randomized trials have provided more different results. In fact, the study having the greatest significance published up to now, that of Shumaker et al. (2003), not only did not find a protector effect on cognitive performance but also found an increased risk of cognitive deterioration[61].

Studies in women and men with gender identity disorder under masculizing or feminizing hormone treatment

A recent line of investigation has focused on the study of cognitive performance of patients with sexual identity disorder before and after administration of sex reassignment hormone therapy. Gender identity disorder refers to a discomfort with one' own biological gender and with a greater identification with the other gender. This entails significant psychological and social repercussions[63]. Man to woman transsexual hormone treatment is based on the administration of anti-androgens plus estrogens and that of woman to man transsexual on the administration of androgens. The studies conducted are detailed in the following.

Van Goozen et al. (1994) conducted a preliminary study with 22 woman to man transsexual patients, who were administered a battery of neuropsychological tests that measured verbal and visuospatial functions prior to the initiation of androgen hormone therapy and at three months of its onset[64]. These authors found that the administration of androgens in the woman to man transsexual group significantly improved spatial aptitude tasks and worsened verbal fluency tasks. In another study, the same author replicated the previous findings of the beneficial effect of hormone treatment in the man to woman transsexual group with two groups of patient (35 woman to man transsexuals and 15 man to woman transsexuals). On the contrary, worse performance was found in the visuospatial tasks in the man to woman transsexual group although verbal fluency improved after hormone treatment[65]. Miles et al. (1998) studied the effect of hormone treatment administration in memory tasks in a sample of 59 man to woman transsexuals[66]. These authors found that the transsexual patients who received estrogen treatment improved in verbal learning tasks (verbal paired associates of the Weschler Memory Scale), but not in other memory tests or in verbal fluency or spatial aptitude tasks in regards to the group who did not receive treatment. Slabbekorn et al. (1999), from the same research group of Van Goozen (1994), replicated to the same study again with 20 man to woman transsexuals and 25 woman to man transsexuals before and at three months of the hormone treatment[67]. To do so, they subjected these patients to cognitive tasks that have demonstrated equal performance based on gender (verbal reasoning), tasks in which greater performance has been demonstrated in men (mental rotation in two dimensions, mental rotation in three dimensions, and a visualization task), and to tasks in

which better performance is found in women (verbal fluency, fine motricity and perceptual speed). Androgen administration in woman to man transsexuals increased performance in spatial aptitude tasks, and did not modify performance in the rest. On the contrary, hormone treatment in transsexuals from man-to-woman (administration of estrogens plus anti-androgens) worsened performance in visuospatial tasks, although to a lesser degree. The authors suggest that this could be due to the organizing effects of the sex hormones on the brain structures related with spatial aptitude.

As a whole, these studies in transsexuals suggest that hormone treatment modifies some cognitive functions. Specifically, androgen treatment seems to improve visuospatial capacity and estrogen plus anti-androgen treatment improves verbal capacities. However, the results must be replicated in similar studies to confirm these findings.

CONCLUSIONS

There is contrasted scientific evidence on the differences in gender based cognitive capacities. Women exceed men in verbal tasks, perceptual speed and fine motor skill and also in memory and verbal learning tasks. Men exceed women in visuospatial tasks and mathematical problem solving and in visual memory tasks. No clear differences have been found for gender in tasks that imply attention and working memory. The studies that try to clarify the influence of sex hormones on cognitive capacitates have demonstrated differences based on hormone levels, although, as a whole, the results should be cautiously interpreted due to their limitations. A large part of them have been done with a reduced subject sample. Many did not adequately control the type of hormone treatment administered (estrogen, androgen, estrogen plus progestin, estrogens plus anti-androgens, etc.). Several did not control the test-retest effect. Finally, few studies controlled potential confounding variables (educational level, intelligence quotient, mood state). In spite of this, as a whole, these studies suggest that sex hormones are capable of modifying cognitive capacities. Given that the modifications are much clearer in subjects exposed to pathological hormone levels during fetal and/or prepubertal development in regards to those studies that evaluate hormone influence in adult subjects (after puberty), these results suggest that sex hormones have a permanent organizing effect on brain structures that support the cognitive functions during brain development.

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