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Sex differences in episodic memory: Minimal influence of estradiol

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Abstract

Sex differences exist for several cognitive tasks and estrogen has been suggested to influence these differences. Eighteen men and 18 women were matched on age and estradiol level. Potential sex differences were assessed in episodic memory, semantic memory, verbal fluency, problem solving, and visuospatial ability. Significant sex differences, favoring women, were found for tasks assessing episodic memory. Correlations between estradiol level and cognitive performance were significant for face recognition in females. Since sex differences remained in verbal episodic memory tasks and face recognition despite matched levels of estradiol, circulating estradiol does not appear to be of paramount consequence for observed sex differences in episodic memory.

Keywords: Estradiol; Sex differences; Episodic memory; Sex hormones; Cognition

1. Introduction

Sex differences have been well established in several cognitive spheres since the seminal work of Maccoby and Jacklin in 1974 (Halpern, 1992, 1997). Men typically excel in spatially oriented tasks whereas women usually have better verbal fluency (Hyde & Linn, 1988; Voyer, Voyer, & Bryden, 1995). In the domain of memory, sex differences have been reported in episodic memory with women typically outperforming men (see Herlitz, Nilsson, & Bäckman, 1997). Women outperform men on episodic memory tasks when the to be remembered items are words (Hill et al., 1995; Kramer, Delis, & Daniel, 1988), stories (Hultsch, Masson, & Small, 1991), concrete pictures (Herlitz, Airaksinen, & Nordström, 1999), faces (Herlitz & Yonker, 2002; Lewin & Herlitz, 2002; Wahlin et al., 1993), locations (Eals & Silverman, 1994), and odors (Lehrner, 1993). These differences are consistent across ages ranging from 5 (Kramer et al., 1988) to 75 (Herlitz et al., 1997). However, no sex differences are found on non-verbal episodic memory tasks, and men outperform women when the to be remembered items are visuospatial in nature (Lewin, Wolgers, & Herlitz, 2001).

The precise explanation for the obtained sex differences in episodic memory is not known, although biological factors are believed to have some influence on the differences. For example, sex differences have been found with respect to brain activation in recent PET studies (Nyberg, Habib, & Herlitz, 2000; Ragland, Coleman, Gur, Glahn, & Gur, 2000). Nyberg and colleagues examined sex differences and episodic memory and found that, even though there was an overlap in male and female brain activation patterns, subtle activation and deactivation differences were apparent between men and women. Others have found that resting activity in the left temporal lobe was positively associated with episodic memory performance in women (Ragland et al., 2000).

In addition, there is some evidence indicating that fluctuating hormone levels influence cognitive performance. For example, a few studies have found that young women performed at a higher level on visuospatial tasks when estrogen levels were lower, than when

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estrogen levels were higher (Hampson, 1990; Hausmann, Slabbekoorn, Van Goozen, Cohen-Kettenis, & Gunturkun, 2000; Postma, Winkel, Tuiten, & van Honk, 1999). However, studies of endogenous estrogen in postmenopausal women have not always found an association between cognition and endogenous estrogen (Barrett-Connor & Goodman-Gruen, 1999; Yaffe, Grady, Pressman, & Cummings, 1998a), and research investigating the contribution of hormone replacement therapy (HRT) on cognitive performance in postmenopausal women has yielded conflicting results. Some studies reported beneficial effects of HRT on cognition (Kampen & Sherwin, 1994; Kimura, 1995; Maki, Zonderman, & Resnick, 2001; Robinson, Friedman, Marcus, Tinklenberg, & Yesavage, 1994; Sherwin, 1988), whereas other studies have reported no effect of HRT on cognition (Barrett-Connor & Kritz-Silverstein, 1993). Taken together, the results from both controlled trials and observational studies are difficult to interpret, due primarily to methodological inconsistencies (Haskell, Richardson, & Horwitz, 1997; Hogervorst, Williams, Budge, Riedel, & Jolles, 2000; Yaffe, Sawaya, Lieberburg, & Grady, 1998b).

Even though results from behavioral studies examining estrogen and cognition have been inconsistent, basic animal research clearly demonstrates estrogen's impact on the brain, particularly on systems that could be important for memory functions. Estrogen influences neurotransmission in the brain by stimulating a significant increase in both dopamine$_2$ receptors and density of serotonin binding sites (Fink, Sumner, Rosie, Grace, & Quinn, 1996). Estrogen increases dendritic spines in the hypothalamus and the hippocampus (McEwen, Alves, Bulloch, & Weiland, 1997; McEwen & Woolley, 1994), increases synaptic plasticity (Naftolin, Leranth, Perez, & Garcia-Segura, 1994), and enhances neuronal growth (Brinton, Proffitt, Tran, & Luu, 1997a, 1997b). These animal studies suggest that estrogen can play a role in cognitive abilities, however, the precise mechanism of estrogen's action on cognitive functions has yet to be determined.

Guided by persistent sex differences in verbal episodic memory performance and findings from the estrogen research domain, we aspired to better understand the contribution of active estradiol on sex differences in episodic memory by examining endogenous estradiol levels in older men and women. Men and women were matched on estradiol level, thereby keeping constant one possible contributor to the sex differences in episodic memory (Herlitz et al., 1997; Hill et al., 1995; Schaie & Willis, 1993; Zelinski, Gilewski, & Schaie, 1993). Therefore, if circulating estradiol is a major contributor to sex differences in episodic memory, we hypothesized that men and women with similar estradiol levels should exhibit similar episodic memory performance.

2. Method

2.1. Participants

Participants in our study were taken from the Betula Study on Memory, Health and Aging. The Betula study is a population-based, longitudinal prospective study (for a detailed description of purposes and study design, see Nilsson et al., 1997). All Betula participants were voluntarily recruited through community outreach efforts in Umeå, Sweden and ranged in age from 35 to 85. Individuals with mental retardation, dementia, visual or auditory handicap, or individuals who were not native Swedish speakers were excluded from the sample. All participants received an examination of memory functions, medical examination with blood testing, a health status interview, and questionnaires on social, economic issues, and critical life events. The health examination and blood sampling were done approximately one week prior to the cognitive testing. Because stable endogenous hormone levels were of concern, we selected those participants who were 55 years or older and women who underwent natural menopause. In order to control for medication effects on cognitive abilities, only participants who claimed no medication usage or only occasional usage of pain relievers, cold/flu preparations, diuretics, or antacids were considered further in the present study. Women were then matched to men on estradiol level (within 3.0 pmol/L) and age (within 5 years), resulting in 18 men and 18 women. As can be seen in Table 1, one-way ANOVAs yielded no differences between men and women in age, estradiol level, body mass index (BMI), education, and on a global

Table 1
Participant characteristics

	Women ($N = 18$)		Men ($N = 18$)	
	M	*SD*	*M*	*SD*
Hormones				
Estradiol,[a] pmol/L	94.38 ± 14.71		94.62 ± 14.64	
Testosterone, Free pg/mL	2.91 ± 2.15		$48.81 \pm 13.42^{***}$	
DHEA-S, nmol/L	2.41 ± 1.25		$4.31 \pm 2.40^{**}$	
Health				
Age, years	61.1 ± 6.8		60.28 ± 6.29	
BMI	27.4 ± 4.5		26.1 ± 3.3	
Smoke regularly (%)	33.3		11.1^{*}	
Education, years	9.3 ± 3.6		11.3 ± 3.5	
MMSE[b]	28.1 ± 1.3		28.0 ± 1.3	

[a] Normal estradiol range for postmenopausal women, 37–110 pmol/L and for men, 73–184 pmol/L (Greenspan & Strewler, 1997).

[b] MMSE (Mini-Mental State Examination; Folstein, Folstein, & McHugh, 1975) is a global measure of cognitive functioning.

$^{*}p < .09$.

$^{**}p < .01$.

$^{***}p < .001$.