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Sex Differences in Cognition in Healthy Elderly Individuals

Cynthia A. Munro, PhD[1], **Jessica M. Winicki, BA**[4], **David J. Schretlen, PhD**[1], **Emily W. Gower, PhD**[2], **Kathleen A. Turano**[3], **Beatriz Muñoz, MSc**[2], **Lisa Keay, PhD**[6], **Karen Bandeen-Roche, PhD**[5], and **Sheila K. West, PhD**[2]

[1]Department of Psychiatry and Behavioral Sciences, The Johns Hopkins University School of Medicine

[2]Dana Center for Preventive Ophthalmology, The Johns Hopkins University School of Medicine

[3]Lions Vision Center, Wilmer Eye Institute, The Johns Hopkins University School of Medicine

[4]Johns Hopkins School of Nursing, Johns Hopkins Bloomberg School of Public Health

[5]Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health

[6]George Institute for Global Health, Sydney University, Sydney, Australia

Abstract

Sex differences in patterns of cognitive test performance have been attributed to factors, such as sex hormones or sexual dimorphisms in brain structure, that change with normal aging. The current study examined sex differences in patterns of cognitive test performance in healthy elderly individuals. Cognitive test scores of 957 men and women (age 67–89), matched for overall level of cognitive test performance, age, education, and depression scale score, were compared. Men and women were indistinguishable on tests of auditory divided attention, category fluency, and executive functioning. In contrast, women performed better than men on tests of psychomotor speed and verbal learning and memory, whereas men outperformed women on tests of visuoconstruction and visual perception. Our finding that the pattern of sex differences in cognition observed in young adults is observed in old age has implications for future studies of both healthy elderly individuals and of those with cognitive disorders.

Keywords

Cognitive; sex differences; elderly; organizational effects; sexual dimorphism

INTRODUCTION

A consistent finding among studies of sex differences in cognitive test performance is that women outperform men on tests of verbal abilities, whereas men perform better than women on tests of visuospatial skills (Halpern, 1992; Maccoby & Jacklin, 1974). These differences, typically ranging from 0.3 to 0.9 standard deviation units (for a review, see Andreano & Cahill, 2009), have been purported to reflect sex differences in biological factors such as neuronal lateralization (Gur et al., 2000) areas of relative brain metabolism (Li et al., 2004), region-specific brain dimorphisms (Cowell et al., 1992), and/or circulating hormone levels (Silverman et al., 1999).

Address correspondence to: Cynthia A. Munro, Ph.D., Department of Psychiatry and Behavioral Sciences, The Johns Hopkins University School of Medicine, 600 N. Wolfe St., Meyer 218, Baltimore, Maryland 21287, telephone: 410-614-7785, fax: 410-955-0504, cmunro@jhmi.edu.

Many of the factors thought to underlie sex differences in cognition in young individuals are affected by normal aging. For example, functional neuroimaging studies document decreasing lateralization with age (Bracco et al., 2010), Sex hormone levels, also thought to be related to sex differences in cognition, decline with age, and, at least in men, low testosterone levels are associated with poorer cognitive functioning. The relation between circulating levels of sex hormones and cognition have been examined in several studies. Testosterone in particular has been related to performance on visuospatial tasks (Thilers, Macdonald, & Herlitz, 2006), and appears to have an increasing influence on these tasks with advancing age in men but not women (Thilers et al, 2006). Given that the prevalence of hypogonadism in older men is estimated at approximately 20% for community-based studies (Araujo et al., 2007) to almost 40% in clinic-based studies (Mulligan et al., 2006), it is likely that men's advantage on tests of visuospatial skills would be expected to diminish with advancing age. The association between estrogen and cognition in elderly women is less clear, with lifetime exposure to estrogen being associated with better performance in some cognitive domains but worse performance in other cognitive domains (Ryan, Carrière, Scali, Ritchie, & Ancelin, 2009).

To the extent that advancing age affects factors thought to underlie sex differences in patterns of cognitive functioning, these differences might not be expected to persist into old age. To our knowledge, only three studies have compared the cognitive test performance of men and women specifically among older adults. In a large sample of men and women aged 20 to 64, Jorm and colleagues (2004) found that women outperformed men on a test of verbal memory and that the magnitude of this difference did not vary with age (Jorm, Anstey, Christensen, Rodgers, 2004). Their study did not, however, include tests of visuospatial skills, on which men typically have an advantage, and their sample was limited to individuals younger than age 65. In a more recent study of 452 individuals aged 60–64, women outperformed men on a test of verbal learning whereas men outperformed women on tests of working memory and simple reaction time (Maller, Anstey, Reglade-Meslin, Christensen, Wen, & Sachdev, 2007). Visuospatial skills again were not assessed. Finally, Van Hooren and colleagues (2007) compared the cognitive test performance of men and women aged 67 to 81 years. The only sex difference they observed was on a word-list learning task, on which women performed better than men. As with the studies by Jorm and colleagues (2004) and Maller and colleagues (2007), the authors did not include tasks of visuospatial skills.

The aim of the current study was to determine whether sex differences in cognition that are observed among young adults could be observed in a sample of healthy elderly individuals. Whereas prior studies of this type have not included tasks on which men traditionally have an advantage, the current study included a comprehensive battery of tests, including those on which both sexes have demonstrated an advantage in samples of young adults.

METHOD

Subjects

Subjects were selected from participants of the Salisbury Eye Evaluation and Driving Study (SEEDS). The SEEDS is a longitudinal study of vision, cognition, and driving in older individuals on Maryland's Eastern Shore. To be recruited into the SEEDS, residents of the greater Salisbury, Maryland metropolitan area were invited to participate through letters sent by the Maryland Department of Motor Vehicles to all drivers aged 67 years or older registered as of May 1, 2005. The letters outlined the study and requested participation, indicated by return of a postcard. Potential subjects were then contacted to arrange for a home visit, during which they received oral and written descriptions of study aims and procedures, and provided written informed consent. Demographic characteristics and medical conditions were queried using structured questionnaires. Subjects were then scheduled for a clinic visit, during which they underwent assessments of vision and cognition through tests administered by trained technicians. The current results are from data obtained in round 1 of the study (July 2005–June 2006). Of 1425 participants, data from 957 (477 men), ranging in age from 67–88 years, were analyzed for the current study. The SEEDS is conducted under the auspices of the The Johns Hopkins Medical Institutions' review board.

Study procedures

Study visits were conducted in two parts. First, participants were interviewed at their homes, during which data were collected on demographic and medical information. Second, participants were seen in the SEEDS clinic, during which they underwent assessment of health status, mood, vision, and cognition. Cognitive test data obtained during the round 1 study visits were used for the current analyses.

Cognitive test battery

Mini Mental State Exam (MMSE; Folstein, Folstein, & McHugh, 1975)—This 30-item gross cognitive screening measure assesses orientation, attention, language, and construction.

Brief Test of Attention (BTA; Schretlen, Bobholz, & Brandt, 1996)—In this divided auditory attention task, participants listen to tape-recorded lists of letters and numbers of increasing length, and are required to state how many letters or numbers were contained within each list. Each item is scored as either correct or incorrect. For this study, we administered only the first 10 trials.

Trail Making Test (TMT; Halstead, 1947)—This timed test measures visuomotor skills as well as flexibility to shift sets under time pressure. Part A requires a subject to consecutively connect circles numbered 1–25, as quickly as possible. Part B requires a subject to consecutively connect circles while alternating between numbers (1–13) and letters (A-L), as quickly as possible. Performance is based on time required to complete each part.

Letter Fluency (Borkowski, Benton, & Spreen, 1967)—This task measures the ability to orally generate as many different words as possible that begin with a particular letter (*s* & *p*). The raw score is the number of words generated within one minute for each letter.

Category Fluency (Borkowski et al., 1967)—In this word-list generation task, participants are allotted one minute to orally generate as many words as possible belonging to a particular semantic category (animals & supermarket items).

Hopkins Verbal Learning Test-Revised (HVLT-R; Brandt & Benedict, 2001))—This word-list learning task requires the participant to recall a list of 12 words (4 words from each of three semantic categories), after each of 3 oral presentations. After approximately 20 minutes, delayed recall is assessed, followed by a yes-no recognition trial.

Beery-Buktenicka Developmental Test of Visuo-Motor Integration (VMI; Beery, 1997)—This test of visuoconstruction requires the participant to copy 24 figures of progressive difficulty. Items are scored as pass/fail.

Visual Perception Test—

This is a computerized test developed by AAA in which degraded traffic signs are presented and participants are required to identify, from an array of choices, which sign is the target sign. Number of errors, ranging from 0 to 10, were recorded.

Matching procedure

Men and women were matched for overall cognitive test performance, age, education, Geriatric Depression Scale score (30-item version; Yesavage, Brink, Rose, Lum, Huang, Adey, et al., 1983), and MMSE score. To match men and women on overall cognitive test performance, each cognitive test score was transformed into a z-score. The mean z-score across the entire test battery was then computed for each subject. Frequency matching was used to equate men and women on the variables of interest, which reduced the sample size for the current study from 1425 subjects to 957 subjects.

Statistical Analysis

Independent-samples t-tests or chi square tests, as appropriate, were used to compare demographic variables. To compare men and women on cognitive test scores, a multivariate analysis of variance (MANOVA) was used with sex as the independent variable, global cognitive test score entered as a covariate, and all cognitive test scores entered as dependent variables. Because the racial composition between men and women differed, the MANOVA was repeated with race entered as a covariate.

RESULTS

Demographic data

Table 1 summarizes study participants' demographic characteristics. The men and women included in this study ranged in age from 67 to 88, were predominantly Caucasian, and had completed between 1 and 2 years of college on average.

Cognitive test performance in men and women

As shown in Table 2, the pattern of cognitive test performance differed between men and women. Specifically, women had better scores on a test of psychomotor speed and visual search (TMT part A), and verbal learning and memory (HVLT-R). Conversely, men outperformed women on tests of letter fluency, visuoconstruction (VMI) and visual perception. Effect sizes (Cohen's *d*) for significant differences ranged from .096 (for letter fluency) to .400 (for HVLT-R Trials 1–3). Entering race as a covariate did not change the results.

DISCUSSION

The aim of this study was to determine whether sex differences in cognitive test performance observed in young adults can be observed in a sample of older adults. Our results indicated that the same pattern of sex differences observed in younger individuals was apparent in our cohort. Specifically, women outperformed men on tests of psychomotor speed and verbal learning and memory, whereas men performed better than women on tasks of visuoconstruction and visual perception.

Our finding that sex differences in cognition are apparent in late life suggests that the influence of factors underlying these differences is not attenuated by normal aging. Which factors are most influential in maintaining sex differences in cognitive test performance throughout adulthood remains to be determined, but one possibility is that early-life influences on sexual dimorphisms interact with environmental factors to maintain the differences. Indeed, sex differentiation of the brain is often attributable to the morphological and neurochemical effects of gonadal hormones on brain development. These alterations are thought to lead in some cases to the phenotypic expression of sex differences in adulthood (McEwen, 1983).

The notion that organizational, as opposed to activational, effects on brain dimorphism has been suggested to account for why sex differences persist over the lifespan. Results from at least some studies examining the relation between circulating hormones and cognitive functioning, however, would argue against this idea (Puts, Rodrigo, Bailey, Burriss, Jordan, & Breedlove, 2010). Moreover, preclinical studies have shown that adult hormone manipulations can completely reverse brain sexual dimorphism in some respects (Foy, Chiaia, & Teyler, 1984). Thus, age-related declines on levels of circulating hormones, which appear to have effects on cognition, do not appear to be adequate to diminish the sex differences in cognition that are observed among younger individuals. Examination of sex differences in cognition across the adult-age span is needed to determine whether the magnitude of sex differences in cognition that we observed in this study, while significant, might nevertheless reflect a decrease from that observed among younger adults.

An alternative explanation for why sex differences observed in younger adults are seen among older individuals is that sex differences in other factors associated with cognition emerge in later life. One such factor is vitamin D insufficiency, which has been shown to be more strongly associated with visuospatial skills in women than in men in one study (Seamans, Hill, Scully, Meunier, Androllo-Sanchez, Polito, et al., 2010) although another study did not find an association between vitamin D levels and visuospatial skills in men or women when assessed with a different test (Menant, Close, Delbaere, Sturkieks, Troller, Sachdev, et al., 2012). Another factor is the prevalence of white matter disease, which has been shown to be greater in women than in men with advancing age, and has been implicated as contributing to the increased prevalence of dementia in women compared to men (de Leeuw, de Groot, Achten, Oudkerk, Ramos, et al., 2001). The degree to which other factors affecting cognition become differentially prevalent in men and women with age is an area of future inquiry.

Our finding of a sex difference in cognitive test performance among elderly individuals suggests future studies of cognition among older adults should account for sex. Results from the current study appear to have particular relevance to studies of patients with mild cognitive impairment or frank dementia. Accounting for sex in such studies would maximize the precision with which we can detect cognitive decline, as doing so would increase our ability to detect subtler deficits than we would otherwise be able to appreciate.

This study has several strengths. First, this study represents to our knowledge the largest sample of elderly adults with data from a comprehensive cognitive test battery, which allowed for a comparison of various domains. Second, the men and women in this study were matched for overall level of cognitive functioning, allowing for a comparison of domains of cognition within a sample whose overall level of cognitive functioning was equivalent.

Weaknesses of this study include that it was limited to drivers. This limitation likely restricted the sample to include only those at the higher end of the continuum of cognitive functioning, reducing the representativeness of the sample. However, the fact that our participants may represent the healthier and higher-functioning older individuals may be desirable for our research question, for which we did not wish to have results confounded by sex differences in prevalence of diseases affecting cognition. Nevertheless, we cannot determine whether our results would generalize to individuals who have stopped driving, or to those who have never driven, perhaps for reasons unrelated to health status. Another weakness of this study is that this sample was restricted to one geographic area. Thus, we cannot know whether the cognitive test performance of the participants in this study is representative of those in other geographic locations.

CONCLUSION

We report a sex difference in cognitive test performance among a large sample of older individuals that parallels that seen among younger sample, suggesting that early-life influences on cognition persist into late life. Our findings emphasize the importance of taking into account sex differences in future studies of not only healthy individuals, but in elderly patients with disorders affecting cognition.

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Table 1

Subject demographics.

	Men	**Women**	***p***
Sample size	477	480	
Age, Mean (SD)	76.0 (5.0)	76.0 (5.1)	.997
Race, Number (%)			.007
Caucasian	432 (90.6)	404 (84.2)	
African-American	42 (8.8)	74 (15.4)	
Asian	1 (0.2)	2 (0.3)	
Other	2 (0.4)	0 (0.0)	
Education, Years (SD)	13.5 (2.1)	13.7 (2.6)	.105
Geriatric Depression Scale	3.3 (3.3)	3.6 (3.0)	.169

Table 2

Cognitive test scores in men and women.

Test[a]	Men	Women	*p*	Effect Size[d]
Mini Mental State Exam	28.46 (1.32)	28.59 (1.43)	.156	−.094
Brief Test of Attention, number correct	6.61 (2.21)	6.71 (2.37)	.848	−.044
Trail Making Test, number of seconds				
Part A[b]	51.06 (23.60)	46.32 (19.72)	.002	.218
Part A number of errors	0.17 (0.45)	0.14 (0.40)	.308	.070
Part B	125.87 (72.28)	117.84 (56.57)	.113	.124
Part B number of errors	0.74 (1.20)	0.71 (1.08)	.662	.026
Letter Fluency, raw score[c]	25.09 (8.09)	24.34 (7.45)	.022	.096
Category Fluency, raw score	39.52 (9.10)	39.27 (8.51)	.197	.028
Hopkins Verbal Learning Test-Revised				
Trials 1–3[b]	22.44 (4.66)	24.28 (4.53)	< .001	−.400
Delayed Recall[b]	7.45 (2.81)	8.08 (2.89)	< .001	−.221
Discrimination[b]	10.14 (1.47)	10.43 (1.75)	.011	−.179
Test of Visuo-Motor Integration[c]	18.84 (3.40)	17.97 (3.34)	< .001	.258
Motor Free Test of Visual Perception, number of errors[c]	2.74 (2.13)	3.39 (2.49)	.010	−.281

[a]Values represent mean (standard deviation).

[b]Women performed better than men on this measure.

[c]Men performed better than women on this measure.

[d]Cohen's *d*