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Gender differences in neuropsychological performance in individuals with atherosclerosis: Impact of vascular function

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Abstract

This study was conducted to assess gender differences in cognition in elderly individuals ($N = 88$; 38 women, 50 men) with atherosclerotic vascular disease (AVD) and to determine whether these were attributable to differences in vascular health. Assessments included neuropsychological testing and measurement of forearm vascular function using venous occlusion plethysmography. There was a significant female advantage on multiple neuropsychological tests. This gender effect was reduced somewhat but remained significant when controlling for education and vascular function. Our study suggests that gender differences in cognition persist into older age and are not primarily due to gender differences in vascular health.

Keywords

Gender; Cognition; Vascular disease; Neuropsychology; Vascular function

Introduction

Gender differences in cognitive abilities have been extensively studied and widely debated. Although there are no significant differences between males and females in general intelligence (Colom, Juan-Espinosa, Abad, & Garcia, 2000; Jensen, 1998), gender differences in specific cognitive abilities have been frequently reported. Gender differences in verbal abilities generally show a female advantage, although the existence and magnitude of such differences depend on which component of language is being assessed. Females tend to perform better than males on tasks of word fluency, spelling, articulation, and verbal memory (for review, see Kimura, 1999). Males typically tend to perform better than females on some tests of visuospatial abilities, though there is considerable variability among tasks.

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Visuospatial ability, like the verbal domain, is not a unitary concept. Rather, it is generally divided into three categories based on Linn and Petersen's (1985) factor analysis. These categories are *mental rotation*, the ability to visualize an object that has been rotated in space, *spatial perception*, the ability to accurately judge spatial relationships while ignoring distracting information, and *spatial visualization*, the ability to manipulate complex visuospatial information through multiple processing stages. The most consistent and reliable male advantage is found on tests of mental rotation of spatial stimuli (Peters et al., 1995; Voyer, Voyer, & Bryden, 1995). When gender differences are reported in episodic memory, they typically favor females. This advantage is seen in word recall (Kimura & Clarke, 2002), story recall (Hultsch, Masson, & Small, 1991), face recognition (Herlitz & Yonker, 2002), spatial location (Eals & Silverman, 1994), and odor recognition (Lehrner, 1993).

These general patterns seem to emerge in childhood, peak in early adolescence, and persist throughout adulthood. It remains unclear whether they extend into old age, and the literature is replete with contradictions. Several studies have reported preserved patterns of gender differences in old age. Bleecker, Bollawilson, Agnew, and Meyers (1988) found a female verbal memory advantage in older adults, with gender differences increasing with advancing age. Similarly, other studies have found that older males perform better on tasks of spatial rotation (Parsons, Rizzo, van der Zaag, McGee, & Buckwalter, 2005; Schaie, Maitland, Willis, & Intrieri, 1998). However, some have reported that gender differences disappear altogether (Buckwalter et al., 1996; Corey-Bloom et al., 1996). Moreover, Jorm, Anstey, Christensen, and Rodgers (2004) found that when controlling for current health state and health habits, no gender differences were observed on tests that typically favor males, while tests with a female advantage showed magnified gender effects.

The disagreement about the nature of cognitive gender differences is striking, but not entirely surprising. Part of the observed inconsistency is likely due to the large variety of tests used. There is considerable disagreement among researchers about the definitions of many cognitive constructs, and, consequently, the measures that they utilize and the specific abilities that they test can vary (Caplan, Macpherson, & Tobin, 1985; Halpern, 2000). Because many cognitive domains are not unitary constructs, but rather are composed of a variety of specific abilities in which gender differences vary, there is difficulty comparing findings across broad domains.

As previously mentioned, Jorm et al. (2004) found a significant mediating effect of current health state and health habits on gender differences in cognition in old age. One specific health state that has been a subject of relatively little cognitive research is the gender difference in vascular health. Although the prevalence and severity of vascular disease between men and women is similar after menopause, the onset of illness in men is nearly a decade earlier (Jacobs & Eckel, 2005; Medina, Aranda, Verdugo, Kato, & Owen, 2003). Vascular disease has been consistently linked to cognitive dysfunction, thus potentially placing men at increased risk for cognitive impairment at earlier ages. Additionally, a study by Kaye, Decarli, Luxenberg, and Rapoport (1992) found that the onset of age-related decline in brain volume occurs in males in their 50s, while women do not begin this atrophy until their 60s. Coffey et al. (1998) also found gender-specific atrophy patterns, with men showing greater age-related changes in specific brain structures than women, which could be vascular in nature. Thus, the impact of this gender disparity in vascular health on neuropsychological performance is of interest.

The purpose of this study was two-fold. First, we sought to determine whether there were gender differences in cognition in a sample of elderly individuals with vascular disease. Gaining a better understanding of gender differences in neuropsychological performance is

important because of its association with quality of life. Second, we wanted to determine whether gender differences in vascular health (measured as vasodilator function) could account for any observed gender differences in neuropsychological performance.

Method

This research was approved by the University of Iowa Institutional Review Board, and all participants provided written informed consent for participation following a thorough discussion of the project's procedures, risks, and potential benefits.

Participants

A total of 88 elderly individuals (38 women, 50 men; mean age = 68.0 years, $SD = 7.8$; mean education = 14.5 years, $SD = 3.2$) who were already participating in our ongoing study assessing vascular disease and neuropsychological performance were included in this study. All participants were age 55 or older, with an unequivocal diagnosis of atherosclerotic vascular disease (AVD) and a history of one or more of the following: angina pectoris, myocardial infarction, percutaneous transluminal coronary angioplasty, placement of coronary artery stent, and peripheral vascular disease (claudication). The numbers of participants taking various medications were as follows: antihypertensives = 83, statins = 64, nonsteroidal anti-inflammatories = 79, angiotensin-converting enzyme inhibitors = 36, beta blockers = 64, aspirin = 76. Additionally, 4 women were taking an estrogen supplement. No participants were on cognitive enhancing medications. Exclusion criteria included coronary artery bypass grafting, valve replacement, carotid endarterectomy, known history of stroke, head injury with loss of consciousness >30 min, other neurological disorder or systemic illness unrelated to vascular disease that is likely to affect cognition, focal neurological sign, diagnosis of dementia, and current or past severe psychiatric illness (e.g., bipolar affective disorder, schizophrenia). All participants underwent thorough history and physical examinations conducted by a physician, including neurological examination, electrocardiogram (ECG), and fasting blood draw/analysis.

Neuropsychological assessment

The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS; Randolph, 1998) was used to assess level of neuropsychological functioning. This widely used battery consists of 12 subtests, which form five age-corrected domain scores, including Immediate Memory, Delayed Memory, Attention, Language, and Visuospatial Construction. Additionally, an age-corrected Total Scale Score that indicates level of global neuropsychological functioning is determined. Because the RBANS has a limited assessment of executive function, additional tests were utilized. Matrix Reasoning and Similarities subtests of the Wechsler Adult Intelligence Scale–III (WAIS–III; Wechsler, 1997) were used as measures of nonverbal and verbal abstract thinking, respectively. The Stroop color–word interference trial (Stroop, 1935) was used as a measure of selective attention. Wide Range Achievement Test–3 (WRAT–3; Wilkinson, 1993) Word Reading was used to estimate level of premorbid cognitive functioning.

The Symptom Checklist-90-Revised (SCL-90-R; Derogatis, 1994) was used to assess psychological symptoms. This well-established self-report questionnaire asks participants to report the extent to which they are bothered by certain psychological symptoms, ranging from 0 (not at all) to 4 (extremely). It provides *T*-scores for nine domains, including depression, as well as an overall *T* score of overall psychological distress (Global Severity Index).

Vascular function assessment

Beginning the night before testing, participants fasted and refrained from taking any medication until all study procedures were completed the next morning. Forearm blood flow was measured in both arms before and after intra-arterial infusion of the vasoactive agent using venous occlusion plethysmography with mercury-in-silastic strain gauges. This methodology is described in detail elsewhere (Moser et al., 2007). Briefly, this technique is currently the gold standard for measuring resistance vessel function in the forearm, requires virtually no subjective judgment on the part of the technician, and has been shown to yield highly reproducible results in our laboratory. Moreover, vascular function is an intriguing measure because changes occur early in the development of vascular disease, even before development of atherosclerotic plaques (Lopez, Armstrong, Piegors, & Heistad, 1989). Additionally, all known risk factors for AVD are associated with impaired vascular function (Vogel, 1999). Thus, forearm blood vessel function was used as a surrogate indicator of general vascular health. During this procedure, the left brachial artery was cannulated under local anesthesia with a 27-gauge steel needle attached to an 18-gauge epidural catheter. Baseline forearm blood flows were obtained during infusion of 0.9% saline (1 ml/min) for 30 minutes. Acetylcholine (30 μ g/min) and verapamil (100 μ g/min) were then infused separately into the left arm, with each dose infused for 6 minutes.

Acetylcholine causes vasodilation through stimulation of endothelial cell muscarinic receptors, thereby activating endothelial nitric oxide synthase and increasing nitric oxide production, which then relaxes underlying vascular smooth muscle, resulting in resistance vessel dilatation. Verapamil acts directly on vascular smooth muscle cells, causing relaxation without altering endothelial cell function or generating nitric oxide. Thus, the vasodilation that occurs as the result of acetylcholine administration is often referred to as “endothelium dependent” and that occurring in response to verapamil is described as “endothelium independent.” Forearm blood flow was measured during the last 3 minutes of the dose. All participants received infusion of acetylcholine. Due to reasons unrelated to vascular health, vascular response to verapamil was not assessed in 3 women. Blood flows were measured in the noninfused (control) arm at time points identical to those in the infused arm in order to provide a contemporaneous control for random fluctuations in flow.

For the purposes of the current study, the vascular function outcome variables are the mean percentage increases in forearm blood flow in the infused arm after intra-arterial infusion of acetylcholine and verapamil, relative to baseline, adjusted for changes in blood flow in the noninfused arm. Higher values indicated better vessel function. Neuropsychological assessment and blood vessel testing were conducted by separate individuals, each of whom was blind to the other's data.

Statistical analyses

Independent-samples *t* tests were used to determine whether the genders differed with regard to age, education, estimated level of premorbid neuropsychological functioning, global psychological distress, depressive symptoms, vascular risk factors, and blood vessel function (our indicator of vascular health). Chi-square analyses assessed gender differences in prevalence of health-related conditions. Then, a *t* test was used to determine whether there was a significant gender difference in global neuropsychological functioning (RBANS Total Scale Score). When it became clear that there was, additional *t* tests were used to examine gender differences in more specific aspects of neuropsychological function. Finally, a series of analyses of covariance (ANCOVAs) was used to examine gender differences in neuropsychological performance while controlling for education and vasodilator response to acetylcholine. These latter two variables were found to be significantly different between the genders during our initial analyses and were also significantly correlated with global

cognition. Additionally, an identical series of ANCOVAs was used with vasodilator response to verapamil as the vascular covariate. All interaction terms were found to be nonsignificant and thus were not included in the final models.

To determine the magnitude of cognitive gender differences, effect sizes were calculated using the adjusted mean values of neuropsychological scores in the numerator (controlling for education and vascular function), with the adjusted standard deviation in the denominator. Additionally, an effect size was calculated without controlling for vascular function, in order to determine the gender differences accounted for by this variable.

Even though the measures of vascular function used in this study are known to be associated with all known risk factors for AVD, the possibility exists that these measures of vascular function do not completely capture the effects of established risk factors on cognition. Therefore, a follow-up ANCOVA was conducted to examine gender effects on global neuropsychological function (RBANS Total Scale Score) controlling for education, vasodilator response to acetylcholine, and the four vascular-related variables on which the genders significantly differed: LDL (low-density lipoprotein) cholesterol, HDL (high-density lipoprotein) cholesterol, total cholesterol, and triglycerides.

Given that a significant gender difference was found regarding global cognition at the onset of statistical analysis, an alpha level of .05 was used in all follow-up analyses used to investigate gender differences in more specific aspects of cognition.

Results

There were no significant differences between men and women in age, years since cardiovascular disease diagnosis, diabetes, history of renal disease, history of liver disease, psychological distress (SCL-90-R Global Severity Index score), depressive symptoms (SCL-90-R Depression score), or estimated premorbid neuropsychological functioning (WRAT-3 Word Reading). However, women had significantly fewer years of education (women, $M = 13.24$, $SD = 2.28$; men, $M = 15.5$, $SD = 3.41$), $t(84.78) = -3.72$, $p < .001$. Additionally, women had substantially better vascular responses to acetylcholine. There was no significant gender difference in response to verapamil. Descriptive and inferential statistics of vascular function and risk factors can be found in Table 1. Descriptive and inferential statistics of neuropsychological scores can be found in Table 2.

Women showed significantly higher global neuropsychological function (RBANS Total Score) and significantly outperformed men on 5 of the 12 RBANS subtests (List Learning, Semantic Fluency, Coding, List Recall, and List Recognition) as well as on the Stroop interference trial. In contrast, men performed better than women on 1 RBANS subtest (Line Orientation). No gender differences were observed on the Story Memory, Figure Copy, Picture Naming, Digit Span, Story Recall, or Figure Recall subtests. Men and women performed within the average range on all of the RBANS subtests, with the exception of Figure Copy, in which both groups performed in the low average range, and List Recall, in which women performed in the high average range. Additionally, there were no significant differences on the Similarities and Matrix Reasoning subtests of the WAIS-III. When education and vasodilator response to acetylcholine were controlled for, the effect of gender on global neuropsychological function and all subtests remained significant, except for the Coding subtest of the RBANS and the Stroop interference trial, which became nonsignificant. Results were very similar, with an identical pattern of significance when verapamil was the covariate, except for the Coding subtest of the RBANS, in which the gender difference remained significant.

When adding the four vascular risk factors that showed a significant gender difference (LDL cholesterol, HDL cholesterol, total cholesterol, and triglycerides) to the original ANCOVA controlling for education and vasodilator response to acetylcholine, the gender difference on global neuropsychological function remained significant, $F(1, 76) = 6.53, p = .013$.

Controlling for education only, the gender effect size with regard to global cognitive function (RBANS Total Scale Score) was .93. This was reduced to .72, a 23% decrease, when endothelium-dilator function (response to acetylcholine) was entered as an additional covariate, but was still significant ($p = .004$). Please see Table 3 for ANCOVA results.

Discussion

In this sample of older adults with vascular disease, women showed significantly stronger performance than men on a test of global neuropsychological functioning as well as on more specific measures of language, memory, speed, and attention. In contrast, men performed better than women on one test of visuospatial perception. These differences do not appear to be entirely attributable to gender differences in vascular health or education.

Overall, there were significant gender differences on nearly half of all of the cognitive tests. This stands in contrast to findings in which there were no gender differences found on global neuropsychological screening measures (Buckwalter et al., 1996; Corey-Bloom et al., 1996) and verbal memory and ability (Armstrong & Walker, 1994). However, our study replicates findings in which females maintain their advantage on tests of verbal fluency and immediate and delayed memory (Bleecker et al., 1988; Portin, Saarijarvi, Joukamaa, & Salokangas, 1995), and males retain their advantage in visuospatial perception (Collaer & Nelson, 2002; Meinz & Salthouse, 1998; Parsons et al., 2005).

Whereas we assessed individual RBANS subtests, Beatty, Mold, and Gontkovsky (2003) analyzed gender differences on the five RBANS index scores. Similar to our findings, when education was controlled for, women in their study performed significantly better on the Immediate Memory, Delayed Memory, and Language indices, whereas men performed significantly better on the Visuospatial/Construction Index. Additionally, no significant gender difference was found on the Attention Index in their study. As noted previously, gender differences may vary with regard to specific abilities under the same broad domain. Thus, one advantage of our study is the analysis of individual subtests. Because index scores are determined by multiple subtest scores, they may not fully capture the existence and magnitude of gender differences on specific tasks.

With regard to vascular function, women in our sample showed significantly greater forearm vasodilation in response to acetylcholine than men, suggesting relatively superior vascular health among women, specifically endothelium-mediated dilator function (response to acetylcholine). Well-established norms are not available for measures of vascular function as they are for the neuropsychological tests employed in this study. However, using similar methodology, Kanani et al. (1999) found the normal range of vascular function responses to acetylcholine and verapamil to be 400–600%, though participants in that study were substantially younger and also free from atherosclerosis. Thus, participants in our study exhibited impaired vascular function; this may be related to age and/or atherosclerosis.

Even when controlling for this variance in endothelium-dependent and -independent dilator function (and the significant disparity in education), gender differences in neuropsychological function remained significant on most tests. When introducing the four known risk factors that were significantly different between genders as additional covariates, the gender difference in global cognition remained significant. This supports a conclusion that the gender difference in cognitive performance is independent of vascular health.

Though still significant, the magnitude of the gender difference in global cognition was reduced by 23% when controlling specifically for endothelium-dilator function. Intriguingly, gender-related differences in tests of psychomotor speed and selective attention were diminished after accounting for variance in vascular function. These findings comport well with the neuropsychological profile of vascular disease, in which attention and psychomotor slowing are primary deficits in vascular dysfunction (Cohen et al., 2009; Moser et al., 2008). Therefore, it is not surprising that controlling for vascular health would have an effect on gender differences in these constructs.

General trends have shown that men perform better than women on visuospatial tasks, and women outperform men on some tests of language and memory. However, this is a broad generalization, and as our findings show, there is considerable variability within these domains. Some tasks showed large gender differences, while on other tasks no differences were observed. Another controversial topic in cognitive gender difference research concerns the magnitude and practical importance of observed differences. Cohen (1988) proposed that an effect size of 0.2 be interpreted as small, 0.5 as medium, and 0.8 as large, though, as Cohen points out, these terms are relative, are impacted by measurement accuracy, and should be used with caution. Nonetheless, according to these guidelines the female advantages on semantic fluency and immediate and delayed memory tasks were striking. The male advantage on spatial perception was also quite pronounced, similar to the effect size (0.64) on spatial perception found by Linn and Petersen (1985) in their meta-analysis of gender differences in visuospatial abilities.

It is noteworthy that although women had fewer years of education, they still outperformed men on many neuropsychological tests. Van Exel et al. (2001) reported a similar finding and subsequently posited that biological mechanisms, such as differing degrees of atherosclerosis, may account for the observed phenomenon. However, our findings do not support such an exclusive role of atherosclerotic vascular disease because most of our observed gender differences in cognition remained significant even when controlling for differences in vascular health. The fact that the WRAT-3 Word Reading score was similar for men and women is suggestive of similar premorbid neuropsychological function, perhaps more so than their educational history suggests. It is plausible that the education differences in this group may not truly be reflective of premorbid neuropsychological function but actually be indicative of a historical phenomenon in which less emphasis was placed on formal education for women, regardless of level of intellectual functioning.

Future studies are needed to explore alternative variables that may influence cognitive gender differences in the elderly. A growing area of research has focused on the relationships among endogenous and exogenous sex hormones and cognitive decline. The role of hormones in cognitive function is supported by the fact that many gender-specific abilities are influenced by fluctuations in hormone levels (Hogervorst, De Jager, Budge, & Smith, 2004; Kimura & Hampson, 1994). Also, emerging evidence has suggested that estrogen therapy may play a neuroprotective role in old age (for reviews see Amantea, Russo, Bagetta, & Corasaniti, 2005; Yaffe, Sawaya, Lieberburg, & Grady, 1998). However, findings are mixed on the existence and magnitude of associations between hormone levels and cognition. Additionally, the mechanisms underlying their neuroprotective effects are still subject to debate, and more studies are warranted to better characterize their modes of action and assess their potential benefits. Unfortunately, our data do not allow us to assess sex steroid levels, nor draw a conclusion regarding their contribution to the gender difference in neuropsychological performance in our participants.

One important limitation of this study is that our participants all had clinically significant vascular disease, and thus these findings may not be generalizable to healthy older adults.

We chose to study patients with atherosclerosis because there would have been greater vascular dysfunction. However, it is possible that the impact of atherosclerosis on vascular function (and possibly cognition) could have obscured the effects of gender. Gender differences in vascular function in older adults without clinical vascular disease might moderate gender differences in cognition. Moreover, our sample may be unique in that there was no significant gender difference in current age or age of onset of vascular disease, even though men tend to develop the disease nearly a decade before women. It is also important to keep in mind the cohort variables that exist in our population. Especially in context of the significant disparity in female education, our findings may not be reflective of future cohorts in which gender differences in education and life experience become less pronounced. Several studies have noted decreasing gender differences across a variety of cognitive tasks (Colom, Quiroga, & Juan-Espinosa, 1999; Feingold, 1988).

Gender differences in cognition across the lifespan have been widely studied. However, as Halpern (2000) noted, the elderly continue to be an understudied population for this type of research. Our data suggest that differences in vascular function do not explain better cognition in females, even in a population that exhibits vascular disease. With the close association between cognition and quality of life, identifying moderating and mediating variables involved in neuropsychological performance is of importance in an aging society.

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TABLE 1
Gender differences in vascular function and vascular risk factors

Variable	Men		Women		T	P
	M	SD	M	SD		
% Δ in blood flow with acetylcholine	193	132	283	166	2.83	.006
% Δ in blood flow with verapamil	227	114	276	158	1.66	.10
Systolic BP, mm Hg	134	19	139	25	0.92	.34
Diastolic BP, mm Hg	72	11	72	11	0.92	.85
Glucose, mg/dl	117	35	110	26	-0.98	.33
LDL-C, mg/dl	84	23	97	35	2.04	.046
HDL-C, mg/dl	45	9	58	19	4.02	<.001
Total cholesterol, mg/dl	155	29	188	45	3.95	<.001
Triglycerides, mg/dl	126	58	158	81	2.13	.04
Homocysteine	12.11	4.74	11.49	2.99	-0.69	.49
C-reactive protein	3.98	4.95	5.77	7.52	1.30	.20
Body mass index	32	7	30	7	-1.02	.31

Note. Blood flow % Δ is the percentage increase in blood flow in response to intra-arterial infusion of drug, adjusted for changes in blood flow in the noninfused arm (higher scores indicate better function). BP = blood pressure; LDL-C = low-density-lipoprotein cholesterol; HDL-C = high-density-lipoprotein cholesterol.

TABLE 2

Gender differences in neuropsychological performance

Cognitive scores	Men		Women		t	p
	M	SD	M	SD		
WRAT-3 Word Reading	46.2	3.9	46.1	4.2	0.28	.91
RBANS						
Total Scale Score	95.5	11.1	100.5	11.0	2.09	.04
List Learning	24.6	4.9	29.2	3.7	5.00	<.001
Story Memory	17.7	3.3	17.0	3.5	-1.03	.31
Figure Copy	16.6	2.5	16.7	1.9	0.08	.94
Line Orientation	18.0	2.1	16.5	3.1	-2.79	.01
Picture Naming	9.7	0.55	9.7	0.50	0.50	.62
Semantic Fluency	18.0	4.5	21.8	4.5	3.99	<.001
Digit Span	10.1	2.4	9.7	2.4	-0.74	.46
Coding	39.7	6.5	43.1	8.9	2.05	.04
List Recall	5.4	2.4	7.3	1.8	4.06	<.001
List Recognition	19.0	1.5	19.7	0.77	2.80	.01
Story Recall	9.2	1.9	9.5	1.8	0.59	.55
Figure Recall	10.9	4.9	11.8	3.1	1.09	.28
WAIS-III						
Similarities	23.2	5.8	21.9	5.3	-1.09	.28
Matrix Reasoning	14.2	4.7	13.7	5.2	-0.47	.64
Stroop color-word interference	33.6	8.2	37.5	8.2	2.3	.02

Note. WRAT-3 = Wide Range Achievement Test-Third Edition. RBANS = Repeatable Battery for the Assessment of Neuropsychological Status. WAIS-III = Wechsler Adult Intelligence Scale-Third Edition. Degree of freedom (*df*) for all tests = 86, except in the case of Figure Recall (83.4) and List Recognition (76.1), for which *df*s were adjusted due to unequal between-group variances. RBANS Total Scale Score is an age-corrected standard score with a normative mean of 100 and standard deviation of 15. All other scores above are raw scores. All of these raw scores fall within the average range, with the exception of Figure Copy, in which both groups performed in the low average range, and List Recall, in which women performed in the high average range.

TABLE 3
Gender differences in neuropsychological performance when controlling for vascular function and education

Cognitive tests	Controlling for response to					
	Acetylcholine			Verapamil		
	F	p	Effect size	F	p	Effect size
WRAT-3 Word Reading	1.40	.24	0.29	2.45	.12	0.37
RBANS						
Total Score	8.77	.004	0.72	16.05	<.001	0.95
List Learning	30.99	<.001	1.35	35.80	<.001	1.42
Story Memory	0.003	.96	-0.04	0.47	.50	0.16
Figure Copy	2.67	.11	0.40	0.96	.33	0.23
Line Orientation	8.0	.01	-0.68	6.05	.02	-0.59
Picture Naming	0.70	.41	0.21	0.36	.55	0.15
Semantic Fluency	11.18	.001	0.81	17.13	<.001	0.98
Digit Span	0.04	.85	-0.05	0.08	.78	-0.07
Coding	3.16	.08	0.43	8.29	.005	0.69
List Recall	19.74	<.001	1.08	24.05	<.001	1.17
List Recognition	9.0	.004	0.73	11.95	.001	0.82
Story Recall	2.0	.16	0.34	5.06	.03	0.53
Figure Recall	2.28	.14	0.37	2.10	.15	0.35
WAIS-III						
Similarities	0.55	.46	-0.18	0.02	.89	0.03
Matrix Reasoning	0.02	.90	-0.03	<0.001	.99	0.02
Stroop color-word interference	2.32	.13	0.38	1.81	.18	0.33

Note. WRAT-3 = Wide Range Achievement Test-Third Edition. RBANS = Repeatable Battery for the Assessment of Neuropsychological Status. WAIS-III = Wechsler Adult Intelligence Scale-Third Edition. Effect sizes are Cohen's *d* values calculated using adjusted means; *df* for all acetylcholine tests = 1, 84; *df* for all verapamil tests = 1, 81. All significant differences favored women (as indicated by positive value effect sizes), with the exception of RBANS Line Orientation, which favored men. As noted in the text, response to acetylcholine is an indicator of endothelium-dependent vascular function, while response to verapamil is an indicator of endothelium-independent vascular function.