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GENDER DIFFERENCES IN COGNITIVE ABILITY FROM AGE 40 TO 79

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ABSTRACT

This study, a cross-sectional study of adults who were administered the CNS Vital Signs test battery when it was being standardized, investigated whether there are gender differences in the rate of neurocognitive decline with age. As a group, men scored better on tests of visual memory, executive function and psychomotor speed. Women scored better in tests of verbal memory, processing speed, and attention. Regression analysis indicated significant effects: men declined more sharply in tests of memory, and women declined more sharply in tests of processing and psychomotor speed.

INTRODUCTION

The results of multiple studies are consistent in demonstrating gender differences in neurocognitive performance: females, on average, perform better than males in tests of fluency, verbal memory, fine motor skills and perceptual speed; males tend to perform better on tests of visual memory and visuospatial problem solving {1, 2}. Gender differences, however, are not very big and they are far outweighed by variability among individuals. Thus, cognitive gender differences, though interesting in the abstract, have little practical import.

One area where gender differences may be meaningful is in the study of cognitive decline associated with aging. Despite some evidence of greater age-related deterioration of the brain in males than in females, gender differences in rates of cognitive aging have proved inconsistent {3, 4, 5, 6, 7, 8, 9}. This technical matter may have a bearing on clinical studies of mild cognitive impairment (MCI) and Alzheimer's disease (AD). MCI may be more common in men than women {10} but AD is generally thought to be more common in women {11, 8}; when juxtaposed, these two opinions are mutually opposed. Both, however, suffer from lack of replication. American studies tend to report equal rates of AD in men and women while European studies show higher rates in women {12}. Such inconsistencies are likely to be methodological in origin {5, 13, 4, 8}.

In this report, we took advantage of a large database of normal, healthy Americans who had been tested with a broad-spectrum computerized neurocognitive test battery to examine cognitive changes from age 40 to 79 relative to gender and other relevant variables.

METHODS

This was a cross-sectional study of adults who had been administered the CNS Vital Signs test battery when the battery was being standardized.

Subjects

During the standardization study, normal subjects were selected if they were in good health, on no intercurrent medications that might have CNS effects, and with no history of psychiatric or neurological disease. Subjects gave their written informed consent to permit their de-identified data to be used for research purposes. In this study, the data from 1352 subjects aged 40-79 were available, 546 males and 806 females. The relevant data are shown in Table 2.

Cognitive Indicators

The CNS Vital Sign (VS7) is a computerized neurocognitive test battery comprised of seven familiar neuropsychological tests that generate ten independent scores. Factor analysis generates four factors. See Table 1 for key to each test.

Test-retest reliability and concurrent validity of the VS7 battery are comparable to similar, conventional neuropsychological tests {20}. The discriminant validity of VS7 has been established in studies of patients with mild cognitive impairment and early dementia {21}; post-concussion syndrome and severe traumatic brain injury {22}; ADHD {23, 24}; depression {25, 26}; schizophrenia and bipolar disorder {27}; and malingering {20}.

Analysis

Scores that did not have a normal distribution were long-transformed or standardized with elimination of outliers who scored more than six standard deviations from the mean. Group

comparisons were done with MANOVA (Multivariate Analysis of Variance), controlling for age, race, gender, education, and self-reported computer familiarity. Regression analysis was by the generalized linear model (SPSS, Statistical Package for the Social Sciences) with the same covariates. Effect sizes were by Cohen's d.

RESULTS

The subjects were comparatively well-educated (16.2 years) and predominantly white (90.5%). Males, as a group, were older and a bit more familiar with computers (ANOVA, Analysis of Variance) (Table 2).

MANOVA (Table 3) indicates highly significant gender differences, although the effect sizes are small. Men, as a group are superior in tests of visual memory, executive function (SAT) and the three tests of psychomotor speed (FTT, SRT, CRT). Women, as a group, are superior in tests of verbal memory, processing speed (SDC), and attention (ST and CPT).

The effect of gender on cognitive aging was measured by linear regression in two ways. In the first, cognitive scores were regressed against age, separately for males and females. Covariates were race, education and computer familiarity. For all of the ten tests, and for both genders, the regressions were highly significant. The comparative slopes of the regression lines indicate gender differences. Cognitive performance declines at a steeper rate in males in tests of memory (VBM and VIM) and attention (ST and CPT). In females, it declines at a steeper rate in tests of cognitive and motor speed (SDC, SDC, FTT, SRT, CRT). The Stroop response time (RT) is one measure of information processing speed that appears to decline more steeply in males (Table 4).

An alternative and more rigorous analysis is to regress cognitive test scores against age for all Ss, and to examine the main effects of age and gender (Table 5). The age X gender interaction is significant for the two memory tests and for four tests of cognitive and motor speed (SDC, SAT, FTT, CRT).

To illustrate aging-related gender differences, Figure 1a shows the decline in composite memory scores (the sum of correct responses on the VBM and VIM tests), in which men decline more steeply, and in Figure 1b the SAT, in which women decline more steeply. The slopes of the linear trendlines diverge with aging.

DISCUSSION

Because the subjects were mostly white and well-educated, these results may not be generally applicable. What occurs in well-endowed brains, however, may only be amplified in people with less in the way of cognitive reserve. An effect in healthy people is likelier to reflect normal brain aging than a disease process.

Although the results of similar studies have not been consistent, our findings are similar to those of Read et al who studied 647 twin pairs from the Swedish Twin Registry, and noted greater deficits in women compared with men at higher ages in symbol digit coding {28}; and also to the results of the Longitudinal Aging Study Amsterdam, which reported better memory performance in aging women. We are not aware of any studies similar to ours, which uses a broad-based neurocognitive battery to assay the relative ageXgender effects of multiple domains, or a computerized battery that is highly sensitive to small differences in psychomotor speed.

There is no paucity of studies, however, that report no gender differences at all in the pattern of cognitive decline {5, 29}. That is surprising, since there is ample evidence that brain

aging occurs differently in men and women. Functional and structural differences in brain aging have been demonstrated using volumetric magnetic resonance imaging and positron emission tomography {6, 30, 31, 32, 33, 34, 35, 36, 37}. The brain undergoes sexually dimorphic changes in gene expression in later life and different categories of genes are predominantly affected in males and females {7}.

Studies of neuroanatomic and neurofunctional correlates of cognitive aging necessarily involve small numbers of subjects, so it is not surprising that the results are diverse and that no specific pattern of brain aging relative to cognitive performance has emerged. In one study of diffusion tensor imaging in healthy adults age-related degradation in anterior brain areas was found to be associated with decreased processing speed, and decline in posterior areas was associated with reduced inhibition and greater task switching costs. Poorer episodic memory was associated with age-related differences in central white matter regions. Age-related decline in cognitive skills and their putative neuroanatomic substrates support the view that age-related cognitive declines are unlikely to represent a unitary process {38}.

It is not unlikely, therefore, that gender contributes to the diversity of processes that govern cognitive aging. If it is true, for example, that women have greater blood flow in the mid-temporal brain region {33, 37} that might explain their comparative resistance to memory decline. The fact that they decline in speeded cognitive processes suggests relative vulnerability in anterior cortical and subcortical structures. There is evidence from positron emission tomography studies have indicated that the in vivo availability of dopamine D(2)-like receptors declines with age in the human brain. Although the availability of D(2)-like receptors in the frontal cortex is higher in women than in men, they decrease with age with the fastest rate in healthy women in the frontal cortex {34}.

The fact that the differences we found between men and women were very small renders the comparison to neuroanatomic and neurofunctional studies speculative if not facile. Our results suggest that large numbers are necessary to elicit reliable differences between the genders. Nor do our data, taken from a healthy group of well-educated people, address how differential rates of aging-related morbidity in men and women might affect the aging by gender equation.

CONCLUSIONS

It appears that cognitive aging occurs differently in men and women. The differences are small but highly significant, and, in this study, they are internally consistent. Memory declines more steeply in men than in women, irrespective of the fact that women, as a group, perform better in verbal memory and men in visual memory. Tests of psychomotor speed decline more steeply in women, whether in a purely motor task like finger tapping or in measures of cognitive processing speed like coding and shifting attention; and, again, irrespective of group differences in mean scores.

REFERENCES

(1) Torres A, Gómez-Gil E, Vidal A, et al: Gender differences in cognitive functions and influence of sex hormones. *Actas Españolas De Psiquiatría* 2006; *34*(6): 408-415.

(2) Halpern DF: Sex differences in intelligence. Implications for education. *The American Psychologist* 1997; *52*(10): 1091-1102.

(3) Maylor EA, Reimers S, Choi J, et al: Gender and sexual orientation differences in cognition across adulthood: age is kinder to women than to men regardless of sexual orientation. *Arch Sex Behav* 2007; *36*(2): 235-249. doi:10.1007/s10508-006-9155-y.

(4) Aartsen, MJ, Martin M, & Zimprich D: Gender differences in level and change in cognitive functioning. Results from the Longitudinal Aging Study Amsterdam. *Gerontology* 2004; *50*(1): 35-38. doi:10.1159/000074387.

(5) Barnes LL, Wilson RS, Schneider JA, et al: Gender, cognitive decline, and risk of AD in older persons. *Neurology* 2003; *60*(11): 1777-1781.

(6) Coffey CE, Lucke JF, Saxton JA, et al: Sex differences in brain aging: a quantitative magnetic resonance imaging study. *Arch Neurol* 1998; *55*(2): 169-179.

(7) Berchtold NC, Cribbs DH, Coleman PD, et al: Gene expression changes in the course of normal brain aging are sexually dimorphic. *Proc Natl Acad Sci U S A* 2008; *105*(40): 15605-15610. doi:10.1073/pnas.0806883105.

(8) Schmidt R, Kienbacher E, Benke T, et al: Sex differences in Alzheimer's disease. *Neuropsychiatrie: Klinik, Diagnostik, Therapie Und Rehabilitation: Organ Der Gesellschaft Österreichischer Nervenärzte Und Psychiater* 2008; *22*(1): 1-15.

(9) Finkel D, Reynolds CA, Berg S, et al: Surprising lack of sex differences in normal cognitive aging in twins. *Int J Aging Hum Dev* 2006; *62*(4): 335-357.

(10) Petersen RC, Roberts RO, Knopman DS, et al: Prevalence of mild cognitive impairment is higher in men. The Mayo Clinic Study of Aging. *Neurology* 2010; *75*(10): 889-897. doi:10.1212/WNL.0b013e3181f11d85

(11) Viña J, Lloret A: Why women have more Alzheimer's disease than men: gender and mitochondrial toxicity of amyloid-beta peptide. *Journal of Alzheimer's Disease: JAD*, *20 Suppl 2* 2010; S527-533. doi:10.3233/JAD-2010-100501.

(12) Musicco M: Gender differences in the occurrence of Alzheimer's disease. *Funct Neurol* 2009; *24*(2): 89-92.

(13) van Hooren SAH, Valentijn AM, Bosma H, et al: Cognitive functioning in healthy older adults aged 64-81: a cohort study into the effects of age, sex, and education. *Neuropsychology, Development, and Cognition. Section B, Aging, Neuropsychology and Cognition* 2007; *14*(1): 40-54. doi:10.1080/138255890969483.

(14) Rey A: *L'examen clinique en psychologie*. Paris, Presses Universitaires de France, 1964

(15) Smith A: *Symbol Digit Modalities Test (SDMT). Manual (Revised)*. Los Angeles, CA, Western Psychological Services, 1982

(16) Stroop J: Studies of interference in serial verbal reactions. *J Exp Psychol Gen* 1935; *18*: 643-662.

(17) Le TH, Pardo JV, Hu, X: 4 T-fMRI study of nonspatial shifting of selective attention: cerebellar and parietal contributions. *J Neurophysiol* 1998; *79*(3): 1535-1548.

(18) Nagahama Y, Sadato N, Yamauchi H, et al: Neural activity during attention shifts between object features. *Neuroreport* 1998; *9*(11): 2633-2638.

(19) Rosvold HE, Delgado, JM: The effect on delayed-alternation test performance of stimulating or destroying electrically structures within the frontal lobes of the monkey's brain. *Journal of Comparative and Physiological Psychology* 1956; *49*(4): 365-372.

(20) Gualtieri C, Johnson L: Reliability and validity of a computerized neurocognitive test battery, CNS Vital Signs. *Archives of Clinical Neuropsychology: The Official Journal of the National Academy of Neuropsychologists* 2006c; *21*(7): 623-643. doi:10.1016/j.acn.2006.05.007.

(21) Gualtieri C, Johnson L: Neurocognitive testing supports a broader concept of mild cognitive impairment. *American Journal of Alzheimer's Disease and Other Dementias* 2005; *20*(6): 359-366.

(22) Gualtieri C, Johnson L: A computerized test battery sensitive to mild and severe brain injury. *Medscape Journal of Medicine* 2008al *10*(4): 90.

(23) Gualtieri C, Johnson L: Efficient allocation of attentional resources in patients with ADHD: maturational changes from age 10 to 29. *Journal of Attention Disorders* 2006b; *9*(3): 534-542. doi:10.1177/1087054705283758.

(24) Gualtieri C, Johnson L: Medications do not necessarily normalize cognition in ADHD patients. *Journal of Attention Disorders* 2008b; *11*(4): 459-469. doi:10.1177/1087054707305314.

(25) Gualtieri C, Johnson L, Benedict K: Neurocognition in depression: patients on and off medication versus healthy comparison subjects. *J Neuropsychiatry Clin Neurosci* 2006; *18*(2): 217-225. doi:10.1176/appi.neuropsych.18.2.217.

(26) Gualtieri C, Johnson L: Age-related cognitive decline in patients with mood disorders. *Prog Neuropsychopharmacol Biol Psychiatry* 2008c; *32*(4): 962-967. doi:10.1016/j.pnpbp.2007.12.030.

(27) Gualtieri C, Johnson L. A Computerized Neurocogntive Test Battery for Studies of Schizophrenic and Bipolar Patients. *Schizophr Res* 2006a; *81*: 122.

(28) Read S, Pedersen NL, Gatz M, et al: Sex differences after all those years? Heritability of cognitive abilities in old age. *J Gerontol B Psychol Sci Soc Sci* 2006; *61*(3): P137-143.

(29) Finkel D, Reynolds CA, McArdle, JJ, et al: Latent growth curve analyses of accelerating decline in cognitive abilities in late adulthood. *Dev Psychol* 2003; *39*(3): 535-550.

(30) Murphy DG, DeCarli C, McIntosh AR, et al: Sex differences in human brain morphometry and metabolism: an in vivo quantitative magnetic resonance imaging and positron emission tomography study on the effect of aging. *Arch Gen Psychiatry* 1996; *53*(7): 585-594.

(31) Cowell PE, Turetsky BI, Gur RC, et al: Sex differences in aging of the human frontal and temporal lobes. *J Neurosci* 1994; *14*(8): 4748-4755.

(32) Kawachi T, Ishii K, Sakamoto S, et al: Gender differences in cerebral glucose metabolism: a PET study. *Journal of the Neurological Sciences* 2002; *199*(1-2): 79-83.

(33) Ragland JD, Coleman AR, Gur RC, et al: Sex differences in brain-behavior relationships between verbal episodic memory and resting regional cerebral blood flow. *Neuropsychologia* 2000; *38*(4): 451-461.

(34) Kaasinen V, Kemppainen N, Någren K, et al: Age-related loss of extrastriatal dopamine D(2) -like receptors in women. *J Neurochem* 2002; *81*(5): 1005-1010.

(35) Hazlett EA, Byne W, Brickman AM, et al: Effects of sex and normal aging on regional brain activation during verbal memory performance. *Neurobiol Aging* 2010; *31*(5): 826-838. doi:10.1016/j.neurobiolaging.2008.10.005.

(36) Gur RC, Alsop D, Glahn D, et al: An fMRI study of sex differences in regional activation to a verbal and a spatial task. *Brain Lang* 2000; *74*(2): 157-170. doi:10.1006/brln.2000.2325.

(37) Li Z, Matsuda H, Asada T, et al: Gender difference in brain perfusion 99mTc-ECD SPECT in aged healthy volunteers after correction for partial volume effects. *Nucl Med Commun* 2004; *25*(10): 999-1005.

(38) Kennedy KM, Raz N: Aging white matter and cognition: differential effects of regional variations in diffusion properties on memory, executive functions, and speed. *Neuropsychologia* 2009; *47*(3): 916-927. doi:10.1016/j.neuropsychologia.2009.01.001.

TABLES

TABLE 1. TESTS IN THE VS7 BATTERY

MEMORY	
VBM	Verbal Memory Test (14)
VIM	Visual Memory Test (14)
COMPLEX INFORMATION PROCESSING	
SDC	Symbol Digit Coding (15)
RT	Stroop Test Response Time (16)
SAT	Shifting Attention Test (17) (18)
EFFORTFUL ATTENTION	
ST	Stroop Errors
CPT	Continuous Performance Test (19)
MOTOR SPEED	
FTT	Finger Tapping Test
SRT	Stroop Test Simple Reaction Time
CRT	CPT Choice Reaction Time

TABLE 2. DEMOGRAPHIC CHARACTERISTICS OF THE SAMPLE.

GEN	MALE		FEMALE		ALL		ANOVA
	MEAN	SD	MEAN	SD	MEAN	SD	Sig.
N	546		806		1352		
AGE	55.4	10.6	52.5	10.1	53.7	10.4	.000
EDUC	16.3	2.7	16.1	2.4	16.2	2.5	.282
COMPUTER	2.71	0.55	2.61	0.62	2.65	0.59	.015
%WHITE	0.892		0.913		0.905		.732

TABLE 3. GENDER DIFFERENCES IN COGNITIVE TESTS, ALL SS.

	MALE		FEMALE		MANOVA		Cohen's d
	Mean	SD	Mean	SD	F	Sig.	
VBM	50.49	5.456	51.99	5.071	14.787	0.00000	0.28
VIM	45.55	5.162	44.83	5.064	9.285	0.00000	0.14
RT	670.20	109.782	664.35	104.711	27.448	0.00000	0.05
SDC	46.94	12.385	50.81	13.076	54.337	0.00000	0.30
SAT	43.96	14.820	41.78	15.698	28.782	0.00000	0.14
ST	14.46	9.565	13.03	9.261	4.864	0.00022	0.15
CPT	39.44	.950	39.55	.804	6.389	0.00001	0.12
FTT	114.59	16.254	109.03	17.083	32.781	0.00000	0.33
SRT	297.30	71.248	308.14	72.352	13.880	0.00000	0.15
CRT	408.55	48.297	419.31	53.186	10.874	0.00000	0.21

NOTE, Table 3. In these tests, higher scores are better: VBM, VIM, SDC, SAT, CPT.

In these tests, lower scores are better: RT, ST, SRT, CRT.

TABLE 4. REGRESSION ANALYSIS, MALES AND FEMALES

	MALES				FEMALES			
	B	Std. Error	Wald Chi-Square	Sig.	B	Std. Error	Wald Chi-Square	Sig.
VBM	-.118	.0290	16.499	0.0000	-.069	.0246	7.758	0.0053
VIM	-.128	.0254	25.436	0.0000	-.097	.0241	16.098	0.0001
RT	4.052	.5748	49.690	0.0000	3.811	.4835	62.134	0.0000
SDC	-.487	.0620	61.699	0.0000	-.746	.0598	155.924	0.0000
SAT	-.427	.0735	33.691	0.0000	-.665	.0718	85.746	0.0000
ST	.178	.0497	12.823	0.0003	.136	.0490	7.754	0.0054
CPT	-.025	.0047	29.442	0.0000	-.008	.0038	4.472	0.0345
FTT	-.608	.0789	59.281	0.0000	-.709	.0746	90.132	0.0000
SRT	1.238	.3745	10.920	0.0010	2.037	.3494	33.974	0.0000
CRT	1.056	.2570	16.899	0.0000	1.245	.2398	26.977	0.0000

TABLE 5. REGRESSION ANALYSIS, ALL SS

				95% Wald Confidence Interval		Hypothesis Test	
	Parameter	B	Std. Error	Lower	Upper	Wald Chi-Square	Sig.
VBM	AGE	-.129	.0206	-.169	-.088	38.934	.000
	AGE * GEN	.024	.0071	.011	.038	11.933	.001
VIM	AGE	-.089	.0192	-.126	-.051	21.423	.000
	AGE * GEN	-.014	.0066	-.027	-.001	4.702	.030
RT	AGE	3.899	.4067	3.102	4.696	91.922	.000
	AGE * GEN	.015	.1405	-.261	.290	.011	.915
SDC	AGE	-.683	.0471	-.775	-.591	210.516	.000
	AGE * GEN	.039	.0163	.007	.071	5.860	.015
SAT	AGE	-.462	.0559	-.572	-.352	68.230	.000
	AGE * GEN	-.059	.0193	-.097	-.021	9.299	.002
ST	AGE	.174	.0383	.099	.249	20.649	.000
	AGE * GEN	-.012	.0133	-.038	.014	.832	.362
CPT	AGE	-.018	.0033	-.025	-.012	31.339	.000
	AGE * GEN	.001	.0011	-.001	.004	1.718	.190
FTT	AGE	-.448	.0597	-.565	-.331	56.357	.000
	AGE * GEN	-.139	.0205	-.179	-.099	45.761	.000
SRT	AGE	1.426	.2805	.876	1.976	25.831	.000
	AGE * GEN	.157	.0966	-.032	.347	2.646	.104
CRT	AGE	.907	.1914	.532	1.282	22.444	.000
	AGE * GEN	.163	.0661	.034	.293	6.114	.013