Effects of Alcohol- and Cigarette-Use Disorders on Global and Specific Measures of Cognition in Middle-Age Adults*

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ABSTRACT. Objective: This study examined the effects of alcohol- and tobacco-use disorders on global and specific cognitive abilities in middle age. **Method:** The sample consisted of 118 men and 169 women ranging in age from 31 to 60 years ($M [SD] = 43.59 [6.58]$). Lifetime diagnoses were determined from a semistructured interview. Information about current levels of alcohol and cigarette use was also collected. A comprehensive neurocognitive assessment measuring global cognition, memory, and executive-functioning abilities was administered. Baseline cognition was estimated from average composite scores of the Iowa Test of Basic Skills school-achievement tests administered from third through eighth grade. Repeated-measures analysis of variance was used. Covariates comprised baseline cognition, current depression symptoms, and medication use. **Results:** Lifetime alcohol- and tobacco-use disorders

were not associated with cognition among men. Women having a diagnosis of tobacco dependence (according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition [DSM-IV]) performed less well on measures of global cognition and executive functioning. A lifetime diagnosis of DSM-IV alcohol abuse or dependence was associated with higher working memory among women only. **Conclusions:** These results demonstrate few negative effects of alcohol-use disorders on midlife cognition, especially if current consumption is light. Differential susceptibility to the effects of cigarette use on cognition was found with women showing greater deficits in visuospatial abilities, processing speed, and executive-functioning abilities. (*J. Stud. Alcohol Drugs*, 71, 192-200, 2010)

METHODOLOGICAL LIMITATIONS and inconsistencies within existing research make it difficult to evaluate the harmful effects of alcohol use on cognitive functioning in middle age. Given recent encouragement of light drinking for health benefits (Britton et al., 2008; Ferreira and Weems, 2008; French and Zavala, 2007; Karlamangla et al., 2009), we consider examination of unforeseen negative consequences of alcohol consumption an important avenue of continued research (Ngandu et al., 2007; Oscar-Berman and Marinkovic, 2007). In this study, we compared midlife cognition of individuals who met criteria for a lifetime alcohol diagnosis with individuals who did not.

The most notable limitations of current research are the use of partial neuropsychological examinations to assess cognition (Krahn et al., 2003; Leroi et al., 2002; Ott et al., 2004; Richards et al., 2003), inadequate estimates of baseline functioning (Britton et al., 2004; Kalmijn et al., 2002; Ott et al., 2004; Schinka et al., 2002), and a tendency to exclude either men or women (Schinka et al., 2002; Stampfer et al., 2005). The administration of a complete neurocogni-

tive assessment is important in the evaluation of the effects of alcohol on cognition because subtle differences may go undetected as a result of the use of a partial assessment (Davies et al., 2005; Espeland et al., 2006). For example, heavy drinking has been associated with frontal-lobe dysfunction (Davies et al., 2005; Fox et al., 2000), whereas light to moderate drinking is associated with better verbal knowledge and fluency (Espeland et al., 2006). A complete neurocognitive assessment would allow investigation of domain-specific effects as a function of drinking severity.

Including a baseline assessment of cognitive functioning would allow several lines of inquiry that would better characterize the effects of alcohol use on cognition. For example, baseline differences may exist in individuals who later engage in heavy drinking. Thus, any group differences in future cognition may be erroneously attributed to current use (Krahn et al., 2003; Schinka et al., 2002). Baseline cognition may also modify associations between future outcomes and alcohol use. Vulnerability models can be examined by testing interactions between alcohol use and a baseline measure of cognitive functioning (Wood et al., 2002). A significant interaction would suggest differences in susceptibility to the neurotoxic effects of alcohol as a function of premorbid performance.

Finally, reports on gender differences have suggested greater benefits of alcohol use on cognition among women (Britton et al., 2004; Dufouil et al., 1997; Glass et al., 2009; Leroi et al., 2002; McGuire et al., 2007). However, these

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studies have lacked adequate control for baseline functioning, used incomplete neurocognitive assessments, and lacked other potentially important covariates (e.g., depression and medication use) that might influence differences between men and women in midlife.

In conclusion, this study addresses several methodological limitations by administering a comprehensive neurocognitive assessment, including a baseline measure of cognition, and including both men and women. In addition, recent studies suggest alcohol and tobacco may have opposing cognitive effects (Ceballos, 2006; Kalmijn et al., 2002) or may influence different cognitive domains (Glass et al., 2009; Schinka et al., 2002). Given that tobacco use is high among individuals reporting alcohol-use disorders, this study also included lifetime tobacco dependence as a predictor of cognitive functioning.

Method

Participants

Subjects were recruited from a sample of previous participants in the Iowa Adoption Studies, in which researchers studied the gene and environment interaction in the etiology of substance-use disorders (see Yates et al., 1999). Two samples of adoptees were originally selected based on the absence or presence of birth-parent alcohol problems or antisocial behaviors. Data collection for the current study was designed to examine cognitive deficits associated with lifetime substance use while controlling for premorbid cognitive functioning. Therefore, subjects for this study were selected for participation on the basis of available standardized school-achievement data (recruitment pool $n = 467$). We successfully updated substance-use histories and psychiatric and health problems and administered a cognitive assessment for 330 adoptees (a 71% recruitment rate). The mean age of the sample was 43.59 years ($SD = 6.58$, range: 31–60). Average household income was \$40,000–\$49,999 per year. Subjects were predominantly White, non-Hispanic ($n = 311$, 94%), with the remainder of the participants being African American, non-Hispanic ($n = 7$, 2%); African American, Hispanic ($n = 2$, ~1%); White, Hispanic ($n = 8$, 2%); or mixed race ($n = 2$, ~1%).

Measures

Alcohol and tobacco diagnoses. The Semi-Structured Assessment for the Genetics of Alcoholism–II (Bucholz et al., 1994) was used to diagnose lifetime alcohol abuse/dependence and tobacco dependence. Criteria from the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV; American Psychiatric Association, 1994), were used to assign lifetime diagnoses. For alcohol, the presence of abuse or dependence resulted in a positive diagnosis (no

differences on any cognitive measures were found for abuse vs. dependence). DSM-IV substance abuse of alcohol was considered present if the subject endorsed at least one of the following symptoms within the same 12-month period: (a) a failure to fulfill obligations (e.g., work, school, or home), (b) recurrent use of substances in physically hazardous situations (e.g., driving), (c) recurrent substance-related legal problems, or (d) continued use despite recurrent interpersonal problems. DSM-IV dependence on tobacco or alcohol was considered present if the subject endorsed three or more of the following symptoms within the same 12-month period: (a) tolerance defined as an increased need in quantity to achieve the same effect or diminished effect of the same amount, (b) withdrawal or avoidance of withdrawal by using substance, (c) amount of substance taken was more than intended, (d) efforts to cut down are unsuccessful, (e) considerable time is spent to obtain the substance, (f) important activities are reduced because of substance use, and (g) use of substance continues despite physical and psychological problems.

Alcohol and tobacco consumption measures. Participants were asked how many weeks out of the past 26 weeks they drank, how many days they drank during a typical week, and how many drinks they had on a typical day. A four-level alcohol-use grouping variable was created from current use and lifetime alcohol diagnosis: (0) current abstainers with no lifetime alcohol diagnosis, (1) current abstainers with a lifetime alcohol diagnosis, (2) light drinkers (1 to 2 drinks per day), and (3) heavy drinkers (3 or more drinks per day). Participants were also asked to report on the typical number of cigarettes smoked in a 24-hour period. A three-level tobacco-use grouping variable was created: (0) nonsmoker (or <100 lifetime cigarettes), (1) smoked fewer than 20 cigarettes a day, and (2) smoked 20 or more cigarettes a day. Tobacco recency was also coded into a three-level categorical recency variable: (0) nonsmoker (or <100 lifetime cigarettes), (1) at least a month since last smoked, and (2) smoked within the past month.

Medication use. The Semi-Structured Assessment for the Genetics of Alcoholism–II (Bucholz et al., 1994) was also used to collect information about use of medication to treat depression, nervousness, or sleeplessness within the past 30 days. We also collected information about current use of birth-control hormones. Women reported higher rates of medication use than men, 20.7% ($n = 35$) versus 9.6% ($n = 11$); $\chi^2(1, n = 284) = 6.26, p = .012$. Fifteen percent ($n = 25$) of women reported using birth-control hormones.

Neurocognitive assessment. All study participants were given a comprehensive neurocognitive battery assessing global cognition, memory, and executive-functioning abilities. Global cognition was measured by the Wechsler Adult Intelligence Scale–III (WAIS-III; Wechsler, 1997a). The WAIS-III index scores for verbal comprehension, perceptual organization, and processing speed were included as

outcomes. Memory was assessed by the Wechsler Memory Scale-III (WMS-III; Wechsler, 1997b). Index scores for immediate memory, general memory, and working memory were the dependent variables. The remaining measures in the test battery were designed to assess executive-functioning skills and included Connor's Continuous Performance Test, Second Edition (Connors, 2002); the Controlled Oral Word Association Test (Benton and Hamsher, 1976); the Stroop Color Word Test (Golden and Freshwater, 2002); the Comprehensive Trail Making Test (Reynolds, 2002); and the computerized Wisconsin Card Sort Task (Heaton et al., 1993).

Before analyses, we submitted the executive-functioning measures to a principal components analysis. Three factors were identified: (a) attention, which consisted of the Comprehensive Trail Making Test and Connor's Continuous Performance Test, Second Edition (eigenvalue = 2.170; % variance = 30.996); (b) verbal fluency (phonemic verbal fluency [FAS] and animal naming) (eigenvalue = 1.103; % variance = 15.764); and (c) set-shifting/inhibition, which consisted of percent conceptual levels reached on the Wisconsin Card Sort Task and Stroop Color Word Test interference (eigenvalue = 1.072; % variance = 15.319). The z scores for each measure contributing to the respective factor were averaged.

School-achievement tests. School-achievement data were collected from the centralized state records office (1999-2003). The Iowa Test of Basic Skills (ITBS; Hoover et al., 2003) is a standardized school-achievement test battery administered in Iowa classrooms by school districts from third through eighth grade. The mean number of years of school data per subject was 4.82 ($SD = 1.24$, range: 2-6) with 95% of the sample having 3 or more years of data. Achievement scores are reported as state-dependent percentile ranks for each year administered. The composite scores from each available year were averaged to create an overall summary score. Average performance was not associated with number of data points ($r = -.09$, $p = .14$; $n = 284$); therefore, the available composite score was used for the 11 participants with 1 year of data.

Current depression symptoms. The Beck Depression Inventory-Second Edition (Beck et al., 1996) measures current depressive symptoms. The 21-item self-report questionnaire measures severity of depression and includes questions about depressed mood, physical symptoms of depression, and depressed cognitions. Each symptom is rated on a 4-point scale ranging from 0 to 3. Published reliabilities for the total score are high ($\alpha = .92$). The maximum possible total score is 63. We used the total score to measure current depression symptoms.

Birth-parent problems. Adoption agency records were reviewed for evidence of birth-parent alcohol problems or antisocial behaviors. For antisocial personality, most birth parents were identified on the basis of incarceration for a felony conviction or placement in a state training school as a

juvenile (or both). Nonincarcerated birth parents were designated antisocial when adoption agency records indicated one or more DSM-IV antisocial symptoms. Birth-parent alcohol problems were considered present when adoption agency records indicated a history of treatment for alcoholism or when a birth parent was noted to have drinking behavior leading to social or other problems. In the current sample, 34% of the men and 41% of the women had a birth parent with at least one problem.

Procedure

Participants were located throughout the United States. Therefore, a trained research assistant traveled to the participant's home (or a private location near their home). Test administration began in the morning. The WAIS-III was administered first to all participants. A Latin Square design was used to determine the order of the remaining assessments. Test results were double scored and reviewed by a neuropsychologist. Because of equipment failure or incomplete questionnaires, complete data were available for 284 subjects. All procedures were approved by the College of Medicine Human Subjects Internal Review Board.

Statistical analysis

SPSS 17.0 (SPSS Inc., Chicago, IL) was used to conduct all analyses. GLM repeated-measures analysis of variance (ANOVA) was used to examine associations between alcohol- and tobacco-use disorders and cognition. Between-subjects effects were gender, age, average ITBS performance, current depression symptoms, birth-parent problems, medication use, and substance diagnoses. The within-subjects effect was test domain. Three separate repeated-measures ANOVAs were analyzed: (a) the three WAIS-III index scores, (b) the three WMS-III index scores, and (c) the three executive-functioning factor scores. When a significant interaction between substance diagnosis and test domain was found, we conducted follow-up analysis of covariance (ANCOVA) with each domain as a dependent variable. We restricted analyses to subjects with no missing data ($n = 115$ for men and $n = 169$ for women) to ensure that the same participants were included in each repeated measures model. Finally, we used a conservative p value of .01 to determine significance. Our discussion of the findings is limited to significant effects as determined by the conservative cutoff. Results not presented can be obtained from the first author.

Results

Descriptives

Characteristics of alcohol and tobacco use. Descriptives for alcohol and tobacco diagnoses are presented in Table 1. Men were more likely to endorse any lifetime alcohol abuse/

dependence, $\chi^2(1, n = 284) = 8.33, p = .004$. Roughly equal numbers of men and women endorsed alcohol abuse, $\chi^2(1, n = 284) = 1.79, p = .181$, whereas men reported higher rates of alcohol dependence than women, $\chi^2(1, n = 284) = 9.01, p = .003$. Significant differences were found between men and women for current alcohol use, $\chi^2(3, n = 280) = 12.13, p = .007$. Although men and women reported equal rates of current light drinking, men were more likely to report currently drinking three or more drinks a day and women were more likely to report currently abstaining from alcohol. Men and women were diagnosed with tobacco dependence at equal rates, $\chi^2(1, n = 284) = 1.72, p = .189$, and reported similar recency of use, $\chi^2(2, n = 261) = 0.52, p = .773$. However, men were more likely to smoke more than 20 cigarettes a day, whereas women were more likely to smoke less than 20 cigarettes a day, $\chi^2(2, n = 261) = 9.17, p = .010$.

Cross-substance use. To further characterize alcohol and nicotine use in our sample, we computed cross-tabulations between the alcohol-use groups and tobacco dependence, and between the tobacco-use and recency groups and alcohol abuse/dependence (see Table 2). Men diagnosed with alcohol abuse/dependence were more likely to smoke 20 or more cigarettes daily whereas men without a diagnosis were more likely to be nonsmokers, $\chi^2(2, n = 102) = 12.11, p = .002$. Men having a lifetime alcohol-abuse/dependence diagnosis were also more likely to be past smokers, $\chi^2(2, n = 102) = 12.71, p = .002$. No difference in alcohol use was found by tobacco dependence for men, $\chi^2(3, n = 114) = 8.66, p = .034$, or women, $\chi^2(3, n = 166) = 5.84, p = .120$. Among women, the distributions of the tobacco-use groups and recency-of-use groups also differed by lifetime alcohol diagnosis, $\chi^2(2, n = 159) = 11.78, p = .003$, and $\chi^2(2, n = 159) = 10.81, p = .004$, respectively. Women diagnosed with alcohol abuse/dependence were more likely to report

smoking more than 20 cigarettes a day and to report current smoking (see Table 2).

Univariate analyses

T tests were used to examine associations between current depression symptoms and alcohol/tobacco diagnoses and chi-squares tested associations between medication use and diagnoses. Alcohol and tobacco diagnoses were not associated with current depression for men. A medium effect size was found among women for differences in current depression symptoms, with higher symptoms of depression among women reporting lifetime tobacco dependence, $t(167) = -3.03, p = .003$; Cohen's $d = 0.52$. Alcohol abuse/dependence and tobacco dependence were not associated with medication use among men, $\chi^2(1, n = 115) = 0.07, p = .793$, and $\chi^2(1, n = 115) = 2.67, p = .102$, respectively, or women, $\chi^2(1, n = 169) = 3.31, p = .069$, and $\chi^2(1, n = 169) = 2.10, p = .147$, respectively.

T tests were used to examine the effect of current medication use on cognition and current depression symptoms. None of the cognitive measures were associated with medication use among men. However, men taking medication reported higher current depression symptoms, $t(113) = -2.71, p = .008$. The difference corresponded to a large effect size (Cohen's $d = 0.72$; $M_{\text{meds}} [SD] = 10.27 [8.17]$ and $M_{\text{no meds}} = 5.19 [5.64]$). Among women, medication use was significantly associated with perceptual organization, $t(167) = 2.85, p = .005$, and current depression symptoms, $t(167) = -4.12, p < .001$. A medium effect size was found for perceptual organization (Cohen's $d = 0.58$; $M_{\text{meds}} = 99.46 [11.16]$ and $M_{\text{no meds}} = 107.08 [14.77]$) and a large effect size was found for depression symptoms (Cohen's $d = 0.71$; $M_{\text{meds}} = 10.46 [8.20]$ and $M_{\text{no meds}} = 5.37 [6.00]$).

TABLE 1. Descriptives of alcohol and tobacco diagnoses and consumption

Study variables	Men ($n = 115$)		Women ($n = 169$)		<i>p</i>
	<i>n</i>	%	<i>n</i>	%	
Alcohol abuse/dependence	67	49.3	69	40.8	.004
Abuse (<i>n</i> , % positive)	52	45.2	63	37.3	.181
Dependence (<i>n</i> , % positive)	15	13.0	6	3.6	.003
Tobacco dependence (<i>n</i> , % positive)	21	18.3	42	24.9	.189
Alcohol-use groups					.007
Current abstainers no diagnosis	8	7.0	28	17.5	
Current abstainers with diagnosis	14	12.3	17	10.2	
1-2 drinks/day	71	62.3	107	64.5	
≥ 3 drinks/day	21	18.4	13	7.8	
Tobacco-use groups					.010
Nonsmoker or <100 cigarettes lifetime	52	51.0	74	46.5	
<20 cigarettes a day, ever	15	14.7	48	30.2	
≥ 20 cigarettes a day, ever	35	34.3	37	23.3	
Tobacco recency					.773
Nonsmoker or <100 cigarettes lifetime	52	51.0	74	46.5	
Past smoker, at least 1 month	24	23.5	42	26.4	
Current smoker, within past month	26	25.5	43	27.0	

Notes: Percentages represent column percentages. Cell sizes vary because of missing quantity/frequency data.

TABLE 2. Current alcohol and tobacco consumption by lifetime diagnoses

Variable	Men diagnoses			Women diagnoses		
	Absent, <i>n</i>	Present, <i>n</i>	<i>p</i>	Absent, <i>n</i>	Present, <i>n</i>	<i>p</i>
Alcohol-use groups by tobacco dependence			.034			.120
Current abstainers without alcohol diagnosis	8 (8.6%)	0 (0%)		26 (20.8%)	3 (7.3%)	
Current abstainers with alcohol diagnosis	8 (8.6%)	6 (28.6%)		10 (8%)	7 (17.1%)	
1-2 drinks/day	61 (65.6%)	10 (47.6%)		79 (63.2%)	28 (68.3%)	
≥3 drinks/day	16 (17.2%)	5 (23.8%)		10 (8%)	3 (7.3%)	
Tobacco-use groups by alcohol abuse/dependence			.002			.003
Nonsmoker or <100 cigarettes lifetime	28 (71.8%)	24 (38.1%)		52 (57.8%)	22 (31.9%)	
<20 cigarettes a day, ever	5 (12.8%)	10 (15.9%)		24 (26.7%)	24 (34.8%)	
≥20 cigarettes a day, ever	6 (15.4%)	29 (46.0%)		14 (15.6%)	23 (33.3%)	
Tobacco recency by alcohol abuse/dependence			.002			.004
Nonsmoker or <100 cigarettes lifetime	28 (71.8%)	24 (38.1%)		52 (57.8%)	22 (31.9%)	
Past smoker, at least 1 month	3 (7.7%)	21 (33.0%)		20 (22.2%)	22 (31.9%)	
Current smoker, within past month	8 (20.5%)	18 (28.6%)		18 (20.0%)	25 (36.2%)	

Notes: Column percentages in parentheses. Cell sizes may vary because of missing quantity/frequency data.

Correlations were computed to test univariate associations between the cognitive measures, current age, ITBS school achievement, and current depressive symptoms (see Table 3). Older men showed slower processing speed, whereas older women showed poorer set-shifting abilities. Higher average school-achievement performance was associated with better performance on all cognitive measures (except set-shifting/inhibition). Higher depression symptoms were associated with lower perceptual organization scores among men. Women reporting higher current symptoms of depression scored lower on verbal comprehension, working memory performance, and set-shifting/inhibition.

Finally, independent *t* tests were used to examine univariate associations between substance-use diagnoses and cognitive performance (see Table 4 for men and Table 5 for women). Alcohol abuse/dependence did not significantly predict performance on any of the WAIS-III, WMS-III, or executive-functioning measures for men or women. Similarly, ITBS school achievement was not associated with alcohol or tobacco diagnoses for men or women. Tobacco dependence was not associated with cognition in men. Among women, however, tobacco dependence was associ-

ated with lower scores on perceptual organization, $t(167) = 2.84, p = .005$, and processing speed, $t(167) = 2.66, p = .009$. The effect sizes were medium for both indices (perceptual organization: Cohen's $d = 0.52$, and processing speed: Cohen's $d = 0.45$).

Multivariate analyses

Wechsler Adult Intelligence Scale-III index scores: Verbal comprehension, perceptual organization, and processing speed. Lifetime alcohol or tobacco diagnoses were not associated with WAIS-III performance for men (see Table 6). The Tobacco Dependence $\times$ Index interaction was significant for women. Separate ANCOVAs showed that tobacco dependence was associated with perceptual organization, $F(1, 160) = 8.26, p = .005$, and processing speed, $F(1, 160) = 10.95, p = .001$, but not verbal comprehension, $F(1, 160) = 0.01, p = .921$. The effect sizes for the marginal means were small for both perceptual organization (Cohen's $d = 0.39$; $M_{\text{diagnosis}} = 98.67 [16.40]$ and $M_{\text{no diagnosis}} = 105.77 [20.06]$) and processing speed (Cohen's $d = 0.45$; $M_{\text{diagnosis}} = 110.33 [13.93]$ and $M_{\text{no diagnosis}} = 117.29 [17.02]$).

TABLE 3. Correlations between cognitive measures and covariates

Cognitive measures	Men (<i>n</i> = 115)			Women (<i>n</i> = 169)		
	Age	ITBS	BDI-II	Age	ITBS	BDI-II
Verbal comprehension ^a	.13	.65***	-.07	.05	.65***	-.19*
Perceptual organization ^a	-.04	.24**	-.19*	-.02	.42***	-.15
Processing speed ^a	-.22*	.22*	-.14	-.14	.39***	-.13
General memory ^b	.11	.45***	-.13	.06	.31***	-.13
Immediate memory ^b	-.03	.39***	-.11	-.02	.29***	-.11
Working memory ^b	.14	.39***	-.14	-.13	.42***	-.15*
Attention ^c	-.10	.24**	-.10	-.12	.29***	-.09
Verbal fluency ^c	-.09	.28**	.09	-.14	.30***	-.08
Set-shifting/inhibition ^c	-.11	.13	-.04	-.25***	.23**	-.19*

Notes: ITBS = Iowa Test of Basic Skills; BDI-II = Beck Depression Inventory-Second Edition. ^aWechsler Adult Intelligence Scale-III scores; ^bWechsler Memory Scale-III scores; ^cexecutive-functioning scores (standardized).

* $p < .05$; ** $p < .01$; *** $p < .001$.

TABLE 4. Descriptives (mean, standard deviation) for study variables by substance diagnosis for men ($n = 115$)

Study variables	Lifetime alcohol diagnosis			Lifetime tobacco diagnosis		
	Absent, M (SD)	Present, M (SD)	p	Absent, M (SD)	Present, M (SD)	p
Verbal comprehension	108.58 (17.49)	104.58 (11.97)	.174	106.87 (15.22)	103.48 (11.26)	.337
Perceptual organization	107.77 (14.40)	106.00 (12.37)	.481	107.73 (13.32)	102.29 (12.12)	.088
Processing speed	106.98 (14.93)	103.99 (12.16)	.239	106.29 (13.11)	100.52 (14.02)	.075
General memory	104.83 (15.47)	104.94 (12.70)	.968	105.52 (13.62)	102.10 (14.91)	.308
Immediate memory	101.79 (15.97)	103.78 (12.90)	.463	103.46 (13.91)	100.67 (15.47)	.419
Working memory	107.63 (14.55)	104.27 (14.76)	.229	107.15 (14.97)	99.05 (11.60)	.022
Attention ^a	-0.01 (0.82)	-0.21 (0.79)	.191	-0.06 (0.77)	-0.43 (0.90)	.055
Verbal fluency ^a	0.06 (0.94)	-0.23 (0.74)	.066	-0.08 (0.85)	-0.25 (0.79)	.388
Set-shifting/inhibition ^a	-0.04 (0.67)	0.09 (0.75)	.320	0.10 (0.64)	-0.25 (0.95)	.041
ITBS school achievement	55.40 (28.69)	53.57 (27.57)	.732	54.76 (28.45)	52.41 (26.08)	.728
Current depression symptoms	4.94 (5.34)	6.21 (6.53)	.270	4.76 (4.87)	9.81 (8.82)	.018
n	48	67		94	21	

Notes: ITBS = Iowa Test of Basic Skills. ^az scores.

Wechsler Memory Scale-III index scores: Immediate memory, general memory, and working memory. Memory function was not associated with lifetime alcohol or tobacco diagnoses among men (see Table 6). Tobacco dependence was not associated with memory performance; however, a significant interaction was found between lifetime alcohol abuse/dependence and memory domain among women (see Table 6). Follow-up ANCOVA analyses showed non-significant associations of alcohol abuse/dependence with immediate memory, $F(1, 160) = 0.07$, $p = .786$, and general memory, $F(1, 160) = 1.36$, $p = .250$. In contrast, a lifetime alcohol diagnosis was significantly associated with working memory, $F(1, 160) = 6.57$, $p = .011$. The effect for the marginal means was small (Cohen's $d = 0.29$) with higher working memory scores among women diagnosed with lifetime alcohol abuse/dependence ($M_{\text{diagnosis}} = 113.34$ [19.61] and $M_{\text{no diagnosis}} = 107.10$ [23.30]).

Executive functioning: Attention, verbal fluency, and set-shifting/response inhibition. Using the conservative p value of .01, alcohol and tobacco diagnoses were not associated with executive functioning among men (see Table 6). Among women, only tobacco dependence showed a significant as-

sociation with overall executive functioning. Lower marginal means were found among women having a diagnosis. The effect size was small (Cohen's $d = 0.36$; $M_{\text{diagnosis}} = -0.14$ [0.56] and $M_{\text{no diagnosis}} = 0.09$ [0.69]).

Secondary analyses: Tobacco consumption and recency

Because of the significant effects of tobacco dependence on women's cognition, we examined associations between amount and recency of nicotine consumption and the cognitive outcomes. We reanalyzed the repeated-measures ANOVAs with the tobacco variables as separate predictors. The only significant effect was for the association between number of cigarettes typically smoked in a 24-hour period and executive functioning, $F(2, 149) = 6.27$, $p = .002$. Significantly lower executive-functioning abilities were found among women who reported smoking at least 20 cigarettes a day ($p = .003$) compared with nonsmokers ($M_{>20/\text{day}} = -0.18$ [0.55] and $M_{\text{nonsmoker}} = 0.10$ [0.60]). The effect size for the marginal means was medium (Cohen's $d = 0.49$). A medium effect size was also found for the marginal mean difference between light and heavy smokers (Cohen's $d = 0.62$, $p =$

TABLE 5. Descriptives (mean, standard deviation) for study variables by substance diagnosis for women ($n = 169$)

Study variables	Lifetime alcohol diagnosis			Lifetime tobacco diagnosis		
	Absent, M (SD)	Present, M (SD)	p	Absent, M (SD)	Present, M (SD)	p
Verbal comprehension	102.51 (12.79)	101.26 (12.91)	.535	102.31 (11.77)	101.05 (15.68)	.580
Perceptual organization	105.75 (14.97)	105.14 (13.66)	.789	107.28 (14.38)	100.14 (13.27)	.005
Processing speed	115.10 (12.23)	117.32 (12.14)	.247	117.42 (11.48)	111.74 (13.45)	.009
General memory	111.38 (12.35)	107.77 (14.12)	.080	110.28 (12.67)	108.76 (14.72)	.518
Immediate memory	109.72 (13.28)	107.87 (15.25)	.403	109.41 (13.74)	107.62 (15.24)	.477
Working memory	107.75 (15.33)	111.81 (16.95)	.107	110.50 (15.69)	106.10 (17.01)	.124
Attention ^a	0.10 (0.63)	0.09 (0.70)	.977	0.16 (0.64)	-0.09 (0.68)	.036
Verbal fluency ^a	-0.01 (0.78)	0.18 (0.83)	.137	0.11 (0.80)	-0.04 (0.83)	.310
Set-shifting/inhibition ^a	-0.05 (0.75)	-0.01 (0.88)	.726	0.02 (0.72)	-0.21 (0.99)	.098
ITBS school achievement	58.94 (24.42)	56.43 (24.44)	.512	58.42 (24.48)	56.40 (24.34)	.643
Current depression symptoms	5.63 (6.13)	7.58 (7.59)	.067	5.54 (6.51)	9.12 (7.06)	.003
n	100	69		127	42	

Notes: ITBS = Iowa Test of Basic Skills. ^az scores.

TABLE 6. Substance-related effects from repeated-measures analysis of variance predicting WAIS-III and WMS-III index scores and executive functioning factors

Effects	WAIS-III		WMS-III		EF	
	<i>F</i>	<i>p</i>	<i>F</i>	<i>p</i>	<i>F</i>	<i>p</i>
Men (<i>n</i> = 115)						
Alcohol abuse or dependence	1.54	.217	0.23	.633	0.39	.536
Tobacco dependence	0.15	.702	1.90	.171	4.89	.029
Women (<i>n</i> = 169) ^a						
Alcohol Diagnosis × Index	—	—	10.70	.001	—	—
Alcohol abuse or dependence	2.81	.096	0.38	.537	2.80	.096
Tobacco dependence	9.13	.003	0.72	.396	7.19	.008
Tobacco Dependence × Index	7.38	.007	—	—	—	—

Notes: MANCOVA = multivariate analysis of covariance; WAIS-III = Wechsler Adult Intelligence Scale-III; WMS-III = Wechsler Memory Scales-III; EF = executive functioning. Effects containing "Index" reflect significant within-subject interactions. Effects not containing "Index" reflect between-subject main effects. Covariates included birth-parent problems, current age, Iowa Test of Basic Skills (ITBS) school achievement, medication use, birth-control hormones (women only), and current depression symptoms. *Df* for men (1, 107) and for women (1, 160). ^aSignificant covariates. WAIS-III univariate analyses: (a) perceptual organization: ITBS school achievement, $F(1, 160) = 32.88, p < .001$, and medication use, $F(1, 160) = 6.35, p = .011$; (b) processing speed: ITBS school achievement, $F(1, 160) = 27.72, p < .001$. WMS-III univariate analysis: (a) working memory: ITBS school achievement, $F(1, 160) = 35.16, p < .001$; (b) overall EF: ITBS school achievement, $F(1, 160) = 33.22, p < .001$, and current age, $F(1, 160) = 11.99, p = .001$.

.001). Scores for executive-functioning abilities were higher among light (<20/day) smokers ($M_{<20/day} = 0.16 [0.08]$) compared with heavy smokers (>20/day). No difference was found between nonsmokers and women that reported smoking fewer than 20 cigarettes a day ($p = .469$).

Discussion

The analyses presented in this article emphasize the need to include a comprehensive neurocognitive assessment, a measure of baseline cognitive functioning, and both men and women when examining the effects of alcohol consumption on cognition in midlife. Our data showed that lifetime diagnoses of alcohol- and tobacco-use disorders did not predict cognition among men. In contrast, women diagnosed with tobacco dependence showed poorer perceptual organization, processing speed, and executive-functioning abilities after controlling for covariates. The significant effect of tobacco dependence on executive functioning was attributed to amount of tobacco consumed with deficits among women that smoked 20 or more cigarettes a day. Finally, opposing effects for alcohol and tobacco were found for women's memory with higher working memory scores among women diagnosed with lifetime alcohol abuse/dependence. Importantly, controlling for baseline cognition, medication use, and current depressive symptoms did not eliminate these associations.

To understand the nature of our results, we must place the findings within the context of the consumption patterns of our sample. Specifically, the null findings involving lifetime alcohol abuse/dependence could be attributed to the seemingly low levels of current alcohol consumption in our

sample. Only 27% of men diagnosed with a lifetime alcohol-use disorder reported drinking three or more drinks a day in the recent 26 weeks. The remainder of men with a positive diagnosis reported abstaining from alcohol (24%) or averaging one to two drinks per day (49%). The majority of women reported light drinking regardless of diagnosis (66% without and 62% with alcohol abuse or dependence). Therefore, our findings are consistent with other studies demonstrating few negative (and in some cases positive) effects of light alcohol consumption on cognition in midlife (Dufouil et al., 1997; Espeland et al., 2006; Leroi et al., 2002; Schinka et al., 2002).

Another issue that may have influenced the alcohol findings is the fact that the majority of individuals positive for alcohol abuse/dependence met criteria for abuse only. A DSM-IV diagnosis of alcohol abuse requires endorsement of only a single symptom. This low threshold resulted in more than half of our sample being diagnosed with abuse. We compared the frequency of individual lifetime abuse symptoms found in our sample with those reported from a national epidemiological study (Hasin and Beseler, 2009). The highest lifetime occurrence was for endorsement of hazardous use (39.4%), which compares to 42.4% of our sample. Therefore, although our estimate is close to national norms, the diagnosis of alcohol abuse may reflect a low threshold and thus may be indicative of drinking levels that do not have a harmful effect on cognitive functioning.

With regard to smoking, the positive findings for tobacco dependence and typical number of daily cigarettes among women suggest greater susceptibility to the harmful effects of smoking. One possible explanation for our observed differences between men and women could be the role of

hormonal changes (e.g., menopause) that occur in midlife. Animal studies have shown that nicotine reduces serum estradiol (Bjarnason et al., 2004; Byrjalsen et al., 1993) and inhibits the neuronal effects of estrogen (Shingo et al., 2000). Sixty percent of our women were between 40 and 54 years of age, increasing the likelihood of hormonal changes consistent with perimenopause or menopause. It is therefore possible that nicotine may exacerbate the effects of concomitant fluctuations in estrogen levels on cognition in a domain-specific manner (Sherwin and Henry, 2008). A similar argument can be made for the observed benefits of light alcohol use on working memory. There exists some evidence for a combined benefit of light alcohol consumption and estrogen hormone therapy on visuospatial abilities and memory among postmenopausal women (Tivis et al., 2003, 2008). It is possible that light alcohol consumption protected memory abilities among women in the early stages of menopause (Sherwin, 2007). Unfortunately, we did not collect information about hormone therapy or menopausal status.

Although this study has several advantages over previous research, there are limitations to the generalizability of the findings of the study. First, the use of an adoption sample may introduce the possibility of prenatal influences on cognition and other unknown biases. Co-varying ITBS school-achievement scores and birth-parent problems was an attempt to control for this confound. Second, our sample consisted primarily of alcohol abusers and did not allow separate analyses for abuse versus dependence. Findings of alcohol-related cognitive deficits may be more pronounced among individuals endorsing alcohol dependence rather than abuse. Finally, we used a conservative p value ($<.01$) to determine significant findings in our study that may have inflated the observed differences between men and women in these data relative to other studies that have used a more liberal cutoff (Kalmijn et al., 2002; Richards et al., 2003; Schinka et al., 2002). Despite these limitations, this study suggests middle-age women may be more vulnerable to the effects of tobacco dependence on cognition. Future studies should investigate physiological mechanisms that might account for this increased susceptibility.

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