Neuropsychiatric Disease and Treatment

Dovepress

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ORIGINAL RESEARCH

Frontal brain dysfunction in alcoholism with and without antisocial personality disorder

This article was published in the following Dove Press journal:
Neuropsychiatric Disease and Treatment
22 May 2009
Number of times this article has been viewed

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Abstract: Alcoholism and antisocial personality disorder (ASPD) often are comorbid conditions. Alcoholics, as well as nonalcoholic individuals with ASPD, exhibit behaviors associated with prefrontal brain dysfunction such as increased impulsivity and emotional dysregulation. These behaviors can influence drinking motives and patterns of consumption. Because few studies have investigated the combined association between ASPD and alcoholism on neuropsychological functioning, this study examined the influence of ASPD symptoms and alcoholism on tests sensitive to frontal brain deficits. The participants were 345 men and women. Of them, 144 were abstinent alcoholics (66 with ASPD symptoms), and 201 were nonalcoholic control participants (24 with ASPD symptoms). Performances among the groups were examined with Trails A and B tests, the Wisconsin Card Sorting Test, the Controlled Oral Word Association Test, the Ruff Figural Fluency Test, and Performance subtests of the Wechsler Adult Intelligence Scale. Measures of affect also were obtained. Multiple regression analyses showed that alcoholism, specific drinking variables (amount and duration of heavy drinking), and ASPD were significant predictors of frontal system and affective abnormalities. These effects were different for men and women. The findings suggested that the combination of alcoholism and ASPD leads to greater deficits than the sum of each.

Keywords: alcoholism, antisocial personality disorder (ASPD), frontal brain system, neuropsychological deficits, reward system

Introduction

Antisocial personality disorder (ASPD) and alcoholism are often comorbid conditions. Epidemiological and clinical studies consistently have found a strong association between alcoholism and a lifetime history of antisocial personality traits and symptoms among recovering alcoholics.[1–3] Motives for drinking,[4] as well as behaviors such as heavy drinking and alcohol dependence, may be associated with ASPD symptomatology. Moreover, early-onset alcoholics have a severe clinical presentation that may be related to a history of conduct disorder and progression to ASPD,[5,6] and strong associations between ASPD and alcoholism are related to poor treatment outcomes and increased clinical severity.[3]

Several studies have reported that novelty seeking,[5] impulsivity,[7] affective instability,[4] disinhibition,[8] and negative affectivity[9] are related to chronic alcohol use and dependence. Similarly, individuals with ASPD often display a reduced attentional capacity[10] and abnormal perseverative responding.[10–12] These various characteristics associated with alcoholism[13,14] and ASPD[15,16] likely reflect abnormalities in the functioning of frontal brain systems,[11,17,18] although it is not clear whether the presence

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of ASPD symptoms is a risk marker or a reflection of chronic alcoholism.

There is further evidence of possible premorbid frontal abnormalities in individuals at risk for alcoholism, a subset of whom display impulsivity, rule breaking, insensitivity to reinforcement, poor response to social censure and physical punishment, and ASPD.[19–22] Type II alcoholic personalities (early drinking onset, antisocial personality characteristics, and resistance to treatment)[23] may be the most vulnerable to frontal system deficits, as well as to emotional processing difficulties.[24,25] Functional and structural neuroimaging techniques have revealed frontal brain abnormalities in alcoholics and in individuals with ASPD.[13,18,26–28] However, little is known about the characteristics of frontal dysfunction in alcoholics with ASPD symptoms. Therefore, in the present study, in examining the association between alcoholism and ASPD symptoms on neuropsychological tests sensitive to different aspects of frontal system function, we hypothesized that the interaction would reveal greater deficits than the sum of both conditions.

The frontal lobes are connected with all of the other lobes of the brain, and they receive and send fibers to many subcortical structures as well.[29] The posterior region of the frontal lobes controls motor functions, and the anterior region of the frontal lobes (prefrontal cortex) plays a regulatory role within the brain. Prefrontal cortex is host to at least two subsystems: dorsolateral and orbitofrontal (on the ventral surface).[29,30] Whereas the dorsolateral system contains extensive reciprocal connections with other neocortical sites, its connections with limbic sites are less striking than are those of the orbitofrontal system. The dorsolateral system is important for successful performance on tasks that require intact visuospatial, mnemonic, attentional, and executive functions, for cognitive set shifting and rule discovery, and for verbal and spatial working memory (see Fuster,[29] Miller and Cummings,[31] and Royall and colleagues[32] for reviews). By contrast, functions involved in response inhibition and emotional responsiveness have been linked to the ventral surface or orbitofrontal system, which is extensively connected with basal forebrain and limbic structures. The orbitofrontal system is especially important for maintaining normal inhibitory influences on behavior, such as inhibiting abnormal perseverative responding,[30] including disengagement from previously reinforced responses,[33] and control over untoward social behaviors. Research on prefrontal functioning in alcoholics[34] and individuals with ASPD symptoms[11] has suggested that both groups may be more impaired on tasks sensitive to compromised orbitofrontal functioning, as compared to tasks sensitive to dorsolateral prefrontal dysfunction. One purpose of the present study was to employ tests that can evaluate the integrity of both the dorsolateral and orbitofrontal brain systems, in order to determine whether alcoholics with and without ASPD symptoms differ with respect to performance on those tests.

A secondary purpose of the present study was to assess gender differences in disturbances of prefrontal functioning. Characteristics of antisocial behavior that play a role in abnormal aggressive behaviors, affective instability, disinhibition, impulsivity, and impaired problem solving,[35–40] are more pronounced in men than in women. Moreover, recent meta-analytic reviews of frontal system function in ASPD reported that antisocial groups performed worse than non-ASPD groups,[16] and the most robust findings were observed for men. This suggests that there may be key ways in which men and women differ with respect to personality traits,[41] which in turn, may be associated with specific neurological underpinnings. In fact, although many research studies have explored the relationship between antisocial traits and disturbances in frontal brain systems,[24,42] and research on gender differences in alcoholism suggest that women may be more vulnerable than men to its pathological consequences,[43,44] few studies have directly compared alcoholic men and women with respect to ASPD symptoms.[20,45] Likewise, few studies have examined frontal system functioning among male and female participants with comorbid antisocial symptoms and alcohol use disorders.[24,46] We reasoned that if the effect size associated with gender is equivalent for alcoholism and for ASPD, then alcoholic men and women with ASPD symptoms would be similarly impaired. However, if women and men are differently influenced by alcoholism and by ASPD, we expected a more complicated picture to emerge.

Methods

Participants

A total of 345 participants (172 males) took part in the study. All of the participants were right-handed English-speaking men and women from the Boston area, with comparable socioeconomic backgrounds. The groups consisted of 144 abstinent alcoholics (66 with ASPD symptoms), and 201 healthy nonalcoholic control participants (24 with ASPD symptoms). See Table 1 for characteristics of the research participants.

Participation by alcoholic and control participants alike was solicited by the same methods. Many potential participants responded to flyers posted in the Neurology, Psychology, Psychiatry, Medical, and Outpatient Services at

Table 1 Characteristics of the research participants. The significant differences listed here are between alcoholic vs nonalcoholic groups, and between alcoholism and antisocial personality disorder (ASPD) vs non-ASPD groups. Additional statistical comparisons among the four subgroups are described in the text

N = 345 (172 males)	**Nonalcoholic controls without ASPD N = 177 (70 males) Mean (SD) and range**	**Nonalcoholic controls with ASPD N = 24 (17 males) Mean (SD) and range**	**Alcoholics without ASPD N = 78 (40 males) Mean (SD) and range**	**Alcoholics with ASPD N = 66 (45 males) Mean (SD) and range**	**Significant differences between**	
					Alcoholic group, Alc (N = 144) vs nonalcoholic group, non-Alc (N = 201)	**ASPD group (N = 90) vs non-ASPD group (N = 255)**
Age in years	51.25 (16.97)	46.10 (13.83)	53.63 (12.51)	51.65 (9.28)		
Range	18.66–83.64	21.18–74.75	30.52–80.05	26.44–71.36	ns	ns
Education in years	15.73 (2.23)	14.67 (2.10)	15.10 (2.79)	13.58 (2.03)		
Range	11–21	12–20	7–23	9–19	Alc < non-Alc**	ASPD < non-ASPD**
WAIS Full Scale IQ	112.85 (13.80)	109.54 (15.61)	110.10 (13.78)	102.53 (15.23)		
Range	67–151	79–138	80–147	70–139	Alc < non-Alc**	ASPD < non-ASPD**
WAIS Verbal IQ	113.88 (13.36)	109.04 (14.90)	110.21 (14.29)	104.36 (14.48)		
Range	74–155	79–137	80–143	73–131	Alc < non-Alc**	ASPD < non-ASPD**
WAIS Performance IQ	109.03 (14.05)	107.88 (15.59)	108.01 (12.44)	99.62 (15.77)		
Range	65–146	83–140	83–142	67–142	Alc < non-Alc*	ASPD < non-ASPD**
Hamilton Depression Scale	1.24 (2.14)	1.96 (2.66)	1.96 (2.66)	4.50 (4.39)		
Range	0–14	0–9	0–12	0–17	Alc > non-Alc†	ASPD > non-ASPD†
Duration Heavy Drinking (years)	0.06 (0.43)[a]	0.12 (0.45)	15.08 (10.04)	16.77 (9.26)		
Range	0–4	0–2	3–50	3–38	Alc > non-Alc**	ASPD > non-ASPD**
Length of Sobriety (years)	N/A	N/A	6.70 (7.87)	5.21 (8.01)		
Range			0.01–30.32	0.01–30.62	N/A	ns
Quantity Frequency Index	0.22 (0.38)[b]	0.38 (0.43)[c]	7.76 (6.65)	10.90 (8.65)		
Range	0–3.2	0–1.28	0.36–37.98	0.08–36.48	Alc > non-Alc‡	ASPD > non-ASPD‡

Notes: [a]N = 176, [b]N = 173, [c]N = 23; *$p \leq 0.01$, **$p \leq 0.001$; †Significant Alc × ASPD interaction, $F(1, 341) = 5.44$, $p < 0.05$. ‡Significant Alc × ASPD interaction, $F(1, 336) = 4.75$, $p < 0.05$.

the Boston Campus of the Department of Veterans Affairs (VA) Healthcare System, Boston University Medical Center, and VA after-care programs in the Boston area. Other individuals responded to newspaper and Internet advertisements. Informed consent for participation in the research was obtained from each subject prior to testing, and participants were reimbursed for time and travel expenses.

Assessments

Potential participants were given a medical history interview and a modified Computerized Diagnostic Interview Schedule (DIS Version III-Revised[47] or Version IV[48]) which provides psychiatric diagnoses according to criteria established by the American Psychiatric Association (DSM-III-R[49] or DSM-IV[50]). Participants were excluded from further investigation if they endorsed any of the following criteria based on their initial interview, referral sources, medical history, or DIS scores: English was not their first (or one of their first) language(s); history of dyslexia; uncorrected abnormal vision or hearing problem; history of neurological dysfunction (eg, due to alcohol-induced persisting amnestic disorder, major head injury, loss of consciousness for more than 15 minutes, stroke, epilepsy or seizures unrelated to alcohol use or withdrawal); current use of psychoactive medication; history of electroconvulsive shock therapy; and/or history of significant drug use (other than alcohol). Participants were also excluded if they met diagnostic criteria for significant psychiatric disorder such as bipolar disorder, mania, hypomania, and schizophrenia-spectrum disorders.

All of the participants were given a structured interview in which they were questioned about their drinking patterns. A Quantity Frequency Index (QFI), which takes into consideration the amount, type, and frequency of use of alcoholic beverages, either over the last six months (for the nonalcoholics), or over the six months preceding cessation of drinking (for the alcoholics), was calculated for each participant.[51] For the alcoholics, information also was obtained about length of abstinence and the number of years of heavy drinking (duration of heavy drinking [DHD]; quantified as greater than 21 drinks per week). Alcoholic participants met DSM[49,50] criteria for alcohol abuse or dependence for at least five years. All but seven alcoholics had abstained from alcohol use for at least four weeks prior to testing; three were women (two with ASPD symptoms), and four were men (one with ASPD symptoms). Alcoholics with and without ASPD symptoms did not differ with respect to length of sobriety ($t = 1.13$, $p = 0.26$). We excluded control participants who reported periods of prolonged heavy drinking, as determined by the results of our screening interviews; the mean DHD for all nonalcoholics was 0.07 years (range 0–4 years).

Psychometric properties of the assessment instruments are available in the referenced citations for each of the standardized tests that we used. Norms have been established among alcoholics for the Wechsler Adult Intelligence Scale (WAIS), Wechsler Memory Scale (WMS), Wisconsin Card Sorting Test (WCST), and Trails,[52] but to our knowledge, none of the measures we used have norms relevant to ASPD populations. The DIS has been tested for reliability and validity in diagnosing ASPD among substance abusers, including alcoholics.[53,54] Psychometric properties are not available for our medical and alcohol screening interviews.

In our study, we assessed antisocial personality symptoms with the DIS.[47,48] According to the DSM criteria, a diagnosis of ASPD requires antisocial behavior symptoms since age 15, and evidence of conduct disorder with onset before age 15. However, we examined participants who met DSM criteria for ASPD symptoms rather than ASPD diagnosis, because for a large portion of the participants, we had no information regarding a history of conduct disorder before age 15. Thus, we considered syndromal antisocial behavior since age 15. This is an important distinction, because several studies have reported that the presence of conduct disorder among alcoholics with ASPD is associated with more severe alcohol abuse, poorer treatment outcomes, and poorer performance on neuropsychological tests.[3,55] Moreover, among young adults with early onset alcoholism, those with a history of conduct disorder had poorer behavioral inhibition compared to those without conduct disorder.[5]

Procedures

In order to estimate general levels of intelligence and to obtain traditional measures of memory on the participants, we administered the WAIS[56,57] and WMS.[58,59] Three WAIS subtests (Digit Symbol, Block Design, and Picture Arrangement) were used as measures of frontal system function, including: attention, memory, social competency, motor speed, and visuospatial function. We also administered four additional neuropsychological tests that were particularly sensitive to frontal brain dysfunction:[60,61] Trail Making Test;[62] WCST;[63] Controlled Oral Word Association Test (COWAT);[64] and Ruff Figural Fluency Test (RFFT).[65] Table 2 lists the tasks, as well as the various measures derived from each of them.

Trails A is a test of sequential-motor ability requiring individuals to connect an ordered series of numbered circles. Trails B adds a cognitive flexibility/mental-tracking component to the task by requiring the participant to alternate

Table 2 Measures of frontal function

Test	Measure
Trail Making Test (Parts A and B)	• Age and education corrected T-Score
Wisconsin Card Sorting Test (WCST)	• Total number of correct responses • Age and education corrected percentile ranking for perseverative responses • Age and education corrected percentile ranking for conceptual level responses
Controlled Oral Word Association Test (COWAT or FAS)	• Total number of words • Age and education corrected percentile ranking for total number of words • Total number of perseverations
Ruff Figural Fluency Test (RFFT)	• Total number of unique designs
WAIS Digit Symbol subtest	• Age and education corrected scaled score comprised of the coding score (number of symbols correctly copied in 120 seconds)
WAIS Block Design subtest	• Age and education corrected scaled score comprised of the successful completion of up to 14 designs within the time limit (time limits for each design range from 30 seconds for the easiest designs to 120 seconds for the most difficult designs)
WAIS Picture Arrangement subtest	• Age and education corrected scaled score comprised of the correct arrangement of up to 11 pictures completed within the time limit (time limits for each design range from 30 seconds for the easiest arrangements to 120 seconds for the most difficult arrangements)

between number and letter series (1, A, 2, B, etc.). Both measures were transformed to T-Scores using age and education norms.[66] The WCST was administered to examine perseverative responding while set-switching, as well as to measure concept formation. This task was administered manually and scored by computer. Verbal and figural fluency were assessed with the COWAT and the RFFT, respectively. The COWAT (also called the FAS test) required participants to name as many words as they could that begin with the letter F (then A, and then S) within a 60 second period. For the RFFT, participants must draw as many unique designs as possible within 60 seconds by connecting dots in different patterns. The WAIS Performance subtests were administered in part because of their known sensitivity to visuospatial deficits in alcoholics,[13,18] and also because they are sensitive to frontal functions such as attention, memory, and social competence.[67] For the Coding portion of the Digit Symbol subtest, participants copied symbols that are paired with numbers, for 120 seconds. For the Incidental Learning and Free Recall portions, participants were asked to fill in the correct symbols that corresponded with the numbers and to draw as many symbols as they could accurately recall. The Block Design subtest requires participants to assemble nine three-dimensional blocks such that they form patterns displayed on two-dimensional cards. The WAIS Picture Arrangement subtest requires participants to arrange pictures in an order that tells a coherent story involving interactions among people.

Of particular interest, because of their special putative sensitivity to frontal system dysfunction, were the following test measures: Trails A and B T-Scores; percentile ranking of the conceptual level responses and perseverative responses on the WCST; the percentile score and the total number of perseverative responses on the FAS test; the number of unique designs on the RFFT; and the Picture Arrangement subtest of the WAIS.

In addition, we administered the Hamilton Depression Scale[68] and the Profile of Mood States (POMS)[69] to assess affect. The POMS contains well-documented measures of negative affect associated with alcohol use[70,71] and antisocial symptoms,[72] and we included it as an adjunct to our indices of frontal functioning.

Although none of the aforementioned tests can definitively assess deficits specific to damage of different subsystems within prefrontal brain circuitry, the following are considered more sensitive to dorsolateral prefrontal function than to orbitofrontal function:[17,18] Trails T-Scores, WCST Conceptual Responses, FAS Percentile score, RFFT unique designs, and WAIS Digit Symbol and Block Design subtests. The tests considered to be more sensitive to orbitofrontal than to dorsolateral functions are WCST Perseverative Responses, FAS Perseverative Responses, WAIS Picture Arrangement, and measures of affect.

Statistical analyses

Relationships and interactions among variables were analyzed with SPSS Version 16.[73] Hierarchical multiple regressions were conducted to predict performances on the neuropsychological test measures sensitive to frontal

dysfunction, as well as the measures of affect. We selected the variables for inclusion in the analyses by first entering all of the variables of interest, as well as their interactions, into the hierarchical multiple regression models. We then removed the variables that were not significant predictors ($p = 0.10$), one at a time beginning with the interactions. Regression analyses included the following significant predictors: Alcohol group (AL), DHD, QFI, ASPD group, and Gender. Group membership (AL or ASPD) was defined according to the inclusion/exclusion criteria described earlier. Additionally, Age, Education, and Verbal IQ (VIQ) were examined as covariate predictors.

Results

The significant independent variables (ie, predictors) of interest in this study were AL, DHD, QFI, ASPD, and Gender. Table 3 shows the beta, standard error of beta, standardized beta, *t* and *p* values, as well as the bivariate, partial, and part correlations for each predictor in each significant model predicting the outcome measures. In addition, the R^2-Change is listed to denote the additional variance contributed by the final predictor over and above the model with just the other predictors. In the models for the WAIS Digit Symbol Subtest, where there are multiple listings for R^2-Change, the value for ASPD represents the R^2-Change over and above each model with the alcohol variable alone (ie, AL, DHD, or QFI), and the value for Gender represents the R^2-Change over and above each model with that same alcohol variable and ASPD.

When examining the influence of the possible confounding variables of age, education, and VIQ in relation to the measures of frontal and affective functioning, only those predictors that remained significant were retained. In addition, there were significant differences in the duration and amount of drinking among men and women. Therefore, we examined Gender in all our regression analyses, and only retained Gender as a predictor when it remained significant with DHD or QFI in the model. Examination for muliticollinearity of the noncategorical independent variables of DHD and QFI with Age, Education, and VIQ were significant but low: DHD with Age ($r = 0.19$) and with Education ($r = -0.30$); QFI with Education ($r = -0.31$) and with VIQ ($r = -0.24$).

The deficits we observed did not appear to reflect generalized cognitive impairments in the alcoholics with ASPD symptoms. Specificity of their frontal-system deficits was indicated by the observations that (a) the various predictors were significant after we examined the influence of the possible confounding variables of Age, Education, and VIQ, and (b) the interaction of AL × ASPD was not statistically significant with respect to scores on the WAIS Vocabulary subtest, a measure of premorbid crystallized intelligence.[56,74,75]

Measures of frontal function

Trails A and Trails B

For the Trails A T-Score, the DHD × ASPD × Gender interaction was significant ($R^2 = 0.04$, $F(7, 333) = 2.03$, $p = 0.05$). For the Trails B T-Score, the three-way interaction of AL × ASPD × Gender was significant ($R^2 = 0.05$, $F(7, 335) = 2.30$, $p < 0.05$), as was DHD × ASPD × Gender ($R^2 = 0.05$, $F(7, 333) = 2.73$, $p < 0.01$), and QFI × ASPD × Gender ($R^2 = 0.04$, $F(7, 330) = 1.98$, $p = 0.06$). These results suggest that the combination of ASPD symptoms and drinking was associated with poor performance on the Trails A and B tasks, and that these relationships were more pronounced for women than for men.

Wisconsin Card Sorting Task (WCST)

For perseverative responses, the regression model with AL and ASPD as predictors was significant ($R^2 = 0.04$, $F(2, 339) = 7.01$, $p = 0.001$), indicating that the alcoholic and the ASPD groups exhibited increased perseverative responding. For WCST conceptual responses, the regression model with the AL × ASPD interaction was significant ($R^2 = 0.04$, $F(3, 338) = 4.91$, $p < 0.01$), indicating that the combination of alcoholism and ASPD symptoms was associated with worse conceptual scores than would be attributable to either condition alone. DHD and QFI did not significantly predict WCST perseverative or conceptual responses.

Controlled Oral Word Association Test (COWAT or FAS)

For the total number of words generated, two of the alcohol-related measures (DHD and QFI) formed significant models with Gender (DHD: $R^2 = 0.07$, $F(2, 329) = 12.61$, $p < 0.001$; QFI: $R^2 = 0.07$, $F(2, 329) = 12.39$, $p < 0.001$). For age and education corrected FAS percentiles, two of the alcohol variables (AL and QFI) and ASPD formed significant models with Gender (AL: $R^2 = 0.05$, $F(2, 334) = 8.81$, $p < 0.001$; QFI: $R^2 = 0.06$, $F(2, 329) = 9.75$, $p < 0.001$; ASPD: $R^2 = 0.05$, $F(2, 334) = 9.20$, $p < 0.001$). DHD and ASPD also predicted FAS percentiles ($R^2 = 0.03$, $F(2, 333) = 5.20$, $p < 0.01$). The pattern presented was the same for all the drinking variables, that is, increased drinking was associated with fewer words produced. Women also generated more words than men. For FAS total number of perseverations, there was a significant three-way interaction of DHD × ASPD × Gender

Table 3 Regression Models: Beta, Standard Error of Beta, Standardized Beta, *t* and *p* values, as well as the bivariate, partial, and part correlations for each significant predictor for each test measure. "N" represents the number of subjects for which data were available

Test Measure	Predictor	Beta	SE_B	Std. Beta	*t*	*p*†	Bivariate	Partial	Part	R^2-Change
Trails A T-Score	Intercept	46.284	1.192		38.842	<0.001				
N = 341	DHD	−0.031	0.092	−0.029	−0.337	0.736	−0.089	−0.018	−0.018	
	ASPD	3.980	2.372	0.164	1.678	0.094	0.043	0.092	0.090	
	Gender	0.087	1.544	0.004	0.056	0.955	−0.003	0.003	0.003	
	DHD × ASPD	−0.188	0.148	−0.136	−1.272	0.204	−0.086	−0.070	−0.068	
	DHD × Gender	0.026	0.166	0.014	0.159	0.874	−0.070	0.009	0.009	
	ASPD × Gender	4.062	3.999	0.105	1.016	0.310	0.017	0.056	0.055	
	DHD × ASPD × Gender	−0.565	0.315	−0.188	−1.792	0.074	−0.100	−0.098	−0.096	0.009
Trails B T-Score	Intercept	50.986	1.225		41.608	<0.001				
N = 343	Alc	−2.370	2.049	−0.113	−1.157	0.248	−0.109	−0.063	−0.062	
	ASPD	−4.515	2.772	−0.192	−1.629	0.104	−0.037	−0.089	−0.087	
	Gender	−0.986	1.576	−0.048	−0.625	0.532	−0.011	−0.034	−0.033	
	Alc × ASPD	5.278	3.566	0.201	1.480	0.140	−0.060	0.081	0.079	
	Alc × Gender	−0.143	2.832	−0.005	−0.051	0.960	−0.115	−0.003	−0.003	
	ASPD × Gender	15.087	4.866	0.398	3.100	0.002	−0.003	0.167	0.165	
	Alc × ASPD × Gender	−17.716	6.046	−0.409	−2.930	0.004	−0.095	−0.158	−0.156	0.024
Trails B T-Score	Intercept	50.238	1.154		43.535	<0.001				
N = 341	DHD	−0.017	0.089	−0.017	−0.195	0.845	−0.075	−0.011	−0.010	
	ASPD	−2.169	2.298	−0.092	−0.944	0.346	−0.036	−0.052	−0.050	
	Gender	−0.589	1.495	−0.028	−0.394	0.694	−0.010	−0.022	−0.021	
	DHD × ASPD	0.056	0.143	0.041	0.388	0.698	−0.084	0.021	0.021	
	DHD × Gender	−0.082	0.161	−0.043	−0.507	0.612	−0.130	−0.028	−0.027	
	ASPD × Gender	11.299	3.873	0.298	2.918	0.004	−0.003	0.158	0.155	
	DHD × ASPD × Gender	−0.934	0.305	−0.319	−3.061	0.002	−0.151	−0.165	−0.163	0.027
Trails B T-Score	Intercept	50.567	1.158		43.680	<0.001				
N = 338	QFI	−0.129	0.154	−0.083	−0.840	0.402	−0.106	−0.046	−0.045	
	ASPD	−1.817	2.172	−0.077	−0.836	0.404	−0.042	−0.046	−0.045	
	Gender	−1.160	1.510	−0.056	−0.768	0.443	−0.003	−0.042	−0.041	
	QFI × ASPD	0.091	0.211	0.050	0.432	0.666	−0.107	0.024	0.023	
	QFI × Gender	0.139	0.307	0.047	0.454	0.650	−0.114	0.025	0.024	
	ASPD × Gender	7.949	3.553	0.210	2.237	0.026	−0.002	0.122	0.121	
	QFI × ASPD × Gender	−1.021	0.430	−0.276	−2.376	0.018	−0.143	−0.130	−0.128	0.016

(*Continued*)

Table 3 (*Continued*)

Test Measure	Predictor	Beta	SE_B	Std. Beta	*t*	*p*†	Bivariate	Partial	Part	R^2-Change
WCST Perseverative Response Percentile	Intercept	50.525	2.040		24.765	<0.001				
N = 342	AIc	−6.452	3.338	−0.111	−1.933	0.054	−0.160	−0.104	−0.103	
	ASPD	−8.375	3.748	−0.129	−2.234	0.026	−0.171	−0.120	−0.119	0.014
WCST Conceptual Response Percentile	Intercept	50.347	2.163		23.281	<0.001				
N = 342	AIc	−1.074	3.920	−0.018	−0.274	0.784	−0.130	−0.015	−0.015	
	ASPD	0.778	6.243	0.012	0.125	0.901	−0.161	0.007	0.007	
	AL × ASPD	−15.051	7.895	−0.203	−1.907	0.057	−0.204	−0.103	−0.102	0.010
FAS Total	Intercept	42.186	1.031		40.927	<0.001				
N = 336	DHD	−0.135	0.063	−0.117	−2.152	0.032	−0.169	−0.117	−0.114	
	Gender	4.827	1.249	0.211	3.864	<0.001	0.240	0.207	0.204	0.042
FAS Total	Intercept	42.031	1.018		41.297	<0.001				
N = 332	QFI	−0.202	0.094	−0.118	−2.150	0.032	−0.169	−0.118	−0.114	
	Gender	4.810	1.259	0.210	3.822	<0.001	0.239	0.206	0.203	0.041
FAS Percentile	Intercept	50.453	2.569		19.639	<0.001				
N = 337	AIc	−5.508	3.030	−0.098	−1.818	0.070	−0.128	−0.099	−0.097	
	Gender	10.292	2.986	0.186	3.446	0.001	0.202	0.185	0.184	0.034
FAS Percentile	Intercept	56.923	1.888		30.150	<0.001				
N = 336	DHD	−0.265	0.159	−0.096	−1.672	0.096	−0.135	−0.091	−0.090	
	ASPD	−7.266	3.574	−0.117	−2.033	0.043	−0.149	−0.111	−0.110	0.012
FAS Percentile	Intercept	50.210	2.470		20.326	<0.001				
N = 332	QFI	−0.506	0.228	−0.122	−2.217	0.027	−0.165	−0.121	−0.119	
	Gender	9.644	3.055	0.174	3.157	0.002	0.205	0.171	0.169	0.029
FAS Percentile	Intercept	50.273	2.438		20.624	<0.001				
N = 337	ASPD	−6.886	3.420	−0.110	−2.014	0.045	−0.151	−0.110	−0.107	
	Gender	9.755	3.026	0.176	3.224	0.001	0.202	0.174	0.172	0.029
FAS Perseverations	Intercept	1.22	0.164		7.429	<0.001				
N = 335	DHD	0.039	0.013	0.261	3.025	0.003	0.073	0.165	0.161	
	ASPD	−0.186	0.324	−0.056	−0.574	0.566	−0.097	−0.032	−0.031	
	Gender	−0.191	0.213	−0.064	−0.898	0.370	−0.155	−0.05	−0.048	
	DHD × ASPD	−0.039	0.02	−0.204	−1.908	0.057	−0.043	−0.105	−0.101	

	DHD × Gender	−0.069	0.023	−0.256	−3.004	0.003	−0.132	−0.164	−0.16	
	ASPD × Gender	−0.671	0.546	−0.125	−1.23	0.219	−0.133	−0.068	−0.065	
	DHD × ASPD × Gender	0.095	0.043	0.231	2.217	0.027	−0.07	0.122	0.118	0.014
RFFT Unique Designs	Intercept	64.031	5.656		11.321	<0.001				
N = 137	Alc	−15.178	7.547	−0.224	−2.011	0.046	−0.151	−0.172	−0.165	
	Gender	5.948	7.272	0.089	0.818	0.415	0.255	0.071	0.067	
	Alc × Gender	26.065	12.087	0.245	2.156	0.033	0.184	0.184	0.177	0.031
RFFT Unique Designs	Intercept	61.717	5.043		12.239	<0.001				
N = 136	DHD	−0.599	0.327	−0.185	−1.829	0.070	−0.150	−0.157	−0.151	
	Gender	7.269	6.695	0.110	1.086	0.280	0.246	0.094	0.090	
	DHD × Gender	1.515	0.665	0.228	2.278	0.024	0.202	0.194	0.188	0.035
RFFT Unique Designs	Intercept	62.796	4.200		14.952	<0.001				
N = 137	ASPD	−28.004	8.027	−0.297	−3.489	0.001	−0.350	−0.289	−0.279	
	Gender	10.173	5.681	0.153	1.791	0.076	0.255	0.153	0.143	0.021
WAIS Digit Symbol	Intercept	11.741	0.282		41.697	<0.001				
N = 345	Alc	−1.122	0.341	−0.179	−3.290	0.001	−0.281	−0.175	−0.165	
	ASPD	−1.533	0.388	−0.217	−3.946	<0.001	−0.314	−0.209	−0.198	0.050
	Gender	0.798	0.319	0.129	2.498	0.013	0.206	0.134	0.125	0.016
WAIS Digit Symbol	Intercept	11.715	0.280		41.823	<0.001				
N = 344	DHD	−0.058	0.017	−0.186	−3.446	0.001	−0.289	−0.184	−0.172	
	ASPD	−1.591	0.378	−0.226	−4.206	<0.001	−0.313	−0.222	−0.211	0.053
	Gender	0.690	0.324	0.111	2.128	0.034	0.210	0.115	0.107	0.011
WAIS Digit Symbol	Intercept	11.520	0.274		42.002	<0.001				
N = 340	QFI	−0.062	0.025	−0.135	−2.447	0.015	−0.258	−0.132	−0.123	
	ASPD	−1.733	0.386	−0.247	−4.493	<0.001	−0.327	−0.238	−0.227	0.062
	Gender	0.837	0.324	0.136	2.582	0.010	0.222	0.139	0.130	0.017
WAIS Block Design	Intercept	11.897	0.297		40.107	<0.001				
N = 345	Alc	−1.779	0.422	−0.310	−4.216	<0.001	−0.129	−0.223	−0.222	
	Gender	−1.423	0.394	−0.251	−3.613	<0.001	−0.084	−0.192	−0.190	
	Alc × Gender	1.983	0.612	0.264	3.239	0.001	−0.016	0.173	0.170	0.029
WAIS Block Design	Intercept	11.793	0.312		37.796	<0.001				
N = 343	DHD	−0.068	0.024	−0.241	−2.833	0.005	−0.121	−0.153	−0.150	
	ASPD	−1.013	0.623	−0.158	−1.627	0.105	−0.097	−0.089	−0.086	
	Gender	−1.314	0.404	−0.233	−3.249	0.001	−0.077	−0.175	−0.172	

(*Continued*)

Table 3 (*Continued*)

Test Measure	Predictor	Beta	SE_B	Std. Beta	t	$p^{\dagger}$	Bivariate	Partial	Part	R^2-Change
	DHD × ASPD	0.039	0.039	0.106	0.997	0.320	−0.121	0.054	0.053	
	DHD × Gender	0.118	0.044	0.227	2.697	0.007	−0.022	0.146	0.143	
	ASPD × Gender	1.544	1.050	0.150	1.471	0.142	−0.066	0.080	0.078	
	DHD × ASPD × Gender	−0.178	0.083	−0.223	−2.151	0.032	−0.100	−0.117	−0.114	0.013
WAIS Block Design	Intercept	11.641	0.307		37.888	<0.001				
N = 340	QFI	−0.092	0.041	−0.218	−2.227	0.027	−0.103	−0.121	−0.119	
	ASPD	−0.936	0.579	−0.147	−1.618	0.107	−0.106	−0.088	−0.086	
	Gender	−1.290	0.401	−0.230	−3.213	0.001	−0.069	−0.174	−0.171	
	QFI x ASPD	0.043	0.056	0.088	0.770	0.442	−0.127	0.042	0.041	
	QFI × Gender	0.256	0.082	0.319	3.127	0.002	0.007	0.169	0.167	
	ASPD × Gender	1.120	0.948	0.110	1.182	0.238	−0.063	0.065	0.063	
	QFI × ASPD × Gender	−0.266	0.115	−0.266	−2.319	0.021	−0.075	−0.126	−0.124	0.015
WAIS Picture Arrangement	Intercept	10.763	0.203		53.056	<0.001				
N = 345	Alc	0.750	0.367	0.136	2.045	0.042	0.009	0.110	0.109	
	ASPD	0.446	0.587	0.072	0.759	0.448	−0.095	0.041	0.040	
	Alc x ASPD	−1.852	0.741	−0.268	−2.501	0.013	−0.131	−0.134	−0.133	0.018
WAIS Picture Arrangement	Intercept	10.825	0.192		56.361	<0.001				
N = 334	DHD	0.036	0.019	0.131	1.869	0.062	0.002	0.101	0.100	
	ASPD	0.049	0.472	0.008	0.103	0.918	−0.095	0.006	0.006	
	DHD × ASPD	−0.075	0.033	−0.210	−2.283	0.023	−0.123	−0.123	−0.122	0.015
WAIS Picture Arrangement	QFI	0.054	0.034	0.133	1.604	0.110	−0.079	0.087	0.086	
N = 340	ASPD	0.291	0.436	0.047	0.669	0.504	−0.095	0.036	0.036	
	QFI × ASPD	−0.145	0.047	−0.305	−3.083	0.002	−0.175	−0.166	−0.165	0.027
Hamilton	Intercept	1.243	0.214		5.803	<0.001				
N = 345	Alc	0.719	0.387	0.115	1.856	0.064	0.287	0.100	0.092	
	ASPD	0.715	0.620	0.102	1.154	0.249	0.336	0.062	0.057	
	Alc × ASPD	1.823	0.782	0.233	2.332	0.020	0.382	0.125	0.116	0.013
Hamilton	Intercept	0.907	0.283		3.209	0.001				
N = 344	DHD	0.042	0.020	0.134	2.049	0.041	0.293	0.111	0.101	
	ASPD	1.213	0.498	0.173	2.438	0.015	0.335	0.131	0.120	
	Gender	0.643	0.319	0.104	2.015	0.045	−0.012	0.109	0.099	

	DHD × ASPD	0.082	0.034	0.203	2.390	0.017	0.386	0.129	0.118	0.014
POMS Anger	Intercept	39.760	0.732		54.285	<0.001				
N = 262	Alc	1.426	0.779	0.121	1.832	0.068	0.143	0.114	0.111	
	ASPD	3.089	1.042	0.246	2.965	0.003	0.137	0.182	0.179	
	Gender	1.498	0.883	0.127	1.697	0.091	–0.039	0.105	0.102	
	ASPD × Gender	–4.938	1.605	–0.255	–3.076	0.002	–0.066	–0.188	–0.186	0.035
POMS Anger	Intercept	41.122	0.445		92.317	<0.001				
N = 261	DHD	0.076	0.036	0.132	2.139	0.033	0.132	0.132	0.132	
POMS Depression	Intercept	37.351	0.738		50.613	<0.001				
N = 262	Alc	1.978	0.784	0.162	2.522	0.012	0.223	0.155	0.148	
	ASPD	2.496	1.050	0.192	2.377	0.018	0.219	0.147	0.140	
	Gender	–1.461	0.890	–0.120	–1.642	0.102	–0.238	–0.102	–0.096	
	ASPD x Gender	–2.776	1.617	–0.138	–1.716	0.087	–0.051	–0.106	–0.101	0.010
POMS Depression	Intercept	38.131	0.690		55.250	<0.001				
N = 261	DHD	0.051	0.048	0.085	1.058	0.291	0.252	0.066	0.062	
	ASPD	0.296	1.081	0.023	0.274	0.784	0.218	0.017	0.016	
	Gender	–2.128	0.752	–0.174	–2.832	0.005	–0.240	–0.174	–0.166	
	DHD x ASPD	0.134	0.076	0.181	1.758	0.080	0.291	0.109	0.103	0.011
POMS Tension	Intercept	34.498	0.554		62.275	<0.001				
N = 262	Alc	2.150	0.861	0.163	2.497	0.013	0.221	0.153	0.150	
	ASPD	2.079	0.913	0.148	2.277	0.024	0.212	0.140	0.137	0.019
POMS Tension	Intercept	34.658	0.523		66.234	<0.001				
N = 261	DHD	0.111	0.041	0.171	2.700	0.007	0.221	0.166	0.162	
	ASPD	2.172	0.888	0.155	2.446	0.015	0.210	0.151	0.147	0.022

Notes: †Denotes *p* value for the Predictor as well as for the R^2-Change. ‡For models predicting WAIS Digit Symbol, where there are multiple listings of R^2-Change, the value for ASPD represents the R^2-Change over and above the alcohol variable alone, and the value for Gender represents the R^2-Change over and above the alcohol variable and ASPD.

Abbreviations: Alc, alcohol group; ASPD, antisocial personality disorder; DHD, duration of heavy drinking; QFI, Quantity Frequency Index.

($R^2 = 0.08$, $F(7, 327) = 3.92$, $p < 0.001$). This suggests that for individuals without ASPD symptoms, men perseverated more in connection with DHD, whereas men with ASPD symptoms did not; this pattern was not observed for women.

Ruff Figural Fluency Test (RFFT)

Three multiple regression analyses for the RFFT number of unique designs revealed significant effects of AL, DHD, ASPD, and Gender. In the first regression model, the AL × Gender interaction significantly predicted the RFFT scores ($R^2 = 0.10$, $F(3, 133) = 5.01$, $p < 0.01$). The second regression equation with the DHD × Gender interaction for the RFFT was significant ($R^2 = 0.10$, $F(3, 132) = 4.92$, $p < 0.01$). Third, the model with ASPD and Gender was significant ($R^2 = 0.14$, $F(2, 134) = 11.19$, $p < 0.001$). Together, these results indicated that alcoholic men made fewer unique designs than nonalcoholic men, but this relationship was not seen in women. In addition, longer DHDs were associated with fewer unique designs in men, but not in women. Participants with ASPD symptoms scored lower than those without, and the men scored lower than the women.

WAIS subtests (age-scaled scores)

For the WAIS Digit Symbol subtest, three multiple regression analyses were significant (for AL, DHD, and QFI), and in all three of them, ASPD and Gender also were significant predictors (AL: $R^2 = 0.15$, $F(3, 341) = 19.29$, $p < 0.001$; DHD: $R^2 = 0.15$, $F(3, 340) = 19.70$, $p < 0.001$; QFI: $R^2 = 0.15$, $F(3, 339) =$, $p < 0.001$). Thus, each of the three alcohol variables (AL, DHD, and QFI), as well as ASPD symptoms, were associated with impaired Digit Symbol performance, and women scored higher than men.

For the WAIS Block Design subtest, the multiple regression analyses indicated that AL, Gender, and their interaction significantly predicted the scores ($R^2 = 0.06$, $F(3, 341) = 6.84$, $p < 0.001$). Two three-way interactions with drinking variables were significant: DHD × ASPD × Gender ($R^2 = 0.06$, $F(7, 335) = 2.89$, $p < 0.01$) and QFI × ASPD × Gender ($R^2 = 0.06$, $F(7, 332) = 2.90$, $p < 0.01$). Men without a drinking history performed better than the other three groups; that is, they performed better than the nonalcoholic women, and better than the alcoholics of both genders. Increased duration and amount of drinking were associated with lower scores for women with ASPD symptoms; men did not show this connection.

For the WAIS Picture Arrangement subtest, all three alcohol-related predictors significantly interacted with ASPD (AL: $R^2 = 0.03$, $F(3, 341) = 3.44$, $p < 0.05$); DHD: $R^2 = 0.02$, $F(3, 340) = 2.94$, $p < 0.05$); and QFI: $R^2 = 0.04$, $F(3, 336) = 4.49$, $p < 0.01$). Alcoholics with comorbid ASPD symptoms performed significantly worse than alcoholics without ASPD; nonalcoholics did not show this relationship. Similarly, for all individuals with ASPD symptoms, DHD and QFI each predicted lower scores, and individuals without ASPD symptoms did not show this association.

Measures of affect

Hamilton Depression Scale

The regression equation with the AL x ASPD interaction for Hamilton Depression scores was significant ($R^2 = 0.15$, $F(3, 341) = 21.02$, $p < 0.001$). Further, the interaction of DHD × ASPD, along with the predictor of Gender, also significantly predicted Hamilton Depression scores ($R^2 = 0.16$, $F(4, 339) = 17.90$, $p < 0.001$). Comorbidity of ASPD symptoms with alcoholism, especially in alcoholics with a long DHD, was associated with the highest depression scores, and more so for women than for men.

Profile of Moods (POMS) affect scores

On the Anger scale of the POMS, the main effect of AL and the ASPD × Gender interaction were significant predictors ($R^2 = 0.06$, $F(4, 257) = 4.31$, $p < 0.01$). Also, DHD alone was a significant predictor ($R^2 = 0.02$, $F(1, 259) = 4.57$, $p < 0.05$). These findings indicated that high Anger scores on the POMS were associated with increased DHD. In addition, men with ASPD symptoms had higher Anger scores than men without ASPD symptoms, but women did not show this difference. On the POMS Depression scale, the main effect of AL, and the interaction of ASPD × Gender were significant ($R^2 = 0.11$, $F(4, 257) = 8.23$, $p < 0.001$); the men with ASPD symptoms had higher Depression scores than the women. In addition, the main effect of Gender, as well as the DHD × ASPD interaction, significantly predicted POMS Depression scores ($R^2 = 0.12$, $F(4, 256) = 8.81$, $p < 0.001$). In other words, longer drinking histories were associated with increased depression, but even more so in individuals with ASPD symptoms. With respect to the POMS Tension measure, AL, DHD, and ASPD were significant main effects (AL: $R^2 = 0.07$, $F(2, 259) = 9.36$, $p < 0.001$; DHD: $R^2 = 0.07$, $F(2, 258) = 9.79$, $p < 0.001$). These results showed that longer DHDs as well as ASPD symptoms were associated with increased Tension scores.

Discussion

In the present study, we employed a multivariate approach to evaluate the connection between alcoholism and ASPD

symptoms on measures of prefrontal brain functioning. Our findings confirmed results of other studies showing that alcoholism and ASPD, separately, are associated with deficits on tests of frontal brain integrity.[13,55] We found that AL, DHD, QFI, and ASPD were significant predictors on several measures of frontal dysfunction. Moreover, our findings further extended those results by showing that alcoholism and ASPD symptoms, together as comorbid conditions, were associated with synergistic frontal system deficits: They exceeded the sum of frontal deficits attributable to alcoholism plus those attributable to ASPD symptoms. This synergism was observed for tests sensitive both to dorsolateral prefrontal functions (Trails tests, WCST conceptual responses, and WAIS Block Design) and to orbitofronal functions (WAIS Picture Arrangement, and Depression).

With respect to gender differences, some of our results supported findings from the literature that neuropsychological deficits in association with alcohol variables were more pronounced for women than for men,[43,44,76] and conversely, that the deficits with regard to ASPD were more pronounced for men than for women.[36,38,40] However, our gender differences were not consistent across the tasks. Moreover, the men and women in the present study differed with respect to impairments associated with the co-occurrence of alcoholism and ASPD. In the following sections, the findings from each of the measures are discussed in turn, followed by a summary consideration of gender differences.

Trails A and Trails B

The interaction of DHD with ASPD and Gender significantly predicted performance on Trails A in the present study. Stevens and colleagues[42] reported that an interaction of an antisocial profile and family history for alcohol dependence significantly predicted Trails A completion time in men; women were not included in that study. For Trails B, we found significant interactions for each of the alcohol variables with ASPD and Gender. The fact that AL, DHD, and QFI predicted poor performance on Trails B is in concert with observations of Moriyama and colleagues[77] and Davies and colleagues,[78] who also reported deficits in alcoholic patients. Our results further suggested that the Trails deficits, which were associated with a combination of ASPD and drinking, were more pronounced for women than for men.

Wisconsin Card Sorting Task (WCST)

There were significant main effects of AL and ASPD on WCST perseverative response scores. Because the WCST requires set-switching, these findings support the proposed link of orbitofrontal system dysfunction to impulsive and disinhibited behavior.[36,79,80] Moreover, the findings are in concert with those of Deckel,[81] who reported an association of alcoholism and WCST deficits, and those of Oscar-Berman and colleagues[18] who reported an increased number of perseverative responses among alcoholic Korsakoff patients. In addition, in the present study, the AL × ASPD interaction for conceptual level responding suggested greater dorsolateral prefrontal impairments associated with the combined conditions than deficits attributable to either condition alone.

Controlled Oral Word Association Test (COWAT or FAS)

For several of the FAS measures, ie, total number of words generated, age and education corrected percentiles, and perseverations, alcohol-related measures formed significant models with Gender. That is, increased drinking was associated with fewer words produced, and women generated more words than men. There also were significant main effects of AL, DHD, QFI, ASPD, and Gender in the models that predicted FAS percentiles. For FAS total number of perseverations, the significant three-way interaction of DHD × ASPD × Gender suggested that men without ASPD symptoms exhibited a stronger connection between drinking and perseveration than men with ASPD symptoms. This interpretation should be heeded with caution because the overall low frequency of perseverative responses allowed a few individuals to have greater influence on the statistical outcome.[42,82]

Ruff Figural Fluency Test (RFFT)

The interactions of AL with Gender, and DHD with Gender, significantly predicted performance on the number of unique designs on the RFFT. Whereas alcoholic men made fewer unique designs than nonalcoholic men, and longer DHDs in men predicted fewer unique designs, these relationships were not seen in women. Individuals with ASPD symptoms were also impaired on the task. The RFFT is often used as a measure of executive skills, as it requires planning and organizing to produce as many unique designs as possible during the time limit. Since these skills are considered to be controlled by the dorsolateral prefrontal system, our findings support the view that alcohol consumption by men, as well as ASPD symptoms in both genders, contribute to dorsolateral prefrontal dysfunction.

Of note, other studies have examined RFFT performance among alcoholics, and our findings support those of Oscar-Berman and colleagues[18] who found that alcoholic Korsakoff

patients had a significantly reduced number of unique designs on this test. By contrast, Blume and colleagues[82] examined the number of unique designs and perseverative errors on the RFFT among nonabstinent alcoholics, and the investigators did not find the RFFT to significantly predict self-report scores on self-awareness of problem drinking or readiness to change drinking behavior.

WAIS subtests (age scaled scores)

A limited number of studies have used WAIS Performance subtests to assess frontal system dysfunction and social cognitive ability in patients with neurobehavioral disorders. On the Digit Symbol subtest of the WAIS, the main effects of AL, DHD, QFI, ASPD, and Gender significantly predicted performance. These findings support those of others[14,78,83] who found that alcoholics, and in particular alcoholics who drank heavily,[18] performed poorly on this subtest. However, we are among only a few who have reported poor Digit Symbol performance in association with ASPD symptoms.[84] We also confirmed findings that, overall, women performed significantly better than men on Digit Symbol.[85–89]

On the Block Design subtest of the WAIS, the interaction of Gender and AL significantly predicted performance. Alcoholic men, and both alcoholic and nonalcoholic women performed significantly worse than men without a drinking history. Thus, we confirmed results of previous studies showing that alcoholic men are impaired on Block Design.[90] However, in the present study, we found that alcoholic women were equivalent to nonalcoholic women. This finding differs from that of other investigators, who reported that alcoholic women are impaired on Block Design.[91] We attribute the lack of impairment in our sample of alcoholic women to their long sobriety durations (mean of 6.6 years) and limited number of additional psychiatric diagnoses compared to other samples.[91] The women with ASPD symptoms – but not the men – had lower scores in association with longer durations and higher amounts of drinking.

On the Picture Arrangement subtest of the WAIS, the interaction of ASPD with each of the three alcohol variables (AL, DHD, and QFI), significantly predicted performance. Picture Arrangement performance involves widespread frontal brain regions, because successful performance requires the weighing of multiple options and possible outcomes of a social situation presented to the participant, while at the same time, using working memory to organize the pictures cohesively. The Picture Arrangement subtest has been used previously to assess frontal system function.[92-94] In addition, orbitofrontal deficits are presumed, because several studies have found this subtest to measure social cognitive functioning in patients with psychiatric diagnoses[95,96] (although there is no general consensus for this assumption).[96] We also found that alcoholics with ASPD symptoms performed worse on Picture Arrangement as DHD increased. Our findings are robust, since the AL × ASPD, DHD × ASPD, and QFI × ASPD interactions significantly predicted Picture Arrangement scores, thereby supporting the view that individuals with ASPD symptoms who drink excessively have greater impairments on frontal tasks than those who drink less.

Measures of affect

Several studies have reported relationships between alcoholism, ASPD, negative affectivity, and emotional dysregulation.[8,34,97–99] The findings from this study support those previous findings, indicating that, indeed, there were significant interactions between ASPD and drinking variables (AL and DHD) on the Hamilton Depression Scale: Alcoholics with ASPD symptoms had higher Depression scores than nonalcoholics, and Depression scores were higher in individuals with ASPD symptoms as their drinking durations increased. While taking into consideration this interaction, Depression scores were higher in women than in men. Once more, these findings support an association between ASPD symptoms and frontal system dysfunction beyond that attributable to alcoholism alone.

On all three measures of the POMS, ie, Anger, Depression, and Tension, the alcoholics scored higher than the nonalcoholics, and the participants with ASPD symptoms scored higher than those without. Higher Anger and Depression scores also were associated with increased duration of drinking, and individuals with ASPD symptoms who drank for the longest time had the highest Depression scores. Finally, in concert with other research,[100] we found that men with ASPD symptoms had higher Anger and Depression scores on the POMS than did women.

Gender

With respect to gender, our results confirmed the findings of others, showing that women performed better than men on the FAS test[92,101–104] and the WAIS Digit Symbol subtest,[85–89] whereas men performed better than women overall on the Block Design subtest.[85,88] A more complex pattern of gender interactions was observed with respect to alcohol-related variables and ASPD symptoms for all of our measures except for the WCST and the WAIS Picture Arrangement Subtest, in which we observed no gender differences. Overall, our results

did not support those of other investigators who reported that women were generally more vulnerable to the effects of alcoholism than men.[44,76,105] That is, for three measures, FAS perseverations, RFFT, and Block Design, men were more impaired in relation to alcohol variables than women,[41,106,107] while the opposite was found for the Trails tests.

The results of the present study confirmed and extended previous findings that alcoholic as well as nonalcoholic men have more ASPD symptoms than women.[3,45] Additionally, men with ASPD symptoms had higher negative affect scores on the POMS in comparison to women.[100] Furthermore, for FAS perseverations and Block Design, the ASPD-related differences were larger for alcoholic men than women. For the Trails tests, the relationship with ASPD symptoms and alcohol variables was more pronounced in women.

Limitations

Psychometric properties are not available for our medical and alcohol screening interviews, and although norms have been established with alcoholic participants for the WAIS, WMS, WCST, and Trails, we know of no norms relevant to ASPD populations for the measures we used in our study. Additionally, and as noted earlier, we characterized our ASPD group as having "ASPD symptoms," because measures of the presence or absence of conduct disorder were not available from many participants. Therefore, our sample of individuals with ASPD symptoms may not be representative of patients with a formal psychiatric diagnosis of ASPD. In any case, our results demonstrated a clear synergism between alcoholism and ASPD symptoms with respect to the presence of frontal deficits.

Another limitation of this study is that we did not examine ASPD severity (as measured by number of symptoms) among alcoholics and nonalcoholics. Stevens and colleagues[42] reported that a greater number of ASPD symptoms were associated with slightly decreased scores in verbal abstraction, a measure of executive cognitive function. Further investigations of ASPD symptom severity and the effects of alcoholism on executive function are needed.

Additionally, exclusion criteria for participation in our study included significant psychiatric disorder such as bipolar disorder, mania, hypomania, and schizophrenia-spectrum disorders. However, other personality pathology, including panic disorder, posttraumatic stress disorder, and disorders characterized by high levels of impulsivity (eg, borderline), were not exclusion criteria and might confound associations of antisociality and alcohol use disorders with the neuropsychological deficits examined in this study.

Conclusions

This study examined the influence of alcoholism and ASPD symptoms on neuropsychological test performance sensitive to frontal brain dysfunction in men and women. We found that men and women were affected differently by the comorbidity of alcoholism and ASPD symptoms, depending upon the task. We also observed impairments, unrelated to gender differences, in performance between alcoholics with and without ASPD symptoms on measures of dorsolateral and orbitofrontal frontal system integrity. As hypothesized, there were significant interactions of alcohol-related measures with ASPD on several neuropsychological tests. In addition, we found that the drinking variables and ASPD were strong predictors of negative affect. That is, ASPD (or an interaction with ASPD) predicted significantly over and above alcoholism and duration of heavy drinking. In other words, we obtained evidence that the combination of alcoholism and ASPD symptoms led to greater deficits than the sum of each.

It has been reported[55] that among ASPD subjects, increased alcohol consumption predicted poor neuropsychological performance. Thus, clinicians treating patients with alcoholism may provide more effective treatment when considering that personality disorders such as ASPD contribute to frontal dysfunction resulting in impulsivity, disinhibition, compulsivity, negative affectivity, and emotional dysregulation. These factors are related to drinking behaviors, which in turn, can complicate treatment and lead to poor treatment outcomes. Therefore, ASPD symptoms must be carefully examined in order to facilitate accurate and timely evaluations of alcoholic patients, as well as to anticipate and counter potential difficulties inherent in treating dual diagnosis patients.

Acknowledgments

This research was supported by funds from the US Department of Health and Human Services, NIAAA (R01-AA07112 and K05-AA00219) to Boston University, and by funds from the Medical Research Service of the US Department of Veterans Affairs. Claribel Yu and Kimberly Wall helped with data collection.

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