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A Profile of Neuropsychological Deficits in Alcoholic Women

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Neuropsychological deficits, most notable in executive, visuospatial, and functions of gait and balance, are detectable in alcoholic men even after a month of sobriety. Less well established are the severity and profile of persisting deficits in alcoholic women. The authors used an extensive test battery to examine cognitive and motor functions in 43 alcoholic women who were sober, on average, for 3.6 months. Functions most severely affected in alcoholic women involved visuospatial and verbal and nonverbal working memory processes as well as gait and balance. Areas of relative sparing were executive functions, declarative memory, and upper-limb strength and speed. The authors found that lifetime alcohol consumption was related to impairment severity on Block Design (Wechsler Adult Intelligence Scale—Revised, D. Wechsler, 1981) and verbal and nonverbal working memory, suggesting a dose effect of alcohol abuse. The alcohol-related deficits in working memory, visuospatial, and balance implicate disruption of prefrontal, superior parietal, and cerebellar brain systems.

Numerous studies have identified a pattern of mild to moderate neuropsychological deficits that can occur in detoxified alcoholic men. Deficits have consistently been observed in executive functions, visuospatial abilities, psychomotor speed, and balance tasks (for reviews, see Kleinknecht & Goldstein, 1972; Oscar-Berman, 2000; Oscar-Berman & Hutner, 1993; Parsons, Butters, & Nathan, 1987; Sullivan, 2000). To date, fewer studies (cf. Nixon & Glenn, 1995) have examined neuropsychological functioning in alcoholic women. As a group, alcoholic women have been reported to drink less (Kessler et al., 1994; York & Welte, 1994), exhibit more psychiatric comorbidities (Brady & Randall, 1999), and metabolize alcohol differently than men (Li et al., 2000; Lieber, 2000). Because of these drinking and metabolic differences observed between men and women, the effects of alcohol on the cognitive and motor abilities in women cannot necessarily be generalized from those observed in men. Therefore, neuropsychological functions should be examined specifically in women as they have been so extensively studied in men.

The studies that have been conducted on alcoholic women (a) generally report neuropsychological deficits in the same cognitive areas as have been reported in detoxified alcoholic men and (b) feature problems in executive functions and visuospatial abilities (Glenn, 1993; Hochla & Parsons, 1982; Nixon & Glenn, 1995; Parsons et al., 1987). In light of the general finding that women, on average, drink less than men, drink for a shorter period of time than men, and yet display comparable cognitive deficits, it has been hypothesized that women are especially vulnerable to the toxic effects of alcohol (Glenn, Parsons, Sinha, & Stevens, 1988; Hochla & Parsons, 1982; Nixon & Glenn, 1995). However, in contrast to this assertion are studies (e.g., Silberstein & Parsons, 1979) showing alcoholic women to have milder cognitive deficits than men, although deficits tend to be in the same functional domains. Thus, it remains controversial whether alcoholic women display the same severity or pattern of deficits as documented in alcoholic men and whether observed sex differences are related to differences in lifetime alcohol consumption rates.

A series of structural brain imaging studies from our laboratory (Pfefferbaum, Lim, Desmond, & Sullivan, 1996; Pfefferbaum et al., 1992; Pfefferbaum, Sullivan, Mathalon, & Lim, 1997; Sullivan, Deshmukh, Desmond, Lim, & Pfefferbaum, 2000; Sullivan, Marsh, Mathalon, Lim, & Pfefferbaum, 1995) have consistently reported correlations between regional brain volumes and age in alcoholic men, with older alcoholic individuals showing greater structural brain abnormalities than younger alcoholic individuals when compared with age-matched control subjects. This age–alcohol interaction has been observed even after accounting for actual lifetime consumption of alcohol or du-

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ration of illness (Pfefferbaum et al., 1992, 1997). Early studies have revealed significant influences of age on cognition and have served as the foundation of the premature aging hypothesis of alcoholism (Ryan & Butters, 1980, 1984). However, unlike the magnetic resonance imaging literature, interactions between age and alcohol effects have been inconsistent in neuropsychological investigations, with some studies reporting correlations (Fein, Bachman, Fisher, & Davenport, 1990; Hochla & Parsons, 1982) and others not (Becker, Butters, Hermann, & D'Angelo, 1983; Ellis & Oscar-Berman, 1989; Grant, Adams, & Reed, 1984; Oscar-Berman, Clancy, & Weber, 1993; Shelton, Parsons, & Leber, 1984). Eckardt, Stapleton, Rawlings, Davis, and Grodin (1995) found younger alcoholic men, aged 18 to 35 years, to be free of significant cognitive and motor deficits. Another neuropsychological study of alcoholic men, spanning a 40-year age range, showed both patterns, with an age–alcohol interaction being present in motor tests of gait and balance but not in cognitive tests (Sullivan, Rosenbloom, & Pfefferbaum, 2000). Discrepancies may arise in part from discounting the potential of sex differences in alcohol and age–alcohol interaction sequelae. Indeed, it remains undetermined whether age–alcohol interactions characterize neuropsychological abilities in alcoholic women.

This study examined a wide range of cognitive and motor functions in alcoholic women compared with age-matched control women. The measures used in this study were chosen because of their demonstrated sensitivity to circumscribed brain lesions of the neocortex, limbic system, and cerebellum (cf. Sullivan, Deshmukh, et al., 2000; Sullivan, Shear, Zipursky, Sagar, & Pfefferbaum, 1994), which included brain regions commonly compromised in alcoholism. We hypothesized that alcoholic women as a group would show the same pattern of neuropsychological deficits that have been observed in alcoholic men, which included compromise in executive functions, visuospatial abilities, and gait and balance. We also examined whether the severity of deficits would be related to age or alcohol consumption variables.

Method

Subjects

Subjects included 43 alcoholic women (see Table 1) recruited from inpatient and outpatient programs at the Veterans Affairs Palo Alto Health Care System, from outpatient programs at Stanford Medical Center, and from community treatment programs (age range = 28–63 years). Potential subjects who gave their consent were initially screened by examination of their treatment records if available and by a following phone interview. Those who passed the initial screening process came to the laboratory for a detailed clinical assessment that included a medical history, physical examination, electrocardiogram, clinical blood panel, and structured psychiatric interview (Structured Clinical Interview for the *DSM–IV* [SCID], First, Spitzer, Gibbon, & Williams, 1995). Subjects were excluded if they had ever met *Diagnostic and Statistical Manual of Mental Disorders—Fourth Edition* (*DSM–IV*, American Psychiatric Association, 1994) criteria for schizophrenia or bipolar disorder, had a history of medical or neurological illness or trauma, had suffered a head injury involving loss of consciousness for more than 30 min, or were currently taking medications or illicit drugs that affected the central nervous system (CNS). Subjects were tested on an outpatient basis after periods of sobriety ranging from 2 to 15 months (M = 3.6 months, SD = 3.1 months).

Of the 43 alcoholic women, only 11 were free of any other lifetime Axis I *DSM–IV* comorbidities; 9 had met criteria for only one other Axis I *DSM–IV* diagnosis (depression, panic disorder, posttraumatic stress disorder, dysthymia, or substance dependence); the rest had met criteria for two or more other Axis I *DSM–IV* diagnoses. Comorbidities most frequently seen included depression (n = 12), cocaine abuse or dependence (n = 8), cannabis abuse or dependence (n = 6), and polysubstance dependence (n = 4).

The control women were selected on the basis of age from a larger group of 47 women (age range = 20–85 years) who had been recruited from the community to participate in studies of normal aging and to serve as a healthy comparison group for other patient populations studied in our laboratory (e.g., Cahn-Weiner et al., 1999; Fama et al., 1997; Pfefferbaum, Rosenbloom, Deshmukh, & Sullivan, 2001; Sullivan, Rosenbloom, Desmond, & Pfefferbaum, 2001). Age-adjusted norms were derived for each neuropsychological measure from the maximum number of control women for whom scores were available; for 14 of the 19 measures,

Table 1
Subject Group Characteristics

Characteristic	Mean		Standard deviation		*t* test
	Control	Alcoholic	Control	Alcoholic	*p*
Age (years)	42.8	42.1	13.2	9.5	*ns*
Education (years)	15.8	14.7	1.7	3.2	*ns*
Handedness score[a]	18.7	21.7	5.0	14.7	*ns*
NART IQ	114.8	110.0	5.4	8.5	< .01
BDI[b]	1.4	10.2	1.9	8.9	< .01
MMSE	28.7	28.1	1.3	1.6	*ns*
DRS	141.1	139.3	2.6	3.6	*ns*
Lifetime alcohol intake (kg)	22.5	521.6	43.9	364.3	< .01

Note. All subjects were women aged 28 to 65 years. There were 27 women in the control group and 43 women in the alcoholic group. NART = National Adult Reading Test; BDI = Beck Depression Inventory; MMSE = Mini-Mental State Examination; DRS = Dementia Rating Scale.
[a] Right-handed = 14 to 32. [b] Range = 0–29; depressive symptoms ≥ 14.

$n \geq 30$ (sample sizes range = 20–47). Group comparisons were based on a subset of 27 control women matched in mean age to the group of alcoholic women (see Table 1). Control subjects were initially screened with the SCID, a medical history, and a physical examination. Control subjects were excluded if they (a) had a history of medical or neurological illness or trauma that could affect the CNS, (b) had ever met either *Diagnostic and Statistical Manual of Mental Disorders—Third Edition, Revised* (American Psychiatric Association, 1987) or *DSM–IV* criteria for a major psychiatric disorder including substance dependence or abuse in the past year, or (c) had reported a period of time lasting more than 1 month when they had drunk more than two standard drinks each day.

Each alcoholic and control subject underwent a structured interview assessing lifetime alcohol consumption (Skinner, 1982; Skinner & Sheu, 1982). The interviewer started from the age at which the subject first drank regularly (at least one drink per month) and elicited quantity (how many drinks per day) and frequency (how many drinks on average per month). Drinks of each type of alcoholic beverage (wine, beer, spirit) were standardized to units containing approximately 13.6 g of absolute alcohol.

As a group, the alcoholic women had lower National Adult Reading Test (NART) IQ scores (an estimate of premorbid intelligence; Nelson, 1982) and higher lifetime alcohol use than the control subjects (see Table 1). On average, the alcoholic women had been abstinent from alcohol for 3.6 months and had consumed 23 times more alcohol during their lifetime than the controls had. The groups did not differ significantly in education or in Mini-Mental State Examination (Folstein, Folstein, & McHugh, 1975) scores. All subjects gave written informed consent after the nature of the study, and procedures were fully explained to them. Subjects were compensated for their time.

Neuropsychological Tests

Subjects were administered an extensive battery of neuropsychological tests designed to cover a broad range of cognitive and motor functions. The protocol included standard neuropsychological tests as well as experimental tests, which were developed to assess specific component processes of cognitive and motor abilities. On the basis of published research (Sullivan, Rosenbloom, & Pfefferbaum, 2000; Sullivan et al., 1994), we classified selective measures a priori to represent six cognitive or motor domains (executive functions, short-term memory and fluency, declarative memory, visuospatial abilities, upper-limb motor ability, and balance) and formed composite scores for each domain. Not all subjects completed all tests. The composites were based on those developed for Sullivan et al.'s (2000) study of men, but in a few instances, the test forms used in the women's study were from more recent test revisions. Specifically, the men received the original form of the Wechsler Memory Scale (Wechsler, 1945), whereas the women received the revised form; the men received the Jones-Gotman and Milner version of the nonverbal fluency test (Jones-Gotman & Milner, 1977), whereas the women received the Ruff version (Ruff, 1988); and only the women received the Wechsler Adult Intelligence Scale—Revised (WAIS–R, Wechsler, 1981) Block Design test.

Executive functions. Executive function scores included the number of categories achieved and the percentage of perseverative errors on the Wisconsin Card Sorting Test (WCST, Heaton, 1981; Milner, 1963; Sullivan et al., 1993), the number correct on a 14-item digit ordering task (Cooper, Sagar, Jordan, Harvey, & Sullivan, 1991), the time it took to complete a sequencing task (Trails B), and the score obtained on the Picture Arrangement subtest of the WAIS–R. These tasks have been shown to be sensitive markers of frontal lobe lesions.

The WCST required subjects to sort a deck of 128 cards on the basis of one of three principles: color, form, or number of symbols displayed on each card. After correctly sorting 10 consecutive cards, the examiner changed the sorting principle without warning the subject. Scores used in these analyses were the number of categories completed and the percentage of perseverative errors (Heaton, 1981). For the digit ordering test, subjects listened to an array of numbers and then repeated them back to the examiner in ascending order (Cooper et al., 1991). Trails B required the subject to connect numbers and letters in alternating and ascending order (Lezak, 1995). WAIS–R Picture Arrangement subtest assessed the subject's ability to sequence the events of an action or a story and is considered an executive function measure (cf. McFie & Thompson, 1972; Sullivan, Sagar, Gabrieli, Corkin, & Growdon, 1989).

Short-term memory and fluency. The tests chosen to represent this domain have been shown to rely on the integrity of the orbitofrontal cortex (Milner, 1964; Stuss & Benson, 1983). The Brown–Peterson distractor tests (Brown, 1958; Peterson & Peterson, 1959) used consonant trigrams in the verbal form and block triplets in the nonverbal form as the memoranda letter (Sullivan, Corkin, & Growdon, 1986). Retention intervals were 0, 3, 9, and 15 and were filled with a verbal (serial 3 s) distractor in the verbal task and a nonverbal (finger phalanx matching) distractor in the nonverbal task. The verbal fluency test required subjects to write as many words as possible starting first with the letter *s* (for 5 min) and then four-letter words starting with the letter *c* (for 4 min, Milner, 1964; Thurstone, 1944). The nonverbal fluency test (Ruff Figural Fluency Task) required subjects to draw unique designs in prearranged arrays of five dots (Ruff, 1988). The score was the total number of unique words or designs produced in each of these verbal and nonverbal fluency tasks.

Declarative memory. Declarative memory was assessed with the General Memory Index of the Wechsler Memory Scale—Revised (Wechsler, 1987), the Memory subscale score of the Dementia Rating Scale (DRS; Mattis, 1988), the Warrington's Recognition Test for words and faces (Warrington, 1984), and the Rey–Osterrieth Complex Figure Test (Osterrieth & Rey, 1944; Rey, 1942). The Rey–Osterrieth recall score was expressed as a ratio of the drawing copy score to account for individual differences in drawing ability and to differentiate the memory component from the visuospatial component of this task. The tests chosen to represent the declarative memory domain assess medial temporal lobe and/or diencephalic structural integrity.

Visuospatial abilities. The following tests were chosen because of their association to the integrity of parietal and occipital brain regions underlying the visuospatial abilities assessed by these tests. In the Hidden Figures Test (Corkin, Rosen, Sullivan, & Clegg, 1989; Thurstone, 1944), the subject traced simple figures that were embedded in more complex ones and were scored for the number correct. In the Rey–Osterrieth Complex Figure Test, the subject copied a complex design; scoring was based on Taylor's (Taylor, 1969) 36-point system. The WAIS–R Block Design subtest required the subject to put together sets of blocks to match pictures of designs presented to them; the designs were of increasing difficulty.

Upper-limb motor ability. Upper-limb motor ability consisted of grip strength and fine finger movement tasks. Grip strength was assessed with a hand dynamometer. Measurements from the left and right hand were averaged for an overall score. Fine finger movement was assessed with a device that required the subject to turn a knurled rod, using coordinated movement of the thumb and forefinger (Corkin, Growdon, Sullivan, Nissen, & Huff, 1986).

These tests are related to basal ganglia and precentral gyrus integrity (Cooper et al., 1991; Leonard, Jones, & Milner, 1988).

Gait and balance. Gait and balance were assessed with the Walk-a-Line Ataxia Battery (Fregly, Graybiel, & Smith, 1972), which consisted of three parts, each performed first with eyes open and then with eyes closed. First, the subject stood with feet placed heel-to-toe with arms folded across the chest for 60-s trials. Next, the subject stood on one foot for 30-s trials. Finally, the subject walked heel-to-toe for 10 steps. Each condition was performed twice unless the subject achieved a perfect score on the initial trial. These tasks assess the integrity of the anterior superior vermis of the cerebellum in patients with alcoholism (Sullivan, Deshmukh, et al., 2000; Victor, Adams, & Collins, 1989).

Statistical Analysis

Age-corrected standardized *Z* scores were calculated for each test on the basis of age regression analysis of the test scores across all the control women subjects for whom data were available. The *Z* score for each subject represented the extent to which that subject deviated from the norms for her age. By definition, the mean *Z* score of each test in the control group was 0 ± 1 *SD*. For the alcoholic women, the mean age-corrected *Z* scores represented the extent of disease-related impairment on that test, free of the effects of normal aging. The use of standardized *Z* scores allowed us to compare all measures on the same scale and to examine age–alcohol interactions having accounted for observed effects of normal aging.

To reduce the number of variables for analysis, we formed six theoretically determined composite scores, following our previously described method (Sullivan, Rosenbloom, & Pfefferbaum, 2000; Sullivan et al., 1994): executive functions, short-term memory and fluency, declarative memory, upper-limb motor ability, visuospatial abilities, and gait and balance. Each composite was derived by taking the mean of the *Z* scores for all tests available for each subject represented in that composite.

To examine group differences, we first conducted a 2 (group) $\times$ 6 (cognitive domains) analysis of variance (ANOVA), which included the subset of 35 alcoholic women and 17 control women with scores for all composites. Main effects were followed up by *t* tests ($p < .05$ significance level used) for each individual cognitive domain assessed. Subsequent analyses examined group differences on individual test measures and included the maximum number of subjects with test scores. Measures that demonstrated marked (1 *SD*) impairment in the alcoholic women were examined individually. The contribution of age, NART IQ, and lifetime alcohol consumption to age-corrected deficits were assessed with correlation analyses, multiple regression, and analysis of covariance (ANCOVA).

Results

Group Differences in Composite Cognitive and Motor Test Scores

The six composite scores for each group are presented in Figure 1. A 2 (group) $\times$ 6 (composite score) ANOVA indicated a significant group effect, $F(1, 50) = 5.54$, $p = .02$ but not a Group $\times$ Composite interaction, $F(5, 250) = 1.10$, *ns*. Follow-up *t* tests revealed significant performance deficits in the alcoholic group on five of the six composites ($p \leq .04$); the alcoholic and control women did not significantly differ on the upper-limb composite.

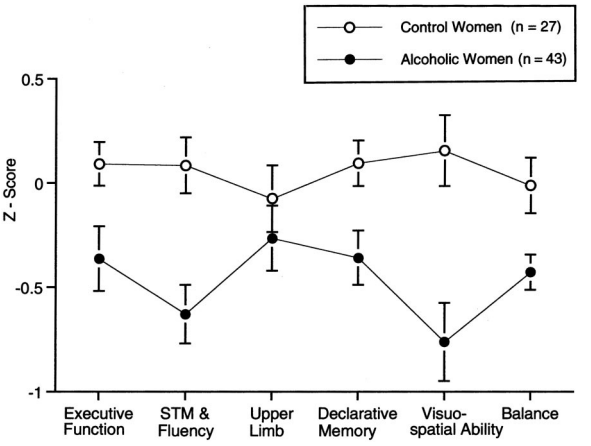

Figure 1. Profile of mean ($\pm$ *SEM*) composite scores for alcoholic women and control women. STM = short-term memory.

ANCOVAs were conducted to examine whether the group differences on the main variables persisted after we controlled for premorbid intelligence with the NART IQ, which was significantly lower in the alcoholic group than in the control group. Group differences on the short-term memory and fluency, $F(1, 60) = 5.78$, $p < .02$; visuospatial, $F(1, 63) = 4.97$, $p < .03$; and balance, $F(1, 54) = 4.88$, $p < .03$, domains remained significant, and there was a statistical trend observed on the memory domain, $F(1, 67) = 3.04$, $p < .09$. However, the group difference on the executive domain did not endure when controlling for NART IQ, $F(1, 67) = 0.69$, $p = .41$.

Group Differences in Performance on Individual Cognitive and Motor Tests

The profile of scores on individual cognitive tests revealed salient ($\geq .75$ *SD*) deficits in verbal and nonverbal short-term (working) memory, DRS Memory subtest, and Block Design (see Figure 2). These scores indicated that the performance deficit observed in the alcoholic group for the short-term memory and fluency composite was solely attributable to short-term memory but not to fluency impairments. In particular, group differences on the verbal and nonverbal task total scores were tested with a 2 (group) $\times$ 2 (task) repeated measures ANOVA, which yielded only a significant group effect, $F(1, 59) = 16.98$, $p < .01$, but neither a task effect, $F(1, 59) = 1.13$, *ns*, nor an interaction, $F(1, 59) = 1.64$. Follow-up analysis revealed that the alcoholic group had significantly lower total scores on both the verbal, $t(60) = 3.16$, $p < .01$, and the nonverbal, $t(59) = 3.36$, $p < .01$, test conditions. For reference, raw scores of the individual tests are presented in Table 2.

We examined the short-term memory impairment more closely by testing rates of forgetting over retention intervals. Raw scores were used in the analysis, permitting examination of forgetting curves of the control group as well as of the alcoholic group. For the verbal short-term memory task, a repeated measures ANOVA across interval (0, 3, 9, and

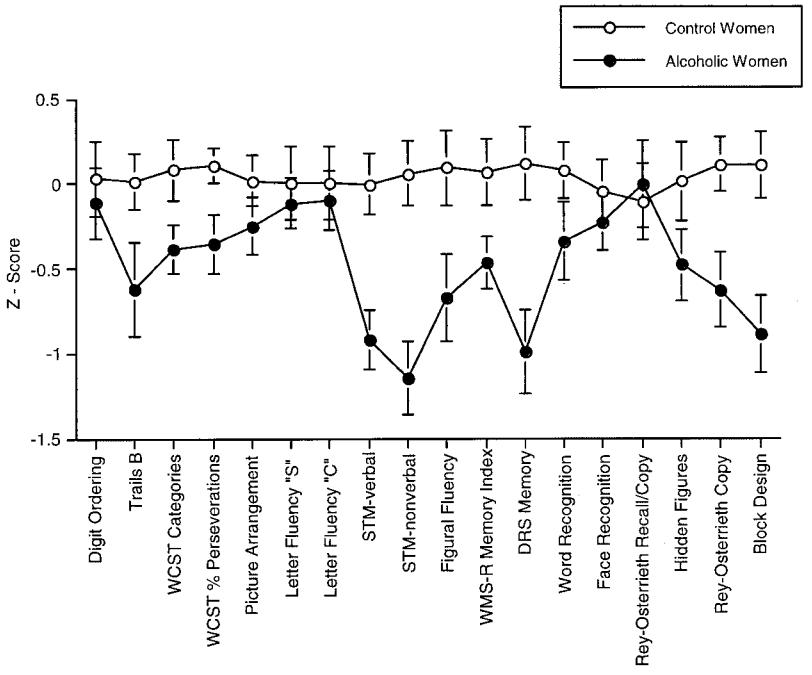

Figure 2. Profile of mean (± *SEM*) individual test measures for alcoholic women and control women. WCST = Wisconsin Card Sorting Test; STM = short-term memory; WMS–R = Wechsler Memory Scale—Revised; DRS = Dementia Rating Scale.

15 s) indicated significant group, $F(1, 60) = 10.00$, $p < .01$, and interval, $F(3, 60) = 60.52$, $p < .01$, effects and a significant Group × Interval interaction, $F(3, 180) = 2.87$, $p < .04$ (see Figure 3). This same pattern was observed on the nonverbal short-term memory task. Repeated measures ANOVA revealed significant group, $F(1, 59) = 11.38$, $p < .01$, and time interval, $F(3, 59) = 87.64$, $p = .01$, effects and a significant Group × Interval interaction, $F(3, 177) = 3.00$, $p < .04$ (see Figure 3). Perfect scores at the 0-s retention interval indicated that all subjects were able to perform both conditions. When the ANOVAs were recalculated excluding the 0-s retention interval because of ceiling level performance, the effects of group verbal, $F(1, 60) = 9.72$, $p < .01$, and group nonverbal, $F(1, 59) = 11.80$, $p < .01$, and the effects of interval verbal, $F(1, 60) = 31.89$, $p < .01$, and interval nonverbal, $F(1, 59) = 30.63$, $p < .01$, endured but the interactions did not, verbal, $F(1, 60) = 1.13$, *ns*; nonverbal, $F(1, 59) = 0.43$, *ns*.

Correlates of Neuropsychological Test Scores

None of the six age-corrected neuropsychological composite scores correlated significantly or even approached significance with age, time sober, or total lifetime alcohol consumption. Although the alcoholic women reported significantly more depressive symptoms than the control women did, $t(56) = 3.74$, $p < .01$, Beck Depression Inventory (Beck & Steer, 1993) scores were not significantly predictive of scores on any of the six cognitive or motor domains (executive functions, $r = .07$; short-term memory and fluency, $r = -.003$; declarative memory, $r = .10$; upper-limb motor ability, $r = -.01$; visuospatial, $r = .24$; and gait and balance, $r = -.07$).

In contrast to the composite scores, several individual age-corrected test measures showing the greatest deficits were modestly correlated (one-tailed) with lifetime alcohol consumption: block design, $r = -.33$, $p < .03$; verbal short-term memory, $r = -.29$, $p < .04$; nonverbal short-term memory, $r = -.36$, $p < .02$. In addition, *Z* scores of the number of categories sorted on the WCST correlated with the duration of drinking in the alcoholic women ($n = 37$, $r = -.40$, $p < .02$). None of these *Z* scores (which were corrected for age-related variation observed in the control women) correlated with age in the alcoholic women. In this sample of alcoholic women, the total amount of alcohol consumed in a lifetime ($r = .12$), the duration of current sobriety ($r = -.01$), and the duration of disease ($r = .27$) did not correlate significantly with age. These correlations indicate that the alcohol consumption–performance correlations are probably not due to the fact that older women drank more because they had more years to drink.

Discussion

This group of alcoholic women, who had been abstinent on average for 3.6 months, exhibited a similar pattern of sparing and impairment in cognitive tests as previously reported in alcoholic men, who had been abstinent on average for only 1 month (Sullivan, Rosenbloom, & Pfefferbaum, 2000). The functional areas most severely implicated

Table 2
Raw Scores of Individual Tests (Mean, Standard Deviation, and Number of Subjects)

Test	Mean		Standard deviation		Sample size	
	Alcoholic	Control	Alcoholic	Control	Alcoholic	Control
Executive functions						
Digit ordering	84.24	85.16	7.23	5.62	38	19
Trails B	78.56	57.23	49.42	26.44	43	22
WCST categories	6.58	7.98	3.07	3.01	38	27
WCST % perseverations	14.94	10.98	10.78	5.98	37	27
WAIS–R picture arrangement	12.11	13.15	4.55	3.54	37	26
STM and fluency						
Letter fluency *S*	42.95	46.05	13.21	16.44	37	20
Letter fluency *C*	15.08	15.95	7.60	7.11	37	20
STM verbal	74.60	85.30	13.47	12.14	38	24
STM nonverbal	71.85	81.94	12.62	9.33	37	24
Figural fluency	81.34	91.48	25.44	18.99	35	25
Declarative memory						
WMS–R memory index	106.39	114.44	14.68	15.12	39	27
DRS memory	23.51	24.37	1.19	0.76	37	19
Word recognition	47.40	48.50	3.85	2.34	35	24
Face recognition	42.35	43.04	4.68	4.11	34	24
Rey–Osterrieth recall copy	0.48	0.48	0.19	0.15	38	21
Visuospatial ability						
Hidden figures	28.58	34.90	15.18	13.74	38	19
Rey–Osterrieth copy	26.26	29.74	6.25	3.12	38	21
WAIS–R Block Design	30.38	37.32	10.75	7.23	37	25
Upper limb						
Grip strength in left hand	21.50	21.05	5.93	7.55	34	25
Grip strength in right hand	23.56	23.19	5.79	6.72	36	24
Fine finger movements in left hand	80.80	82.09	14.08	13.80	38	23
Fine finger movements in right hand	93.15	97.09	18.86	13.15	38	23
Gait and balance						
Romberg eyes open	109.92	111.50	23.64	21.38	38	18
Romberg eyes closed	45.97	66.61	39.54	46.67	38	18
Walk a line eyes open	16.73	20.00	5.27	0.00	38	18
Walk a line eyes closed	4.11	6.22	3.59	5.65	38	18
Stand on left leg eyes open	55.71	57.61	16.89	10.14	38	18
Stand on left leg eyes closed	20.46	29.50	16.32	21.99	37	18
Stand on right leg eyes open	53.80	57.50	20.16	10.61	39	18
Stand on right leg eyes closed	16.74	31.61	13.38	22.52	38	18

Note. WCST = Wisconsin Card Sorting Test; WAIS–R = Wechsler Adult Intelligence Scale—Revised; STM = short-term memory; WMS–R = Wechsler Memory Scale—Revised; DRS = Dementia Rating Scale; Rey–Osterrieth = Rey–Osterrieth Complex Figure Test.

in the women, showing at least a −0.75 *SD* difference from healthy controls, involved short-term working memory and visuospatial abilities. On the short-term memory and fluency composite, almost 80% of the sample of alcoholic women (compared with 50% of controls) had negative *Z* scores, indicating performance below the norm for their age, with 24% performing more than 1 *SD* below the mean. When only the short-term memory tests were considered, 45% of alcoholic women had scores falling 1 *SD* below the mean. On the visuospatial abilities composite, 38% performed more than 1 *SD* below the mean. Thus, despite some overlap in score distributions, the alcoholic group displayed a downward shift in the distribution of scores relative to the control group. The presence of deficits at the −1 *SD* level, even after the alcoholic women's average abstinence of about 3 months, demonstrates the resistance of these functions to early recovery (cf. Nixon & Glenn, 1995).

The salient deficits in composite scores observed in alcoholic women are in line with deficits we had reported in alcoholic men, who on average exhibited a 0.67 *SD* deficit on the visuospatial composite (Sullivan, Rosenbloom, & Pfefferbaum, 2000) compared with a mean 0.76 *SD* deficit in women. Similarly, the alcoholic men showed a 0.54 *SD* deficit, relative to their male control group, on the short-term memory and fluency composite compared with a mean 0.63 *SD* deficit in women. However, when the memory and fluency components of this composite were considered separately, a different pattern emerged. Although neither alcoholic group was impaired on the fluency tests, both groups were impaired on the short-term memory tests, with the deficit in the women (1.10 *SD*) being about 0.50 *SD* larger than that in the men (0.65 *SD*). The performance disadvantage in the women was greater on the nonverbal task (1.20 *SD* in women vs. 0.43 *SD* in men) than on the verbal task (0.92 *SD* in women vs. 0.87 *SD* in men). Interpretation of these standard deviation comparisons must be cautioned by the fact that the standard deviations are not directly comparable, given that they were derived from different sets of norms based on test composites consisting of incompletely overlapping sets of measures.

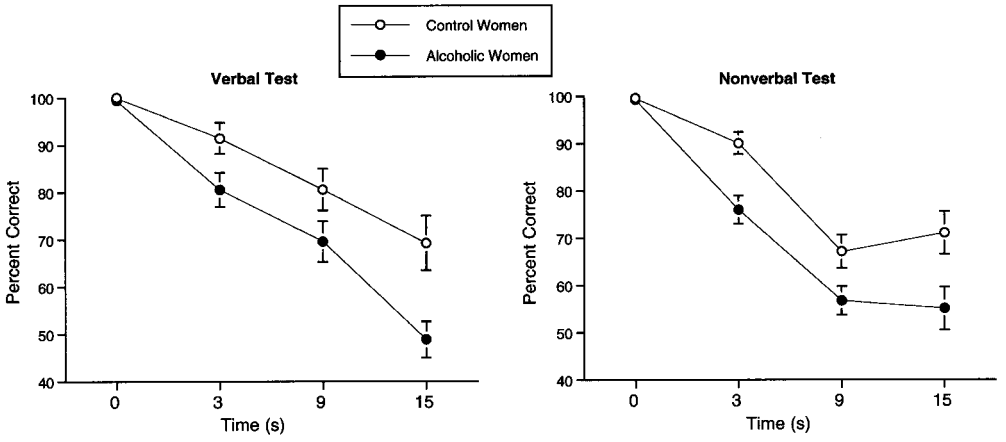

Figure 3. Forgetting curves ($M \pm SEM$) for the verbal and the nonverbal working memory tests in the alcoholic and control groups.

Compared with alcoholic men (described in Sullivan, Rosenbloom, & Pfefferbaum, 2000) who had a 1.20 *SD* deficit relative to their male control group, alcoholic women were more mildly impaired in gait and balance function, with an average *Z* score of 0.41 *SD* deficit. An additional sex difference was the absence of an age–alcohol interaction in the balance scores of the alcoholic women compared with the alcoholic men, who did display such a relationship in ataxia. It remains to be established whether women have a special protective factor, which is at least partially resistant to presumably cerebellar function, or whether women drink at a safer level than men, at least with respect to functional cerebellar integrity.

The extent of impairment in the general cognitive domains, once age corrected, did not show correlations with age. Lack of evidence for accelerating cognitive deficits over the course of the illness in alcoholic women is consistent with the Sullivan, Rosenbloom, and Pfefferbaum (2000) report in men. This finding is in stark contrast to neuroimaging studies that have consistently shown significant age–alcohol interactions, with older alcoholic subjects having greater brain volume deficits than expected for their age (Pfefferbaum et al., 1992, 1996, 1997; Sullivan, Deshmukh, et al., 2000; Sullivan et al., 1995). One speculation is that despite changes in brain structure (e.g., Pfefferbaum et al., 1995; Pfefferbaum, Sullivan, Rosenbloom, Mathalon, & Lim, 1998; Shear et al., 1995) and function (e.g., Brandt, Butters, Ryan, & Bayog, 1983; Martin et al., 1995; Parsons, 1986; Sullivan, Rosenbloom, Lim, & Pfefferbaum, 2000) for the better with alcohol abstinence and for the worse with continued drinking, age may pose a greater limitation on brain volume changes than on functional changes, whether measured with neuropsychological or functional imaging probes.

Despite the greater endorsement of depressive symptoms in the alcoholic women compared with the control women, depression indices were not predictive of performance either for better or for worse. In contrast to depressive symptoms, alcoholism variables of total amount of lifetime alcohol consumption were modest predictors of severity of cognitive impairment. The measures showing these relationships were the Block Design subtest and verbal and nonverbal short-term memory tests, which were the functions severely affected in the alcoholic women. These relationships support the possibility of cognition's graded vulnerability to alcohol dependence, that is, a dose effect of alcohol abuse. Such relationships are seldom observed in alcoholic men and may arise from the fact that, in contrast to women (Wilsnack & Wilsnack, 1995), men's lifetime alcohol consumption levels exceed the threshold above which dose effects can be detected. Indeed, in our own samples, the alcoholic men drank 2.5 times (1,356 kg) more alcohol in their lifetimes than the alcoholic women drank (522 kg). In younger drinkers, who have not yet accumulated the extensive drinking history of their older counterparts, modest relationships have been observed between cognitive performance and lifetime alcohol consumption or length of sobriety (Eckardt et al., 1995). Similar relationships were present in a controlled quantitative longitudinal study of brain structure in older alcoholic men when the period of examination was restricted to a 5-year interval following a month of enforced abstinence. In that group, smaller cortical gray matter volumes correlated with larger amounts of alcohol consumed during a 5-year interval and with a greater number of days meeting alcohol dependence criteria (Pfefferbaum et al., 1998). Other factors that can have serious impacts on cognitive and motor abilities operate through nutritional (cf. Langlais, Zhang, & Savage, 1996; Victor et al., 1989) and hepatic mechanisms (cf. Butterworth, 1993; Tarter & Edwards, 1986). These factors were not considered in this study and require prospective examination in future studies.

In conclusion, components of cognitive and motor functions most affected by alcohol dependence in women involved visuospatial working memory processes, which have been documented as typical areas of deficit in alcoholic men. The verbal and nonverbal working memory tasks showed similar overall impairment severity and rate of

forgetting across retention intervals. Areas of relative sparing included executive functions (provided the level of education was taken into account), declarative memory (also spared in alcoholic men), upper-limb strength, and movement speed. Although we cannot discount the possibility of deficits preexisting alcoholism and possibly connected with family history of alcohol abuse (e.g., Begleiter & Porjesz, 1990; Hill & Steinhauer, 1993; Tarter, Jacob, & Bremer, 1989), the relationships present between certain cognitive deficits and alcohol consumption variables indicate that at least a portion of these relationships is attributable to abusive alcohol drinking itself. The working memory and visuospatial deficits that were detectable in these alcoholic women suggest a disruption of the integrity of the corticocortical circuitry involving prefrontal and superior parietal regions (Selemon & Goldman-Rakic, 1988). Although abnormalities in these brain regions of alcoholic women have not yet been identified with imaging techniques aimed at quantifying brain macrostructure (Pfefferbaum, Rosenbloom, et al., 2001), interruption of the pathways of the prefrontal-parietal brain system may be detectable with imaging techniques targeting brain microstructure (Pfefferbaum et al., 2000), chemistry (cf. Estilaei et al., 2001; Mann, Gunther, Stetter, & Ackermann, 1999; Seitz et al., 1999), or function (e.g., Pfefferbaum, Desmond, et al., 2001; Tapert et al., 2001). By contrast, impairment in gait and balance implicates cerebellar dysfunction, a structure–function relationship that has been shown in alcoholic men (Sullivan, Deshmukh, et al., 2000).

The results of this study have implications for therapy. Namely, in selecting rehabilitation strategies for alcoholic women, clinicians need to recognize that even after 3 months of abstinence, women, like their male counterparts, have persistent deficits in cognition and postural stability that may influence treatment efficacy and recovery.

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