Cognitive Performance in Long-Term Abstinent Elderly Alcoholics

George Fein and Shannon McGillivray

Background: To date, there is a wealth of literature describing the deleterious effects of active alcoholism on cognitive function. There is also a growing body of literature on the extent of cognitive recovery that can occur with abstinence. However, there is still a dearth of published findings on cognitive functioning in very long-term abstinence alcoholics, especially in the elderly population.

Methods: The current study examines 91 elderly abstinent alcoholics (EAA) (49 men and 42 women) with an average age of 67.3 years, abstinent for an average of 14.8 years (range 0.5 to 45 years), and age and gender comparable light/nondrinking controls. The EAA group was divided into 3 subgroups: individuals that attained abstinence before age 50 years, between the ages 50 and 60 years, and after age 60 years. Attention, verbal fluency, abstraction/cognitive flexibility, psychomotor, immediate memory, delayed memory, reaction time, spatial processing, and auditory working memory were assessed. The AMNART and cranium size were used as estimates of brain reserve capacity, and the association of all variables with alcohol use measures was examined.

Results: Overall, the EAA groups performed comparably to controls on the assessments of cognitive function. Only the abstinent in group before 50 years of age performed worse than controls, and this was only in the domain of auditory working memory. EAAs had larger craniums than their controls. This effect was strongest for those who drank the longest and had the shortest abstinence. Such individuals also performed better cognitively.

Conclusions: Our data showed that elderly alcoholics that drank late into life, but with at least 6 months abstinence can exhibit normal cognitive functioning. Selective survivorship and selection bias probably play a part in these findings. Cognitively healthier alcoholics, with more brain reserve capacity, may be more likely to live into their 60s, 70s, or 80s of age with relatively intact cognition, and to volunteer for studies such as this. Our results do not imply that all elderly alcoholics with long-term abstinence will attain normal cognition.

Key Words: Alcoholism, Long-Term Abstinence, Cognition, Neuropsychology, Aging.

THE DELETERIOUS EFFECTS of chronic alcoholism on cognitive functioning have been well documented for over a century beginning as early as the 1880s with Wernicke and Korsakoff (Korsakoff, 1887; Wernicke, 1881). In the 1980s, Finlayson et al. (1988) reported that among patients receiving treatment for alcohol-related disorders, up to 23% had dementia of some type. More recent studies have continued to investigate the harmful effects of chronic alcohol abuse on brain structure and function (Brun and Andersson, 2001; Butterworth, 1995; Diamond and Messing, 1994; Emsley et al., 1996; Harper and Matsumoto, 2005; Heap et al., 2002; Kim et al., 2002; McMurtray et al., 2006; Mochizuki et al., 2005; Ratti et al., 1999; Saxton et al., 2000; Schmidt et al., 2005; Smith and Atkinson, 1995; Victor, 1994).

In more recent years, there has also been a shifting of focus towards examining the extent of cognitive recovery that can occur with sustained abstinence. There are a number of studies reporting the persistence of cognitive deficits in alcoholics with relatively short-term abstinence (Block et al., 2002; Di Sclafani et al., 1995; Fama et al., 2004; Fein et al., 1990; Moriyama et al., 2006; Munro et al., 2000; Sullivan et al., 2000b, 2002; Tedstone and Coyle, 2004; Zinn et al., 2004), especially in executive function, memory, and spatial processing. However, there is encouraging evidence from studies examining alcoholics with slightly longer abstinence durations that suggests that recovery or improvement in these domains can occur (Bates et al., 2005; Munro et al., 2000; Oscar-Berman et al., 2004; Rosenbloom et al., 2004; Sullivan et al., 2000a).

Despite research efforts in studying cognitive recovery in abstinent alcoholics, there is a scarcity of data on long-term abstinence, with most studies focusing on treatment samples and 3- to 12-month follow-up after treatment. The lack of research on cognitive functioning in long-term abstinence is even more pronounced in the elderly population. To our knowledge, there has not been a single study published on the cognitive functioning of elderly alcoholics with very long-term

From the Neurobehavioral Research, Inc., Corte Madera, California, and Honolulu, Hawaii.

Received for publication December 18, 2006; accepted July 4, 2007.

Reprint requests: George Fein, PhD, Neurobehavioral Research, Inc., 201 Tamal Vista Boulevard, Suite 200, Corte Madera, CA 94925; Fax: 415-924-2903; E-mail: george@nbresearch.com

DOI: 10.1111/j.1530-0277.2007.00481.x

abstinence. Studies in the elderly are particularly important because age has been consistently implicated as a major factor modulating the effects of alcohol abuse on brain structure and function (Fama et al., 2004; Goldman et al., 1983; Oscar-Berman et al., 2004). In fact, age is one of the strongest variables modulating the effects of chronic alcohol abuse on brain structure and function.

Furthermore, cerebral reserve capacity (as indexed by premorbid brain size, cranium size, and premorbid IQ) is an important variable to consider when examining cognitive morbidity secondary to any neurodegenerative disease. Cerebral reserve capacity refers to the brain's ability to maintain normal function in the face of neurodegenerative processes (such as Alzheimer's disease, aging, and chronic substance abuse), and is commonly measured using estimates of premorbid brain size (Di Sclafani et al., 1998; Graves et al., 1996; Mori et al., 1997) or premorbid IQ (Satz, 1993; Schmand et al., 1997). In a recent article, we examined in detail, the implications of cerebral reserve capacity for the study of alcohol and drug abuse (Fein and Di Sclafani, 2004).

We recently published a manuscript examining cognitive performance in long-term abstinent (mean abstinence duration 6.7 years), middle-aged alcoholics (mean age 46.8 years) (Fein et al., 2006). The abstinent alcoholics performed comparably to controls in all areas of cognitive functioning, except for a minor deficit in spatial processing. This current manuscript investigates whether or not elderly long-term abstinent alcoholics demonstrate impaired cognitive functioning when compared with age and gender comparable controls. It also examines whether the aging brain is more vulnerable to the effects of heavy drinking on cognitive function by comparing abstinent elderly alcoholics that stopped drinking before 50 years of age, those who stopped drinking between 50 and 60 years of age, and those who stopped drinking after 60 years of age. Furthermore, the manuscript examines the possible effect cerebral reserve capacity has on cognitive functioning in these samples.

MATERIALS AND METHODS

Participants

A total of 143 participants were recruited from the San Francisco Bay Area community by postings at AA meetings, mailings, newspaper advertisements, a local Internet site, and participant referrals. The study consisted of 2 groups, elderly abstinent alcoholics (EAA) and age and gender comparable light/nondrinking normal controls (NC). The EAA group (n = 91) contained 49 men and 42 women, ranging from 58 to 85 years of age (mean = 67.3 years), abstinent from 6 months to 45 years (mean = 14.8 years). The EAA group was divided into 3 sub-groups: (1) individuals that attained sobriety from alcohol before the age of 50 years (EAA1); (2) individuals that attained sobriety between the ages of 50 and 60 years (EAA2); and (3) individuals that attained sobriety after the age of 60 years (EAA3). The inclusion criteria for the EAA groups were as follows: (1) met lifetime DSM-IV (American Psychiatric Association, 2000) criteria for alcohol dependence, (2) a lifetime drinking average of at least 100 standard drinks per month for men, and 80 standard drinks per month for women, and (3) abstinence for at least 6 months. A standard drink was defined as 12 oz beer, 5 oz wine, or 1.5 oz liquor. The control group consisted of 22 men and 30 women, ranging from 60 to 85 years of age (mean = 68.8 years). The inclusion criterion for the NC group was a lifetime drinking average of less than 30 standard drinks per month, with no periods of drinking more than 60 drinks per month.

Exclusion criteria for both groups were as follows: (1) lifetime or current diagnosis of schizophrenia or schizophreniform disorder (assessed by the c-DIS—computerized Diagnostic Interview Schedule) (Robins et al., 1998), (2) history of drug abuse or dependence (other than nicotine or caffeine), (3) significant history of head trauma or cranial surgery, (4) history of significant neurological disease, (5) history of diabetes or stroke, (6) laboratory evidence of hepatic disease, or (7) clinical evidence of Wernicke–Korsakoff syndrome.

Procedures

All participants were fully informed of the study's procedures and aims, and signed a consent form prior to their participation. Participants completed 4 sessions that lasted between an hour and a half and 3 hours, and included clinical, neuropsychological, electrophysiological, and neuroimaging assessments. Normal controls were asked to abstain from consuming alcohol for at least 24 hours prior to any lab visit. A Breathalyzer (Intoximeters, Inc., St Louis, MO) test was administered to all participants. A 0.000 alcohol concentration was required of all participants in all sessions. Subjects were compensated for time and travel expenses upon completion of each session. Participants that completed the entire study were also given a completion bonus.

General Assessment

All participants participated in the following assessments: (1) psychiatric diagnoses and symptom counts were gathered using the c-DIS (Robins et al., 1998), (2) participants were interviewed on their drug and alcohol use using the lifetime drinking history methodology (Skinner and Allen, 1982; Skinner and Sheu, 1982; Sobell and Sobell, 1990; Sobell et al., 1988), (3) medical histories were reviewed in an interview by a trained research associate, (4) blood was drawn to test liver functions, and (5) the Family Drinking Questionnaire was administered based on the methodology of Mann et al. (1985) and Stoltenberg et al. (1998). The Family Drinking Questionnaire asked participants to rate the members of their family as being alcohol abstainers, alcohol users with no problem, or problem drinkers. Family History Density (FHD) was defined as the proportion of first degree-relatives that were problem drinkers.

Neuropsychological Assessment

The neuropsychological assessments were administered in 1 session. The battery began with the administration of the following individual tests: Rey-Osterrieth Complex Figure (copy, immediate, and 20 minute delayed) (Osterrieth, 1944), Trail Making Test A and B (Reitan and Wolfson, 1985), Symbol Digit Modalities Test (written administration only) (Smith, 1968), American version of the Nelson Adult Reading Test (AMNART) (Grober and Sliwinski, 1991), Short Category Test (booklet format) (Wetzel and Boll, 1987), Controlled Oral Word Association Test (COWAT) (Benton and Hamsher, 1983), Paced Auditory Serial Addition Test (PASAT) (Gronwall, 1977), Block Design (WAIS-R) (Wechsler, 1981), Stroop Color and Word Test (Golden, 1978), Fregly Ataxia Battery (Fregly et al., 1973), and the Simulated Gambling Task (Bechara et al., 1994).

After a 15-minute break, the participant completed the MicroCog (MC) Assessment of Cognitive Functioning (standard version) (Powell et al., 1993). The MicroCog is a computer-administered and

-scored test that assesses important neurocognitive function in adults. MicroCog was designed to be sensitive to detecting cognitive impairment across a wide range, and takes into account levels of premorbid intellectual functioning by providing age- and education-level adjusted norms.

Normative scores derived from a nationally representative sample of adults are available for each test, either from the creators or distributors of the tests. *Z*-scores for the neuropsychological domains and measures were computed based on standardized norms adjusted for age [Stroop (Golden, 1978), Short Categories (Wetzel and Boll, 1987), PASAT (Stuss et al., 1988), Block Design (Wechsler, 1997), and Rey (Denman, 1987)]; years of education [AMNART (Schwartz and Saffran, 1987)]; age and years of education [Symbol Digit Modalities (Smith, 1982), MicroCog (Powell et al., 1993)]; and age, gender, and years of education [Trails A and B (Heaton et al., 1991), COWAT (Ruff et al., 1996)]. The Stroop, Symbol Digit Modalities, and the MicroCog test norms are not specific to gender, as gender did not significantly affect scores in the normative samples (Golden, 1978; Powell et al., 1993; Smith, 1982). The AMNART was used to estimate premorbid IQ (Grober and Sliwinski, 1991). The AMNART did not have age norms because the test was designed to be resistant to the effects of normal aging and most neurodegenerative diseases. Additionally, Grober and Sliwinski, (1991) have reported that gender does not influence AMNART scores. The *Z*-scores were standardized so that all positive *Z*-score values indicated superior performance.

The final neuropsychological (NP) battery consisted of the following 9 domains, and their component tests: (1) Attention (Stroop Color, MC Numbers Forward, MC Numbers Reversed, MC Alphabet, MC Word List 1), (2) Verbal Ability (COWAT, AMNART), (3) Abstraction/Cognitive Flexibility (Short Categories, Stroop interference score, Trail Making Test B, MC Analogies, MC Object Match A), (4) Psychomotor (Trails A, Symbol Digit), (5) Immediate Memory (MC Story immediate recall, Rey immediate recall, MC Word List 2), (6) Delayed Memory (MC Story delayed recall, Rey delayed recall), (7) Reaction Time (MC Timers simple and cued), (8) Spatial Processing (MC Tic Tac, MC Clocks, Block Design), and (9) Auditory Working Memory (PASAT at delays of 2.4, 2.0, 1.6, and 1.2 seconds).

Assessment of Premorbid Brain Size

T1-weighted magnetic resonance images (MRIs) (TR/TE/-NEX = 35/5/1: 0.859×0.859 mm^2 in-plane resolution, contiguous 1.3-mm thick slices) were collected on a 1.5 GE Signa Infinity with the LX platform (GE Medical Systems, Waukesha, WI) located at the Pacific Campus of the California Pacific Medical Center in San Francisco, CA. Premorbid brain size was assessed using the FMRIB Software Library's (FSL's) SIENAX procedure (Smith et al., 2002) (http://www.fmrib.ox.ac.uk/fsl/siena/index.html), which produces a measure of the size of an individual's cranium relative to that of the MNI152 template. We recently showed that the FSL measure is comparable to the intracranial vault measure derived from the outer boundary of sulcal CSF from T2-weighted MRIs (Fein et al., 2004). One male from the EAA1 group did not participate in the MRI session for medical reasons, and thus he was not included in analyses of associations with cranium size.

Statistical Analysis

The data were analyzed using the Statistical Package for the Social Sciences (SPSS Inc., 2004). First, a Multivariate Analysis of Variance examining the domain *Z*-scores was carried out using the General Linear Models procedure. To control for multiple comparisons, individual domain *Z*-scores were examined only if the multivariate tests were significant. Within the EAA groups, associations of demographic and alcohol use measures with the cognitive measures were examined using Spearman correlations. For the alcohol dose and cranium size measures, gender means were subtracted for all subjects to remove the known differences between males and females (males drink more and have larger craniums), and to thus increase our sensitivity to detect associations with cognitive measures. We also examined this data using linear regression analyses for each cognitive domain to determine the best predictors of performance in that domain. Some of the controls were used with more than one of the EAA groups so that the comparisons were between an EAA group and age and gender comparable controls.

RESULTS

Demographic and Alcohol Use Variables

The EAA and control groups were similar on age ($F_{1,142} = 1.79$, $p < 0.18$) and AMNART estimated IQs ($F_{1,142} = 1.19$, $p < 0.27$). Compared with controls, the EAAs had fewer years of education (15.7 vs. 16.5 years; $F_{1,141} = 3.47$, $p = 0.06$), slightly larger craniums ($F_{1,141} = 2.74$, $p = 0.10$), and lower family history densities of alcoholism (0.14 vs. 0.32; $F_{1,142} = 21.79$, $p < 0.001$). All of the abstinent alcohol groups had similar levels of education ($F_{2,89} = 1.77$, $p = 0.18$) and AMNART estimated premorbid IQs ($F_{2,90} = 2.71$, $p = 0.07$). Female EAAs had smaller craniums than men ($F_{1,89} = 56.14$, $p < 0.001$), and there was a group by gender interaction ($F_{2,89} = 4.26$, $p = 0.017$), wherein males that achieved abstinence later had larger craniums than males that had achieved abstinence earlier, with the effect size being about one-fourth that of the gender effect. In addition, all of the groups had a similar proportion of individuals that had received treatment for their alcohol use ($\chi^2 = 1.09$, $p = 0.58$). The EAA3 group was significantly older than the other 2 abstinent alcoholic groups. The EAA1 group had a higher proportion of first-degree relatives that were "problem drinkers" than either the EAA2 or EAA3 groups (all *p*-values < 0.07), suggesting a greater genetic loading for alcoholism. The groups also differed on measures of their prior alcohol use. Although all 3 groups had their first drinks at 17 to 19 years of age, the EAA1 group began drinking heavily at a younger age (25.3 ± 6.6 years) than the EAA2 (29.0 ± 8.6 years) and EAA3 groups (34.5 ± 11.5 years). Figure 1 illustrates the differences between the groups in their periods of heavy drinking. Furthermore, males in the EAA3 group had lower lifetime drinking doses (standard drinks/month) than males in EAA1 and EAA2. All the 3 groups had similar durations and doses during their peak alcohol use. Table 1 summarizes the demographic and alcohol use difference among the EAA groups.

NP Performance of the 3 EAA Groups

Multivariate analyses, comparing the 3 EAA groups with each other, revealed significant group differences (Wilks $\lambda_{18,142} = 0.679$, $p < 0.05$). Examining the individual domains showed that the differences were primarily in

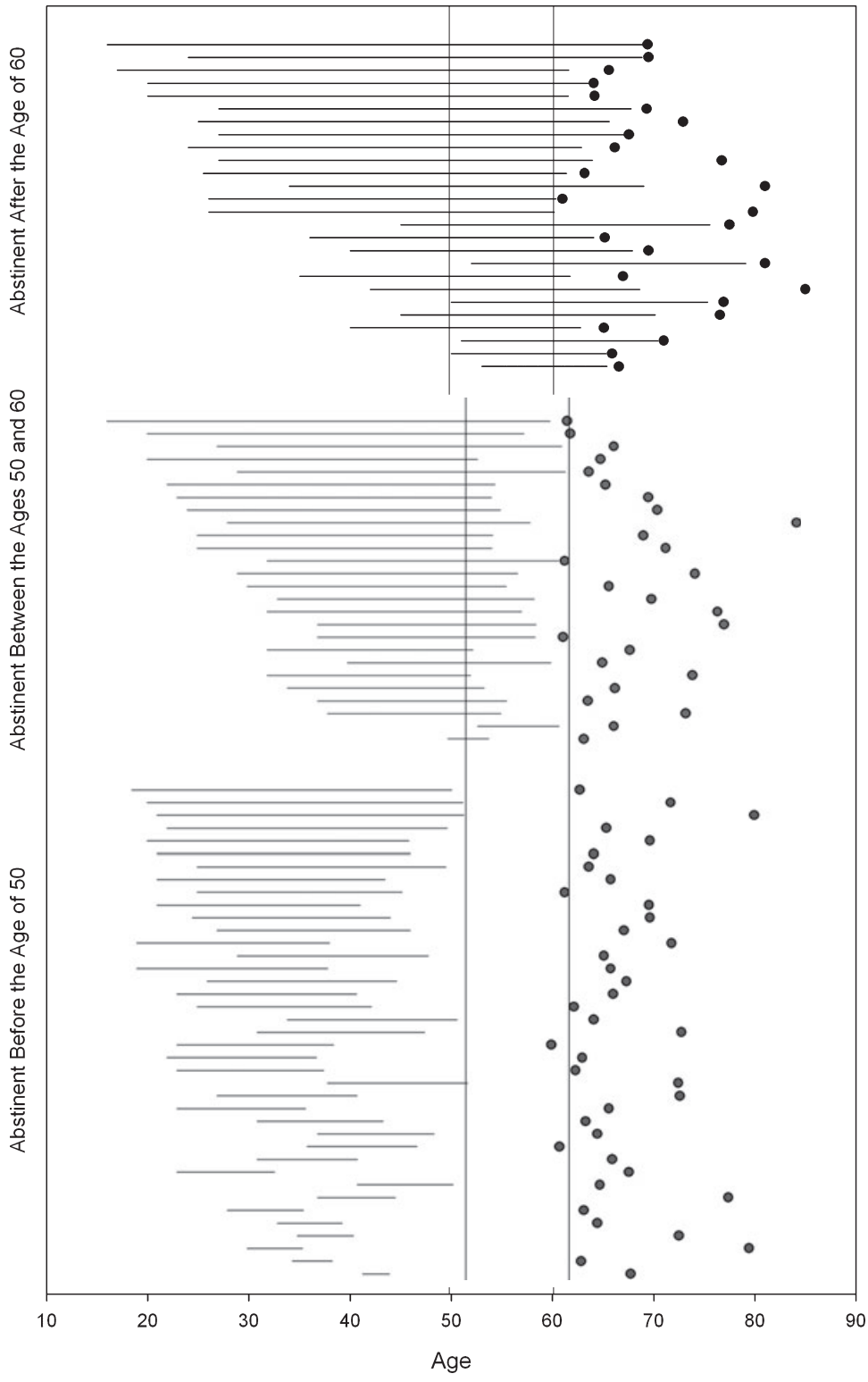

Fig. 1. In the figure, the horizontal lines begin at the onset of heavy drinking and end at the ages at which abstinence was achieved for each member of the abstinent alcoholic groups.

delayed memory ($F_{2,84} = 6.15$, $p = 0.003$) and spatial processing ($F_{2,84} = 3.80$, $p < 0.03$) with the EAA3 performing the best and the EAA1 group performing the worst on both domains. Multivariate analyses did not reveal any significant gender or group by gender effects. However, data uncorrected for multiple comparisons revealed 1 group by gender interaction difference on the assessment of verbal ability ($F_{2,84} = 3.16$, $p < 0.05$).

NP Performance of Individuals That Achieved Sobriety Before 50 Years of Age

Multivariate test analyses revealed a difference between the EAA1 group and their controls (Wilks $\lambda_{9,58} = 0.653$, $p = 0.002$). However, the only individual neuropsychological domain that differed between the groups was auditory working memory ($F_{1,69} = 7.86$, $p = 0.007$), with the abstinent alcoholic group performing poorer than controls. No gender or group by gender differences were observed (see Table 2).

NP Performance of Individuals That Achieved Sobriety Between 50 and 60 Years of Age

The multivariate test did not reveal any group differences (Wilks $\lambda_{9,37} = 0.742$, $p = 0.211$), gender differences, or group by gender interactions. Although not controlled for multiple comparisons, the EAA2 group performed better than controls in the areas of attention ($F_{1,48} = 10.867$, $p = 0.002$), men performed better than women in auditory working memory ($F_{1,48} = 5.11$, $p < 0.03$), and the EAA2 females performed better than the control females on the verbal ability domain ($F_{1,48} = 4.63$, $p < 0.04$) (see Table 3).

NP Performance of Individuals That Achieved Sobriety After 60 Years of Age

Multivariate tests did not reveal group, (Wilks $\lambda_{9,36} = 0.688$, $p = 0.099$) gender, or group by gender interactions. However, uncorrected for multiple comparisons, the EAA3 group performed better than the control sample on the assessments of immediate memory ($F_{1,47} = 6.68$, $p < 0.02$), delayed memory ($F_{1,47} = 4.55$, $p < 0.04$), and reaction time ($F_{1,47} = 6.42$, $p < 0.02$), with no areas in which the EAA3 group performed worse than controls. A group by gender interaction was observed in the assessment of spatial processing ($F_{1,47} = 4.37$, $p < 0.05$) with the EAA3 women performing better than their controls (see Table 4).

Associations Between Neuropsychological Test Scores, Demographic, and Alcohol Use Variables

Within the EAA samples, lifetime duration of alcohol use was positively associated with the average *Z*-score across domains ($r = 0.28$, $p = 0.008$) and with performance in the attention ($r = 0.24$, $p = 0.021$), abstraction/cognitive flexibility ($r = 0.26$, $p = 0.013$), delayed memory ($r = 0.26$, $p = 0.014$), reaction time ($r = 0.22$, $p = 0.034$), and spatial processing ($r = 0.39$, $p < 0.001$) domains. After adjusting for gender, alcohol lifetime dose was negatively correlated with performance in the abstraction/cognitive flexibility ($r = -0.31$, $p = 0.003$) and the spatial processing ($r = -0.21$, $p = 0.042$) domains.

After adjusting for gender, within the control group the cranium size index was positively associated with ability in the domain of abstraction/cognitive flexibility ($r = 0.27$, $p = 0.05$). Within the EAA subjects, the cranium size index was positively associated with average *Z*-score ability ($r = 0.21$, $p = 0.047$) in the domains of abstraction/cognitive flexibility ($r = 0.293$, $p = 0.005$) and spatial processing ($r = 0.24$, $p = 0.021$), with a trend toward an association for reaction time ($r = 0.19$, $p = 0.074$).

Regression analyses showed that the predictors accounted for less than 6% of the variance of all domains except for abstraction/cognitive flexibility (adjusted $r^2 = 14.2\%$) and spatial processing (adjusted $r^2 = 13.9\%$). For abstraction/cognitive flexibility, the predictors were lower average lifetime doses and increased cranium size. For spatial processing, the predictors were longer lifetime duration of alcohol use, longer duration of abstinence, and increased cranium size.

DISCUSSION

This study examined cognitive function in 3 groups of elderly abstinent alcoholics; those who attained abstinence before 50 years of age (EAA1), between 50 and 60 years of age (EAA2), or after 60 years of age (EAA3), all compared with age and gender comparable light/nondrinking controls. The controls had smaller craniums than the abstinent alcoholics, consistent with brain reserve capacity playing a role in cognitive function differences (or the lack thereof) between the groups. The only abstinent alcoholic group to perform significantly worse than their control sample was the EAA1 group, and this was only on the assessment of auditory working memory. However, given that the EAA1 group had significantly fewer years of education than their controls, and that auditory working memory was associated with years of education ($r = 0.23$, $p = 0.008$), this finding should be interpreted with caution. In addition, the EAA1 group had the highest family history density for alcoholism as well as the earliest onset of alcoholism, both implying a higher genetic loading, which may have also contributed to premorbid impairments in auditory working memory in the EAA1 group.

Somewhat surprisingly, the abstinent alcoholics from the EAA2 and EAA3 group performed better than controls on a number of domains; however, those comparisons were uncorrected for multiple comparisons. The EAA2 group performed better than controls on the assessments of attention, verbal ability, and the EAA3 group performed better than controls on the immediate memory, delayed memory, and reaction time assessments. In addition to using published norms, we also calculated age and education adjusted *Z*-scores using our controls as the normative sample. That analysis strategy did not change the findings.

Another interesting result was the alcohol use differences seen between the abstinent alcoholics groups. The individuals that attained abstinence before 50 years of age met criteria for heavy drinking at a younger age than either the EAA2 or EAA3 group (25.3 years old vs. 29.0 years old and 34.5 years old, respectively), and on average drank 53.2 more drinks per

Table 1. Characteristics of the Elderly Abstinent Alcoholic Groups

	Alcoholics that achieved abstinence						Effect size (%)		
	Before 50 years		Between 50 and 60 years		After 60 years				
Variables	Males (n = 16)	Females (n = 23)	Males (n = 16)	Females (n = 10)	Males (n = 17)	Females (n = 9)	Group	Gender	Group × gender
Age (years)	66.4 ± 5.5	65.0 ± 4.7	65.4 ± 4.8	68.6 ± 6.8	70.2 ± 4.8	71.5 ± 9.3	12.6**	0.8	2.9
Family drinking density[a]	0.39 ± 0.30	0.45 ± 0.33	0.19 ± 0.15	0.29 ± 0.26	0.22 ± 0.20	0.35 ± 0.25	8.8*	3.3	0.2
Treated versus untreated[b]	12, 4	15, 8	13, 3	6, 4	12, 5	9, 0	N/A	N/A	N/A
Years education	14.6 ± 2.8	15.9 ± 2.4	16.5 ± 3.1	16.3 ± 3.7	16.2 ± 2.2	14.0 ± 1.8	4.0	0.4	6.5
AMNART (estimated verbal IQ)	116.9 ± 6.5	118.3 ± 5.5	120.2 ± 5.0	120.4 ± 4.1	123.1 ± 5.5	118.2 ± 7.0	6.0	0.9	5.2
Cranium size index	0.80 ± 0.06	0.74 ± 0.04	0.83 ± 0.06	0.76 ± 0.07	0.84 ± 0.04	0.70 ± 0.06	5.2	40.1***	9.2*
Alcohol Use Variables									
Age started drinking	16.4 ± 2.9	18.7 ± 4.6	18.2 ± 4.3	16.0 ± 1.7	18.2 ± 3.5	19.3 ± 2.9	2.9	0.3	6.1
Age at first heavy use	23.3 ± 6.3	26.8 ± 6.6	27.9 ± 10.2	30.7 ± 5.8	35.6 ± 11.7	32.4 ± 11.5	15.3***	0.3	2.7
Duration of active drinking (years)	26.0 ± 6.0	21.4 ± 5.9	35.9 ± 5.9	38.1 ± 3.5	44.5 ± 7.8	44.4 ± 7.4	66.9[c]	0.4	5.4[c]
Average lifetime drinking dose (std. drinks/month)	184 ± 86	159 ± 107	249 ± 218	125 ± 46	127 ± 65	124 ± 61	4.0	4.2	4.2
Lifetime alcohol use (std. drinks)	56,363 ± 24,053	41,088 ± 28,666	98,285 ± 65,401	57,623 ± 24,547	67,209 ± 35,589	62,252 ± 20,472	9.8[c]	6.6*	3.4[c]
Duration of peak drinking (years)	9.9 ± 8.8	5.1 ± 4.1	11.8 ± 8.5	8.9 ± 9.3	15.1 ± 14.3	7.2 ± 3.1	3.3	7.6**	1.1
Peak drinking dose (std. drinks/month)	346 ± 209	383 ± 302	414 ± 243	243 ± 118	268 ± 168	259 ± 125	3.4	1.1	3.7
Alcohol peak use (std. drinks)	32,572 ± 27,707	49,844 ± 19,143	61,616 ± 68,543	20,507 ± 14,619	38,354 ± 28,535	19,038 ± 6,651	3.2	10.4**	2.9
Age at sobriety	43.0 ± 5.7	40.6 ± 5.0	55.0 ± 3.3	54.6 ± 2.4	66.4 ± 4.5	66.8 ± 5.9	83.1[c]	0.7	1.7[c]
Years abstinent	23.3 ± 6.8	24.4 ± 7.3	10.4 ± 6.6	14.1 ± 7.2	3.9 ± 5.1	4.7 ± 5.8	61.5[c]	1.9	0.9[c]

Measures are reported as mean ± standard deviation.

Effect is significant: *$p \leq 0.05$; **$p \leq 0.01$; ***$p \leq 0.001$.

[a]Total number of problem-drinking first-degree relatives divided by the total number of first-degree relatives.

[b]Treated versus untreated is reported as the number of individuals that received treatment for their alcoholism, versus number of those who never received formal treatment for their alcoholism. Chi squared analysis revealed no difference between the groups ($p = 0.58$).

[c]Statistical comparisons on variables directly influenced by or related to the age at which the individuals achieved abstinence are not appropriate, as this was associated with the group selection criteria.

Table 2. Demographics, Neuropsychological Domains, and Individual Tests (Raw Scores) EAA1 Versus Controls

	Alcoholics abstinent before 50 years		Controls		Effect size (%)		
Variable	Male (n = 16)	Female (n = 23)	Male (n = 16)	Female (n = 23)	Group	Gender	Group by gender
Demographics							
Age (years)	66.40 ± 5.49	64.98 ± 4.67	66.86 ± 3.98	65.75 ± 4.56	0.4	1.8	0.0
Years of education	14.59 ± 2.76	15.91 ± 2.41	17.91 ± 2.17	16.13 ± 1.69	9.0**	0.1	6.6*
Neuropsychological domains							
Abstraction/cognitive flexibility	0.06 ± 0.68	−0.06 ± 0.48	0.29 ± 0.65	0.14 ± 0.39	1.8	1.4	0.0
MicroCog analogies	12.5 ± 3.3	11.0 ± 2.5	13.0 ± 2.8	11.4 ± 3.0	0.7	6.8*	0.0
MicroCog object match A	10.4 ± 3.3	10.2 ± 2.4	10.9 ± 2.3	10.8 ± 2.4	1.0	0.1	0.0
Short Categories	40.2 ± 11.1	43.2 ± 10.8	35.6 ± 17.3	36.5 ± 13.7	4.4	0.6	0.2
Stroop-Interference	29.1 ± 8.4	38.0 ± 10.1	35.8 ± 12.0	37.4 ± 7.6	2.5	7.1*	3.5
Trails B	82.4 ± 37.2	81.9 ± 35.2	88.3 ± 32.6	74.9 ± 25.5	0.0	1.1	1.0
Attention	0.16 ± 0.62	0.01 ± 0.34	−0.18 ± 0.70	0.04 ± 0.54	2.9	0.3	3.5
Microcog Alphabet	11.4 ± 0.5	11.4 ± 0.5	11.5 ± 0.6	11.5 ± 0.5	0.5	0.1	0.0
Microcog Numbers Forward	11.5 ± 2.9	10.1 ± 2.2	8.7 ± 3.6	9.8 ± 3.3	6.6*	0.1	4.1
Microcog Numbers Reversed	9.8 ± 4.1	8.7 ± 2.5	7.9 ± 3.8	8.9 ± 2.5	1.3	0.0	2.3
MicroCog Wordlist 1	11.1 ± 2.6	10.9 ± 2.1	10.7 ± 3.2	11.1 ± 2.4	0.0	0.0	0.5
Stroop-Color	64.6 ± 8.4	68.5 ± 11.8	61.7 ± 15.6	68.8 ± 11.0	0.3	5.1*	0.5
Auditory Working Memory	−0.75 ± 1.24	−0.35 ± 0.67	0.17 ± 0.60	−0.16 ± 0.68	10.6**	0.0	4.9
PASAT 2.4 (seconds delay)	28.9 ± 15.3	36.6 ± 9.7	42.8 ± 11.6	38.4 ± 11.1	10.0**	0.4	6.2*
PASAT 2.0 (seconds delay)	30.5 ± 14.5	33.3 ± 13.6	38.2 ± 10.2	33.6 ± 11.0	2.6	0.1	2.2
PASAT 1.6 (seconds delay)	26.8 ± 14.1	26.3 ± 12.5	33.8 ± 8.6	29.4 ± 10.4	4.5	1.2	0.7
PASAT 1.2 (seconds delay)	19.7 ± 11.1	19.3 ± 8.6	24.7 ± 5.2	22.1 ± 7.4	5.4	0.8	0.4
Immediate Memory	0.49 ± 0.54	0.52 ± 0.66	0.51 ± 0.55	0.61 ± 0.56	0.0	0.4	0.0
MicroCog Story Recall	9.1 ± 1.4	9.3 ± 2.0	9.3 ± 1.4	9.3 ± 1.6	0.2	0.2	0.0
MicroCog Wordlist 2	13.8 ± 3.2	14.2 ± 3.6	14.1 ± 1.9	14.3 ± 3.5	0.1	0.2	0.1
Rey-immediate recall	39.1 ± 7.3	38.1 ± 13.1	38.4 ± 13.3	41.1 ± 12.1	0.2	0.1	0.6
Delayed Memory	0.19 ± 0.66	0.30 ± 0.72	0.26 ± 0.75	0.37 ± 0.79	0.0	0.9	0.4
MicroCog Story-Delayed Recall	10.0 ± 3.0	10.3 ± 2.6	9.9 ± 2.9	10.6 ± 3.6	0.0	0.7	0.1
Rey-Delayed Recall	37.1 ± 7.2	38.2 ± 13.4	38.8 ± 12.8	40.0 ± 10.7	0.6	0.3	0.0
Psychomotor	−0.04 ± 0.82	−0.02 ± 0.72	−0.06 ± 0.73	−0.10 ± 0.69	1.3	0.1	0.0
Symbol Digit Modalities	43.1 ± 7.8	47.6 ± 10.6	45.5 ± 5.5	47.3 ± 8.7	0.4	3.3	0.6
Trails A	35.9 ± 9.4	36.3 ± 11.4	37.6 ± 14.5	38.3 ± 12.1	0.6	0.1	0.0
Reaction Time	0.38 ± 0.65	0.45 ± 0.41	0.45 ± 0.50	0.24 ± 0.58	0.4	0.3	1.7
MicroCog Cued Timers	10.9 ± 2.4	11.7 ± 1.7	11.4 ± 1.8	11.1 ± 1.9	0.0	0.3	1.7
MicroCog Simple Timers	11.3 ± 1.9	11.1 ± 1.3	11.3 ± 1.5	10.3 ± 1.9	1.3	3.6	1.1
Spatial Processing	0.22 ± 0.59	0.03 ± 0.42	0.43 ± 0.43	0.24 ± 0.55	2.6	3.9	0.3
Block Design	35.5 ± 9.0	31.7 ± 8.9	40.4 ± 9.8	34.9 ± 10.2	4.4	5.8*	0.2
MicroCog Clocks	12.3 ± 2.0	12.6 ± 1.0	12.6 ± 1.2	12.3 ± 1.7	0.0	0.0	1.5
MicroCog Tic Tac	8.6 ± 2.5	7.7 ± 2.2	8.6 ± 2.1	9.0 ± 2.1	2.1	0.3	1.7
Verbal	1.19 ± 0.41	1.03 ± 0.53	0.90 ± 0.76	0.95 ± 0.53	2.8	0.0	1.2
AMNART (estimated verbal IQ)	120.1 ± 5.1	119.3 ± 4.8	120.2 ± 7.6	118.2 ± 6.4	0.2	1.4	0.3
COWAT	43.4 ± 9.9	41.6 ± 10.0	39.4 ± 11.3	40.8 ± 9.3	1.4	0.0	0.6
Average Z-score	0.21 ± 0.43	0.21 ± 0.37	0.31 ± 0.42	0.26 ± 0.40	0.8	0.1	0.1

Measures are reported as mean ± standard deviation.

Effect is significant: * = $p \leq 0.05$; ** = $p \leq 0.01$.

Units of measurement for the individual tests are as follows:

MicroCog, reported as a scaled score automatically adjusted for age and years of education; Short Categories, total number of errors out of 100; Stroop, number of items correctly identified in 45 seconds; Trails A and B, number of seconds required to complete the trail task; PASAT, number correct out of 60; Rey Immediate and Rey Delayed, maximum score of 72—based on correctly drawing 24 units of the picture with point values from 0 to 3 based on level of correctness; Symbol Digit Modalities, number of correct substitutions in a 90-second interval; Block Design, score is calculated based on seconds taken to complete the design (a score of 0 is given if design cannot be completed in 2 minutes or less; total maximum score attainable = 68); COWAT, number or words participant verbalizes in 3 different 1-minute intervals for letters C, F, and L.

The overall domains abstraction/cognitive flexibility, attention, auditory working memory, immediate memory, delayed memory, psychomotor, reaction time, spatial processing, and verbal are all reported as *Z*-scores.

month than the EAA3 group (adjusted for the difference between the groups in gender composition). The EAA2 group also on average drank 76.8 more drinks per month than the EAA3 group (also adjusted for the difference between the groups in gender composition). Furthermore, the EAA1 group had significantly higher proportions of relatives taht were "problem drinkers" than either the EAA2 or EAA3 group. The combination of a later onset of heavy drinking and a relatively low family history density for alcoholism indicates that the EAA2 and EAA3 groups are late-onset alcoholics, in comparison to the EAA1 group, which has the characteristics of early-onset alcoholics. Interestingly, the alcohol use and family history of the EAA1 participants are highly similar to the participants from our recently published study on 35 to 55-year-old long-term abstinent alcoholics (Fein et al., 2006).

There are a number of possible explanations for our findings. First, selective survivorship may have played a role.

Table 3. Demographics, Neuropsychological Domains, and Individual Tests (Raw Scores) EAA2 Versus Controls

	Alcoholics abstinent between 50 and 60		Controls		Effect size (%)		
Variable	Male (n = 16)	Female (n = 10)	Male (n = 16)	Female (n = 10)	Group	Gender	Group by gender
Demographics							
Age (years)	65.38 ± 4.84	68.62 ± 6.78	66.40 ± 3.15	68.18 ± 6.56	0.1	5.6	0.5
Years of Education	16.50 ± 3.14	16.3 ± 3.68	17.19 ± 2.17	16.20 ± 1.48	0.3	1.2	0.5
Neuropsychological Domains							
Abstraction/Cognitive Flexibility	0.15 ± 0.77	0.33 ± 0.45	0.28 ± 0.60	−0.03 ± 0.40	1.0	0.1	3.5
MicroCog Analogies	11.4 ± 3.2	12.7 ± 3.1	13.1 ± 3.1	10.8 ± 3.2	0.0	0.6	7.7*
MicroCog Object Match A	10.3 ± 2.8	11.3 ± 1.4	11.0 ± 2.1	9.9 ± 2.9	0.6	0.0	4.9
Short Categories	36.7 ± 13.7	35.1 ± 16.0	37.5 ± 17.2	37.8 ± 13.0	0.3	0.0	0.1
Stroop-Interference	33.3 ± 7.8	40.2 ± 6.9	36.3 ± 11.0	35.6 ± 9.8	0.2	2.8	4.3
Trails B	71.9 ± 31.7	77.2 ± 25.9	85.6 ± 31.3	90.2 ± 30.8	4.7	0.7	0.0
Attention	0.17 ± 0.47	0.42 ± 0.54	−0.27 ± 0.71	−0.24 ± 0.58	19.2**	1.8	0.6
MicroCog Alphabet	11.3 ± 0.5	11.7 ± 0.7	11.5 ± 0.6	11.6 ± 0.5	0.1	4.4	1.6
MicroCog Numbers Forward	10.9 ± 3.0	12.5 ± 3.9	7.9 ± 3.4	8.5 ± 4.0	20.7***	2.3	0.5
MicroCog Numbers Reversed	11.1 ± 3.4	9.1 ± 3.5	7.9 ± 4.2	7.7 ± 3.0	9.3*	2.2	1.5
MicroCog Wordlist 1	11.1 ± 3.1	12.5 ± 0.7	10.5 ± 3.2	10.2 ± 3.2	6.3	0.9	2.2
Stroop-Color	64.4 ± 8.9	73.8 ± 8.2	61.7 ± 14.9	62.8 ± 12.0	8.2*	4.9	3.1
Auditory Working Memory	−0.07 ± 0.77	−0.25 ± 0.90	0.10 ± 0.60	−0.85 ± 1.24	1.7	10.2*	5.0
PASAT 2.4 (seconds delay)	38.9 ± 15.2	38.5 ± 15.2	41.2 ± 11.6	25.6 ± 13.7	4.1	8.9*	8.0*
PASAT 2.0 (seconds delay)	38.3 ± 10.5	37.9 ± 7.3	36.9 ± 10.2	24.4 ± 14.9	10.7*	8.2	7.3
PASAT 1.6 (seconds delay)	32.9 ± 9.6	29.8 ± 7.6	32.8 ± 7.7	23.9 ± 15.3	2.3	8.4	2.0
PASAT 1.2 (seconds delay)	22.7 ± 10.3	23.5 ± 7.8	24.6 ± 5.1	17.8 ± 11.3	1.2	3.0	4.6
Immediate Memory	0.78 ± 0.46	0.54 ± 0.90	0.45 ± 0.53	0.44 ± 0.38	3.4	1.7	0.5
MicroCog Story Recall	8.9 ± 1.5	9.3 ± 1.6	9.1 ± 1.3	8.2 ± 1.7	2.6	0.7	4.1
MicroCog Wordlist 2	15.1 ± 1.3	13.9 ± 4.3	13.8 ± 1.9	14.1 ± 1.6	1.2	0.9	2.3
Rey-Immediate Recall	45.7 ± 11.5	38.8 ± 14.3	38.6 ± 12.4	38.8 ± 11.6	2.1	1.8	2.1
Delayed Memory	0.58 ± 0.69	0.38 ± 0.96	0.28 ± 0.74	0.17 ± 0.73	3.2	2.4	0.1
MicroCog Story-Delayed Recall	10.6 ± 2.6	10.6 ± 4.2	10.1 ± 3.1	9.1 ± 3.5	2.3	0.7	0.6
Rey-Delayed Recall	44.9 ± 11.7	38.7 ± 13.5	39.0 ± 11.9	38.7 ± 7.0	1.7	2.1	1.7
Psychomotor	−0.06 ± 0.75	−0.05 ± 0.48	−0.13 ± 0.76	−0.26 ± 0.63	2.5	0.0	0.0
Symbol Digit Modalities	46.6 ± 7.8	49.4 ± 6.6	43.6 ± 6.5	45.3 ± 7.6	5.8	2.5	0.2
Trails A	34.4 ± 9.3	42.8 ± 11.9	36.2 ± 12.9	43.0 ± 15.1	0.2	9.0*	0.1
Reaction Time	0.40 ± 0.68	0.35 ± 0.48	0.46 ± 0.49	0.12 ± 0.50	1.0	2.8	1.6
MicroCog Cued Timers	12.0 ± 1.7	11.2 ± 2.2	11.3 ± 1.9	11.1 ± 2.0	1.0	2.0	0.5
MicroCog Simple Timers	10.5 ± 2.7	11.0 ± 1.4	11.4 ± 1.4	9.7 ± 1.1	0.2	2.9	9.0*
Spatial Processing	0.42 ± 0.66	0.48 ± 0.45	0.37 ± 0.31	0.27 ± 0.55	2.5	0.3	1.4
Block Design	41.2 ± 13.2	38.8 ± 10.9	38.8 ± 9.9	39.0 ± 11.1	0.2	0.2	0.3
MicroCog Clocks	12.0 ± 2.5	13.1 ± 1.3	12.6 ± 1.2	11.5 ± 1.4	2.2	0.0	8.9*
MicroCog Tic Tac	9.4 ± 2.1	8.7 ± 1.3	8.6 ± 1.6	8.6 ± 2.1	1.6	0.8	1.0
Verbal	0.84 ± 0.59	1.36 ± 0.44	0.84 ± 0.76	0.52 ± 0.42	9.5*	1.3	9.3*
AMNART (Estimated Verbal IQ)	118.0 ± 8.3	123.4 ± 5.0	120.1 ± 7.5	115.5 ± 6.6	3.8	0.1	11.0*
COWAT	38.6 ± 11.7	47.6 ± 15.1	38.1 ± 11.3	33.7 ± 6.4	9.1*	1.0	7.9*
Average Z-score	0.36 ± 0.49	0.40 ± 0.32	0.27 ± 0.40	0.03 ± 0.36	8.7*	1.5	2.9

Measures are reported mean ± standard deviation.

Effect is significant: *$p \leq 0.05$; **$p \leq 0.01$; ***$p \leq 0.001$.

Units of measurement for the individual tests are as follows:

MicroCog, reported as a scaled score automatically adjusted for age and years of education; Short Categories, total number of errors out of 100; Stroop, number of items correctly identified in 45 seconds; Trails A and B, number of seconds required to complete the trail task; PASAT, number correct out of 60; Rey Immediate and Rey Delayed, maximum score of 72—based on correctly drawing 24 units of the picture with point values from 0 to 3 based on level of correctness; Symbol Digit Modalities, number of correct substitutions in a 90-second interval; Block Design, score is calculated based on seconds taken to complete the design (a score of 0 is given if design cannot be completed in 2 minutes or less; total maximum score attainable = 68); COWAT, number or words participant verbalizes in 3 different 1-minute intervals for letters C, F and L.

The overall domains abstraction/cognitive flexibility, attention, auditory working memory, immediate memory, delayed memory, psychomotor, reaction time, spatial processing, and verbal are all reported as *Z*-scores.

Heavy alcohol consumption has been shown to negatively impact life expectancy both directly and indirectly (Goldacre et al., 2004; Jarque-Lopez et al., 2001; McDonnell and Maynard, 1985; Ojesjo et al., 1998; Poldrugo et al., 1993; Rehm et al., 2006; Sher, 2005; Wojtyniak et al., 2005). Furthermore the CDC reported that in 2001, there were approximately 75,000 deaths attributable to either excessive or risky drinking in the United States, making alcohol the third leading actual cause of death (Centers for Disease Control, 2004). Given the negative impact of alcoholism on life expectancy, selective survivorship increases the likelihood that cognitively healthier alcoholics are more likely to survive into their 60s, 70s, or 80s of age.

Second, it is possible that maintaining sobriety in the face of cognitive impairment is more difficult as individuals' age. That is, those who were less cognitively intact may have been more likely to relapse into active drinking, and thus were not included in this study.

Table 4. Demographics, Neuropsychological Domains, and Individual Tests (Raw Scores) EAA3 vs Controls

	Alcoholics abstinent after 60 years		Controls		Effect size (%)		
Variable	Male (n = 17)	Female (n = 9)	Male (n = 17)	Female (n = 9)	Group	Gender	Group by gender
Demographics							
Age (years)	70.25 ± 4.84	71.51 ± 9.30	69.79 ± 4.54	71.36 ± 9.46	0.1	1.1	0.0
Years of Education	16.18 ± 2.19	14.00 ± 1.77	16.76 ± 2.54	15.67 ± 1.73	6.0	11.8*	1.4
Neuropsychological Domains							
Abstraction/Cognitive Flexibility	0.30 ± 0.57	0.03 ± 0.86	0.36 ± 0.60	0.26 ± 0.47	0.0	0.1	0.2
MicroCog Analogies	13.1 ± 3.0	12.1 ± 3.6	13.4 ± 3.2	12.2 ± 3.6	0.1	2.9	0.0
MicroCog Object Match A	10.8 ± 2.4	10.1 ± 2.9	11.7 ± 2.0	12.5 ± 1.5	11.6*	0.0	3.0
Short Categories	34.0 ± 13.3	39.0 ± 17.9	38.8 ± 15.3	37.4 ± 16.9	0.3	0.3	1.0
Stroop-Interference	29.5 ± 8.0	34.4 ± 7.8	33.8 ± 10.4	34.3 ± 6.1	1.5	2.4	1.5
Trails B	81.6 ± 28.1	87.4 ± 27.7	84.8 ± 26.2	88.3 ± 23.6	0.1	0.7	0.0
Attention	0.31 ± 0.49	0.13 ± 0.57	−0.05 ± 0.70	−0.03 ± 0.49	6.8	0.0	0.1
MicroCog Alphabet	12.1 ± 0.2	10.3 ± 3.7	11.8 ± 0.5	10.6 ± 3.3	0.0	11.6*	0.3
MicroCog Numbers Forward	11.9 ± 3.5	10.4 ± 2.3	8.9 ± 3.8	9.4 ± 4.8	6.7	0.3	1.8
MicroCog Numbers Reversed	10.7 ± 2.9	10.7 ± 4.7	9.2 ± 3.3	9.9 ± 4.6	2.3	0.2	0.3
MicroCog Wordlist 1	11.3 ± 1.8	11.1 ± 2.8	11.0 ± 3.0	11.8 ± 2.1	0.1	0.4	0.9
Stroop-Color	61.7 ± 8.1	69.8 ± 7.5	59.6 ± 12.2	61.6 ± 8.9	6.4	6.1	2.4
Auditory Working Memory	−0.33 ± 0.76	−0.16 ± 0.77	−0.07 ± 0.57	−0.38 ± 0.50	0.0	0.3	3.0
PASAT 2.4 (seconds delay)	37.8 ± 13.1	37.3 ± 11.1	38.9 ± 10.9	34.1 ± 10.5	0.2	1.2	0.8
PASAT 2.0 (seconds delay)	32.1 ± 9.0	35.7 ± 12.9	34.3 ± 9.7	30.6 ± 8.2	0.6	0.0	3.4
PASAT 1.6 (seconds delay)	27.1 ± 12.7	28.6 ± 15.8	30.7 ± 9.5	25.8 ± 8.8	0.0	0.5	1.8
PASAT 1.2 (seconds delay)	17.3 ± 11.6	21.0 ± 10.7	22.9 ± 7.9	20.1 ± 3.7	1.3	0.0	2.5
Immediate Memory	0.67 ± 0.32	0.70 ± 0.54	0.49 ± 0.50	0.23 ± 0.63	13.2*	0.2	5.4
MicroCog Story Recall	9.1 ± 1.6	9.7 ± 1.6	9.0 ± 1.3	8.4 ± 1.2	5.0	0.0	3.5
MicroCog Wordlist 2	14.2 ± 1.9	15.0 ± 1.7	13.6 ± 2.9	13.4 ± 5.1	2.9	0.3	0.7
Rey-Immediate Recall	43.1 ± 10.4	36.4 ± 11.3	39.5 ± 12.8	30.8 ± 8.3	4.1	10.5*	0.2
Delayed Memory	0.90 ± 0.78	0.72 ± 1.18	1.52 ± 0.80	0.41 ± 0.95	9.4*	0.1	2.1
MicroCog Story-Delayed Recall	12.4 ± 3.5	12.7 ± 5.1	10.9 ± 3.3	11.1 ± 4.2	3.5	0.1	0.0
Rey-Delayed Recall	43.9 ± 10.4	33.9 ± 12.1	39.9 ± 12.8	32.9 ± 9.4	1.2	12.2**	0.4
Psychomotor	−0.04 ± 0.69	−0.26 ± 0.61	−0.06 ± 0.77	−0.62 ± 0.80	6.0	2.3	2.3
Symbol Digit Modalities	43.9 ± 7.1	43.2 ± 8.4	43.6 ± 6.3	40.2 ± 10.2	1.1	1.7	0.8
Trails A	37.7 ± 11.7	42.2 ± 9.7	37.4 ± 12.5	48.1 ± 21.2	1.0	7.0	1.3
Reaction Time	0.72 ± 0.30	0.60 ± 0.24	0.39 ± 0.48	0.36 ± 0.57	12.7*	0.1	0.1
MicroCog Cued Timers	12.6 ± 1.0	11.9 ± 1.2	11.2 ± 1.9	11.8 ± 1.3	6.1	0.0	5.3
MicroCog Simple Timers	11.7 ± 1.6	11.7 ± 0.5	11.2 ± 1.4	10.3 ± 2.3	8.9*	1.7	1.7
Spatial Processing	0.44 ± 0.57	0.36 ± 0.68	0.48 ± 0.54	0.04 ± 0.56	6.4	1.1	9.0*
Block Design	35.8 ± 7.9	34.9 ± 11.4	38.5 ± 9.2	29.1 ± 7.0	0.8	7.6*	5.2
MicroCog Clocks	12.9 ± 1.2	13.0 ± 1.3	12.6 ± 1.5	12.3 ± 2.6	2.0	0.1	0.3
MicroCog Tic Tac	9.1 ± 2.7	8.1 ± 1.8	9.0 ± 2.0	8.1 ± 1.8	0.0	4.0	0.0
Verbal	0.95 ± 0.45	0.94 ± 0.65	0.82 ± 0.70	0.84 ± 0.30	2.3	0.3	0.1
AMNART (Estimated Verbal IQ)	120.8 ± 4.7	119.0 ± 5.7	118.9 ± 7.6	117.3 ± 5.5	2.1	1.8	0.0
COWAT	38.9 ± 9.0	39.8 ± 13.4	37.9 ± 9.0	38.2 ± 4.5	0.4	0.1	0.0
Average Z-score	0.44 ± 0.37	0.34 ± 0.49	0.33 ± 0.37	0.12 ± 0.43	3.8	3.3	0.4

Measures are reported mean ± standard deviation.

Effect is significant: * = $p \leq 0.05$; ** = $p \leq 0.01$

Units of measurement for the individual tests are as follows:

MicroCog, reported as a scaled score automatically adjusted for age and years of education; Short Categories, total number of errors out of 100; Stroop, number of items correctly identified in 45 seconds; Trails A and B, number of seconds required to complete the trail task; PASAT, number correct out of 60; Rey Immediate and Rey Delayed, maximum score of 72—based on correctly drawing 24 units of the picture with point values from 0 to 3 based on level of correctness; Symbol Digit Modalities, number of correct substitutions in a 90-second interval; Block Design, Score is calculated based on seconds taken to complete the design (a score of 0 is given if design cannot be completed in 2 minutes or less; total maximum score attainable = 68); COWAT, number or words participant verbalizes in 3 different 1-minute intervals for letters C, F and L.

The overall domains abstraction/cognitive flexibility, attention, auditory working memory, immediate memory, delayed memory, psychomotor, reaction time, spatial processing and verbal are all reported as *Z*-scores.

Third, it is also possible that the abstinent alcoholics we studied may never have suffered from significant cognitive impairments, even while they were actively drinking. There have been a number of studies through the years that indicate normal cognitive performance in chronic alcoholism is possible (Brokate et al., 2003; Grant et al., 1979; Guthrie and Elliott, 1980; Krabbendam et al., 2000). The greater cranium size in the EAA sample is consistent with this hypothesis. They are also consistent with the findings of Katzman et al. (1988) in a postmortem investigation of Alzheimer's disease. They studied 137 nursing-home residents and found 10 individuals whose autopsy revealed a quantity of neocortical plaques comparable with that observed in patients with Alzheimer's disease, but whose cognitive performance was comparable with that of control subjects (nondemented subjects without Alzheimer's disease or other brain lesions). In addition, the brain weights and number of large neurons in

these cognitively normal patients with a high quantity of plaque were significantly greater than those of the control group. Katzman et al. (1988) concluded that these clinically healthy individuals with a high quantity of plaque had incipient Alzheimer's disease, but were cognitively intact because of a greater neuronal reserve associated with their larger than average brains.

Our results showed that it is possible for elderly alcoholics with at least 6 months abstinence to exhibit essentially normal cognitive functioning, even if they drank during their 50s or 60s. These findings argue against the hypothesis that aging brain is more vulnerable to the effects of alcohol. However, we noted that it is also possible that the aging brain is indeed more vulnerable, but that cognitive deficits resulting from chronic alcohol abuse tend to resolve with significant abstinence, or that a subgroup of elderly alcoholics exist who have sufficient brain reserve capacity to have normal cognitive performance once they have had a reasonable period of abstinence. These results do not suggest by any means that all elderly chronic alcoholics with long-term abstinence will attain normal cognitive function.

Finally, our results suggested that brain reserve capacity is important in modulating the clinical manifestations of chronic alcoholism on cognitive function, especially in an elderly sample. In multigenerational alcohol- or drug-dependent individuals, reduced reserve capacity is a likely result of a less than optimal prenatal and postnatal environments (Fein and Di Sclafani, 2004; Gilman et al., 2007). This reduced reserve capacity may exacerbate cognitive impairments secondary to alcohol abuse, and should be examined as a modulating variable where possible.

ACKNOWLEDGMENTS

This work was supported by Grants AA11311 (GF) and AA13659 (GF), both from the National Institute of Alcohol Abuse and Alcoholism.

REFERENCES

American Psychiatric Association (2000) DSM-IV-TR: Diagnostic and Statistical Manual of Mental Disorders. 4th ed. American Psychiatric Publishing, Washington, DC.

Bates ME, Voelbel GT, Buckman JF, Labouvie EW, Barry D (2005) Short-term neuropsychological recovery in clients with substance use disorders. Alcohol Clin Exp Res 29:367–377.

Bechara A, Damasio AR, Damasio H, Anderson SW (1994) Insensitivity to future consequences following damage to human prefrontal cortex. Cognition 50:7–15.

Benton AL, Hamsher K (1983) Multilingual Aphasia Examination. AJA Associates, Iowa City.

Block RI, Erwin WJ, Ghoneim MM (2002) Chronic drug use and cognitive impairments. Pharmacol Biochem Behav 73:491–504.

Brokate B, Hildebrandt H, Eling P, Fichtner H, Runge K, Timm C (2003) Frontal lobe dysfunctions in Korsakoff's syndrome and chronic alcoholism: continuity or discontinuity? Neuropsychology 17:420–428.

Brun A, Andersson J (2001) Frontal dysfunction and frontal cortical synapse loss in alcoholism—the main cause of alcohol dementia? Dement Geriatr Cogn Disord 12:289–294.

Butterworth RF (1995) Pathophysiology of alcoholic brain damage: synergistic effects of ethanol, thiamine deficiency and alcoholic liver disease. Metab Brain Dis 10:1–8.

Centers for Disease Control (2004) Alcohol-attributal deaths and years of potential life lost—United States, 2001. MMWR Morb Mortal Wkly Rep 53:866–870.

Denman SB (1987) Denman Neuropsychology Memory Scale. SB Denman, Charleston, SC.

Di Sclafani V, Clark HW, Tolou-Shams M, Bloomer CW, Salas GA, Norman D, Fein G (1998) Premorbid brain size is a determinant of functional reserve in abstinent crack-cocaine and crack-cocaine-alcohol-dependent adults. J Int Neuropsychol Soc 4:559–565.

Di Sclafani V, Ezekiel F, Meyerhoff DJ, MacKay S, Dillon WP, Weiner MW, Fein G (1995) Brain atrophy and cognitive function in older abstinent alcoholic men. Alcohol Clin Exp Res 19:1121–1126.

Diamond I, Messing RO (1994) Neurologic effects of alcoholism. West J Med 161:279–287.

Emsley R, Smith R, Roberts M, Kapnias S, Pieters H, Maritz S (1996) Magnetic resonance imaging in alcoholic Korsakoff's syndrome: evidence for an association with alcoholic dementia. Alcohol Alcohol 31:479–486.

Fama R, Pfefferbaum A, Sullivan EV (2004) Perceptual learning in detoxified alcoholic men: contributions from explicit memory, executive function, and age. Alcohol Clin Exp Res 28:1657–1665.

Fein G, Bachman L, Fisher S, Davenport L (1990) Cognitive impairments in abstinent alcoholics. West J Med 152:531–537.

Fein G, Di Sclafani V (2004) Cerebral reserve capacity: implications for alcohol and drug abuse. Alcohol 32:63–67.

Fein G, Di Sclafani V, Taylor C, Moon K, Barakos J, Tran H, Landman B, Shumway R (2004) Controlling for premorbid brain size in imaging studies: T1-derived cranium scaling factor vs T2-derived intracranial vault volume. Psychiatry Res 131:169–176.

Fein G, Torres J, Price LJ, Di Sclafani V (2006) Cognitive performance in long-term abstinent alcoholic individuals. Alcohol Clin Exp Res 30:1538–1544.

Finlayson RE, Hurt RD, Davis LJ, Jr, Morse RM (1988) Alcoholism in elderly persons: a study of the psychiatric and psychosocial features of 216 inpatients. Mayo Clin Proc 63:761–768.

Fregly AR, Smith MJ, Graybiel A (1973) Revised normative standards of performance of men on a quantitative ataxia test battery. Acta Otolaryngol 75:10–16.

Gilman JM, Bjork JM, Hommer DW (2007) Parental alcohol use and brain volumes in early- and late-onset alcoholics. Biol Psychiatry.

Goldacre MJ, Duncan M, Griffith M, Cook-Mozaffari P (2004) Alcohol as a certified cause of death in a 'middle England' population 1979-1999: database study. J Public Health (Oxf) 26:343–346.

Golden CJ (1978) Stroop Color and Word Test: A Manual for Clinical and Experimental Uses. Western Psychological Services, Los Angeles, CA.

Goldman MS, Williams DL, Klisz DK (1983) Recoverability of psychological functioning following alcohol abuse: prolonged visual-spatial dysfunction in older alcoholics. J Consult Clin Psychol 51:370–378.

Grant I, Adams K, Reed R (1979) Normal neuropsychological abilities of alcoholic men in their late thirties. Am J Psychiatry 136:1263–1269.

Graves AB, Mortimer JA, Larson EB, Wenzlow A, Bowen JD, McCormick WC (1996) Head circumference as a measure of cognitive reserve. Association with severity of impairment in Alzheimer's disease. Br J Psychiatry 169:86–92.

Grober E, Sliwinski M (1991) Development and validation of a model for estimating premorbid verbal intelligence in the elderly. J Clin Exp Neuropsychol 13:933–949.

Gronwall DM (1977) Paced auditory serial-addition task: a measure of recovery from concussion. Percept Mot Skills 44:367–373.

Guthrie A, Elliott WA (1980) The nature and reversibility of cerebral impairment in alcoholism; treatment implications. J Stud Alcohol 41:147–155.

Harper C, Matsumoto I (2005) Ethanol and brain damage. Curr Opin Pharmacol 5:73–78.

Heap LC, Pratt OE, Ward RJ, Waller S, Thomson AD, Shaw GK, Peters TJ (2002) Individual susceptibility to Wernicke-Korsakoff syndrome and

alcoholism-induced cognitive deficit: impaired thiamine utilization found in alcoholics and alcohol abusers. Psychiatr Genet 12:217–224.

Heaton RK, Grant I, Maththews CG (1991) Comprehensive Norms for an Expanded Halstead-Reitan Battery: Demographic Corrections, Research Findings, and Clinical Applications. Psychological Assessment Resources, Inc., Odessa, FL.

Jarque-Lopez A, Gonzalez-Reimers E, Rodriguez-Moreno F, Santolaria-Fernandez F, Lopez-Lirola A, Ros-Vilamajo R, Espinosa-Villarreal JG, Martinez-Riera A (2001) Prevalence and mortality of heavy drinkers in a general medical hospital unit. Alcohol Alcohol 36:335–338.

Katzman R, Terry R, DeTeresa R, Brown T, Davies P, Fuld P, Renbing X, Peck A (1988) Clinical, pathological, and neurochemical changes in dementia: a subgroup with preserved mental status and numerous neocortical plaques. Ann Neurol 23:138–144.

Kim JM, Shin IS, Stewart R, Yoon JS (2002) Alcoholism in older Korean men: prevalence, aetiology, and comorbidity with cognitive impairment and dementia in urban and rural communities. Int J Geriatr Psychiatry 17:821–827.

Korsakoff S (1887) Disturbance of psychic activity in alcoholic paralysis. Vestn Klin Psichiat Neurol 4:1–102.

Krabbendam L, Visser PJ, Derix MM, Verhey F, Hofman P, Verhoeven W, Tuinier S, Jolles J (2000) Normal cognitive performance in patients with chronic alcoholism in contrast to patients with Korsakoff's syndrome. J Neuropsychiatry Clin Neurosci 12:44–50.

Mann RE, Sobell LC, Sobell MB, Pavan D (1985) Reliability of a family tree questionnaire for assessing family history of alcohol problems. Drug Alcohol Depend 15:61–67.

McDonnell R, Maynard A (1985) Estimation of life years lost from alcohol-related premature death. Alcohol Alcohol 20:435–443.

McMurtray A, Clark DG, Christine D, Mendez MF (2006) Early-onset dementia: frequency and causes compared to late-onset dementia. Dement Geriatr Cogn Disord 21:59–64.

Mochizuki H, Masaki T, Matsushita S, Ugawa Y, Kamakura K, Arai H, Motoyoshi K, Higuchi S (2005) Cognitive impairment and diffuse white matter atrophy in alcoholics. Clin Neurophysiol 116:223–228.

Mori E, Hirono N, Yamashita H, Imamura T, Ikejiri Y, Ikeda M, Kitagaki H, Shimomura T, Yoneda Y (1997) Premorbid brain size as a determinant of reserve capacity against intellectual decline in Alzheimer's disease. Am J Psychiatry 154:18–24.

Moriyama Y, Muramatsu T, Kato M, Mimura M, Kashima H (2006) Family history of alcoholism and cognitive recovery in subacute withdrawal. Psychiatry Clin Neurosci 60:85–89.

Munro CA, Saxton J, Butters MA (2000) The neuropsychological consequences of abstinence among older alcoholics: a cross-sectional study. Alcohol Clin Exp Res 24:1510–1516.

Ojesjo L, Hagnell O, Otterbeck L (1998) Mortality in alcoholism among men in the Lundby Community Cohort, Sweden: a forty-year follow-up. J Stud Alcohol 59:140–145.

Oscar-Berman M, Kirkley SM, Gansler DA, Couture A (2004) Comparisons of Korsakoff and non-Korsakoff alcoholics on neuropsychological tests of prefrontal brain functioning. Alcohol Clin Exp Res 28:667–675.

Osterrieth PA (1944) Le test de copie d'une figure complex. Archives de Psychologie 30:206–356.

Poldrugo F, Chick JD, Moore N, Walburg JA (1993) Mortality studies in the long-term evaluation of treatment of alcoholics. Alcohol Alcohol Suppl 2:151–155.

Powell DH, Kaplan EF, Whitla D, Weinstraub S, Catlin R, Funkenstein HH (1993) MicroCog Assessment of Cognitive Functioning. The Psychological Corporation, San Antonio, TX.

Ratti MT, Soragna D, Sibilla L, Giardini A, Albergati A, Savoldi F, Bo P (1999) Cognitive impairment and cerebral atrophy in "heavy drinkers". Prog Neuropsychopharmacol Biol Psychiatry 23:243–258.

Rehm J, Patra J, Popova S (2006) Alcohol-attributable mortality and potential years of life lost in Canada 2001: implications for prevention and policy. Addiction 101:373–384.

Reitan RM, Wolfson D (1985) The Halstead-Reitan Neuropsychological Test Battery. Neuropsychology Press, Tucson.

Robins LN, Cottler L, Buckholz K, Compton W (1998) The Diagnostic Interview Schedule for DSM-IV. Washington University School of Medicine, St Louis, MO.

Rosenbloom MJ, Pfefferbaum A, Sullivan EV (2004) Recovery of short-term memory and psychomotor speed but not postural stability with long-term sobriety in alcoholic women. Neuropsychology 18:589–597.

Ruff RM, Light RH, Parker SB, Levin HS (1996) Benton Controlled Oral Word Association Test: reliability and updated norms. Arch Clin Neuropsychol 11:329–338.

Satz P (1993) Brain reserve capacity on symptom onset after brain injury: A formulation and review of evidence for threshold theory. Neuropsychology 7:273–295.

Saxton J, Munro CA, Butters MA, Schramke C, McNeil MA (2000) Alcohol, dementia, and Alzheimer's disease: comparison of neuropsychological profiles. J Geriatr Psychiatry Neurol 13:141–149.

Schmand B, Smit JH, Geerlings MI, Lindeboom J (1997) The effects of intelligence and education on the development of dementia. A test of the brain reserve hypothesis. Psychol Med 27:1337–1344.

Schmidt KS, Gallo JL, Ferri C, Giovannetti T, Sestito N, Libon DJ, Schmidt PS (2005) The neuropsychological profile of alcohol-related dementia suggests cortical and subcortical pathology. Dement Geriatr Cogn Disord 20:286–291.

Schwartz M, Saffran E (1987) Replication and Extension of the British Findings on the Persistence of the Word Pronunciation Skills in Patients With Dementia. The American-NART, Philadelphia, PA.

Sher L (2005) Alcohol use and suicide rates. Med Hypotheses 65:1010–1012.

Skinner HA, Allen BA (1982) Alcohol dependence syndrome: measurement and validation. J Abnorm Psychol 91:199–209.

Skinner HA, Sheu WJ (1982) Reliability of alcohol use indices. The Lifetime Drinking History and the MAST. J Stud Alcohol 43:1157–1170.

Smith A (1968) The symbol digit modalities test: A neuropsychological test of learning and other cerebral disorders, in Learning Disorders (Helmuth J ed), pp 83–91. Special Child Publications, Seattle, WA.

Smith A (1982) Symbol Digit Modalities Test. Western Psychological Services, Los Angeles, CA.

Smith DM, Atkinson RM (1995) Alcoholism and dementia. Int J Addict 30:1843–1869.

Smith SM, Zhang Y, Jenkinson M, Chen J, Matthews PM, Federico A, De Stefano N (2002) Accurate, robust, and automated longitudinal and cross-sectional brain change analysis. Neuroimage 17:479–489.

Sobell LC, Sobell MB (1990) Self-reports issues in alcohol abuse: State of the art and future directions. Behaviorial Assessment 12:77–90.

Sobell LC, Sobell MB, Riley DM, Schuller R, Pavan DS, Cancilla A, Klajner F, Leo GI (1988) The reliability of alcohol abusers' self-reports of drinking and life events that occurred in the distant past. J Stud Alcohol 49:225–232.

SPSS Inc. (2004) SPSS 13.0 for Windows, 13.0 ed. SPSS Inc., Chicago, IL.

Stoltenberg SF, Mudd SA, Blow FC, Hill EM (1998) Evaluating measures of family history of alcoholism: density versus dichotomy. Addiction 93:1511–1520.

Stuss DT, Stethem LL, Pelchat G (1988) Three tests of attention and rapid information processing: an extension. The Clinical Neuropsychologist 2:246–250.

Sullivan EV, Fama R, Rosenbloom MJ, Pfefferbaum A (2002) A profile of neuropsychological deficits in alcoholic women. Neuropsychology 16:74–83.

Sullivan EV, Rosenbloom MJ, Lim KO, Pfefferbaum A (2000a) Longitudinal changes in cognition, gait, and balance in abstinent and relapsed alcoholic men: relationships to changes in brain structure. Neuropsychology 14:178–188.

Sullivan EV, Rosenbloom MJ, Pfefferbaum A (2000b) Pattern of motor and cognitive deficits in detoxified alcoholic men. Alcohol Clin Exp Res 24:611–621.

Tedstone D, Coyle K (2004) Cognitive impairments in sober alcoholics: performance on selective and divided attention tasks. Drug Alcohol Depend 75:277–286.

Victor M (1994) Alcoholic dementia. Can J Neurol Sci 21:88–99.

Wechsler D (1981) Wechsler Adult Intelligence Scale-Revised. The Psychological Corporation, New York.

Wechsler D (1997) Wechsler Adult Intelligence Scale—Third Edition: Administration and Scoring Manual. The Psychological Corporation, San Antonio, TX.

Wernicke C (1881) Lehrbuch der Gehirnkrankheiten fur Aerzte und Studirende, Volume 2. Theodor Fisher, Kassel, Berlin, pp 229–242.

Wetzel L, Boll T (1987) Short Category Test. Booklet Format. Western Psychological Services, Los Angeles, CA.

Wojtyniak B, Moskalewicz J, Stokwiszewski J, Rabczenko D (2005) Gender-specific mortality associated with alcohol consumption in Poland in transition. Addiction 100:1779–1789.

Zinn S, Stein R, Swartzwelder HS (2004) Executive functioning early in abstinence from alcohol. Alcohol Clin Exp Res 28:1338–1346.