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# Comparisons of Korsakoff and Non-Korsakoff Alcoholics on Neuropsychological Tests of Prefrontal Brain Functioning

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## Abstract

**Background—**Evidence suggests that alcoholics exhibit particular deficits in brain systems involving the prefrontal cortex, but few studies have directly compared patients with and without Korsakoff's syndrome on measures of prefrontal integrity.

**Methods—**Neuropsychological tasks sensitive to dysfunction of frontal brain systems were administered, along with standard tests of memory, intelligence, and visuospatial abilities, to 50 healthy, abstinent, nonamnesic alcoholics, 6 patients with alcohol-induced persisting amnestic disorder (Korsakoff's syndrome), 6 brain-damaged controls with right hemisphere lesions, and 82 healthy nonalcoholic controls.

**Results—**Korsakoff patients were impaired on tests of memory, fluency, cognitive flexibility, and perseveration. Non-Korsakoff alcoholics showed some frontal system deficits as well, but these were mild. Cognitive deficits in non-Korsakoff alcoholics were related to age, duration of abstinence (less than 5 years), duration of abuse (more than 20 years), and amount of alcohol intake.

**Conclusions—**Abnormalities of frontal system functioning are most apparent in alcoholics with Korsakoff's syndrome. In non-Korsakoff alcoholics, factors contributing to cognitive performance are age, duration of abstinence, duration of alcoholism, and amount of alcohol consumed.

### Keywords

Alcoholism; Frontal Brain Systems; Korsakoff's Syndrome; Visuospatial Abilities

Alcohol-related brain damage has been associated with a variety of neuropsychological changes, among which are deficits in cognitive, emotional, and behavioral functioning (Bates and Convit, 1999; Bates et al., 2002; Oscar-Berman, 2000; Parsons, 1996; Rourke and Loberg, 1996). Although neuropathologic and neuroimaging findings have noted global atrophy in the brains of alcoholics, there is mounting evidence that alcoholics (especially over age 50) exhibit particular deficits in brain systems involving the prefrontal cortex (e.g., Di Sclafani et al., 1995; Moselhy et al., 2001; Oscar-Berman, 2000; Sullivan, 2000). Further



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evidence in support of frontal system dysfunction in alcoholism comes from work with patients with alcohol-induced persisting amnestic disorder (alcoholic Korsakoff patients). Frontal system deficits are clearly present in Korsakoff patients (Oscar-Berman, 2000; Oscar-Berman and Evert, 1997; Sullivan, 2000), as evidenced both by their brain pathology (Harper, 1998) and by the results of comparative neuropsychological studies that have used behavioral tests that are highly sensitive to frontal lobe damage in human and nonhuman animals alike (Oscar-Berman and Bardenhagen, 1998). Although neuroimaging and neuropsychological test results have confirmed frontal system damage in Korsakoff patients, the findings have been less conclusive regarding non-Korsakoff alcoholics (Oscar-Berman, 2000). However, few studies have directly compared groups of Korsakoff and non-Korsakoff alcoholics on measures of prefrontal integrity (Krabbendam et al., 2000). The primary purpose of this study, therefore, was to compare the contributions of prefrontal neurobehavioral dysfunction in alcoholics with and without Korsakoff's syndrome.

Frontal deficits in alcoholics are most pronounced in older individuals (over 50 years of age). Neuropathologic analyses provided some of the earliest insights into the relationship between alcoholism and aging. Courville (1966) noted cerebral atrophy in postmortem analyses of brains of alcoholics; the pathology resembled the brain shrinkage that occurs with normal chronological aging. The atrophy was most prominent in the frontal lobes, and it extended back to the parietal lobes. These findings were replicated by others who reported abnormal ventricular enlargement and widening of the cerebral sulci of alcoholics in relation to increasing age (Pfefferbaum and Rosen-bloom, 1993). Additionally, Pfefferbaum et al. (1997) conducted regional magnetic resonance imaging analyses of cortical integrity and found evidence that the frontal lobes were especially vulnerable in both young and old alcoholics and that this cortical loss was exacerbated in elderly people. Other studies of frontal lobe function with older alcoholics have confirmed reports of a correlation between impaired neuropsychological performance (e.g., executive control skills) and decreased frontal lobe perfusion or metabolism (Adams et al., 1993, 1998).

Because frontal deficits in alcoholics are most pronounced after age 50 and because frontal changes occur with normal chronological aging (Parkin and Java, 1999; for reviews, see Oscar-Berman and Schendan, 2000; Rourke and Loberg, 1996; Sullivan, 2000), another goal of this study was to measure whether the manifestations of alcoholism and aging are similar or synergistic. If the effects of alcoholism and aging are similar, alcoholics will evidence cognitive decline regardless of the age at which problematic drinking began (Eckhardt et al., 1980; Noonberg et al., 1985). If the effects of alcoholism and aging are synergistic, vulnerability to alcoholism-related brain damage will be magnified in problematic drinkers over age 50, after the normal manifestations of aging generally begin (Jones and Parsons, 1971; Klisz and Parsons, 1977). Thus, older people who have abused alcohol would experience proportionately greater age-related cognitive decline than their nonalcoholic peers, whereas younger alcoholics would show no cognitive impairments relative to younger control participants. In Korsakoff's syndrome, the question of similarity versus synergism of alcoholism and aging is especially important because most Korsakoff patients are over 50 years of age, and their frontal deficits may be confounded by age (Oscar-Berman and Evert, 1997). The approach we took was to administer neuropsychological tests that are sensitive to detecting prefrontal brain damage in groups of alcoholic patients and nonalcoholic controls

(NC) between the ages of 26 and 83 years; alcoholics with Korsakoff's syndrome ranged in age from 52 to 74 years.

Another neuropsychological characteristic common to alcoholics and elderly nonalcoholic individuals is that they exhibit a decline in visuospatial abilities (Oscar-Berman and Schendan, 2000; Parsons, 1996; Rourke and Loberg, 1996). In fact, decline in visuospatial competence in these two populations was an important line of evidence behind the notion that alcoholism may lead to premature aging of the central nervous system (Oscar-Berman and Schendan, 2000; Wilkinson and Carlen, 1982). Because the right hemisphere (RH) of the brain is more involved than the left hemisphere in visuospatial functions, in this study we also included a group of patients with RH damage. The RH patients provided baseline comparison data for visuospatial decline resulting from alcoholism and aging, and they also served as a control group for the effects of brain damage unrelated to alcoholism.

# METHODS

## Subjects

Seventy-seven men and 67 women participated in this study (Table 1). All of the participants were right-handed, native English speakers from the Boston area, with comparable socioeconomic backgrounds. They comprised the following 4 groups: (1) 50 abstinent non-Korsakoff alcoholics (AL; 33 men) aged 30 to 71 years; (2) 6 male Korsakoff patients aged 52 to 74 years; (3) 6 patients (4 men) with RH lesions due to cerebrovascular disease, aged 56 to 71 years; and (4) 82 healthy NCs (34 men) aged 26 to 83 years. The damage in three of the RH patients (two men) was in the right frontal region, and in the other three patients (two men), the damage was located in the right parietal region.

Participation of the subjects was solicited from advertisements and from the Neurology, Psychology, Psychiatry, Medical, and Outpatient Services of Boston University Medical Center; the Department of Veterans Affairs Healthcare System Boston Campus; and Veterans Affairs aftercare programs in the Boston area. Informed consent for participation in the research was obtained from each subject before testing (and from patients' representatives, when needed), and participants were reimbursed for time and travel expenses. Complete evaluation of each subject typically required 7 to 9 hr of testing over a minimum of 2 days, although the Korsakoff and RH patients often required more time. The participants were given frequent breaks, and a session was discontinued and rescheduled if a subject indicated fatigue.

A medical history interview and a vision test were administered to the participants, as was a series of questionnaires (e.g., handedness; alcohol and drug use) to ensure that they met the inclusion criteria for the study. All but the Korsakoff and RH groups were also given a computer-assisted, shortened version of the Diagnostic Interview Schedule (Robins et al., 1989), which provides lifetime psychiatric diagnoses according to DSM-IV (American Psychiatric Association, 1994) criteria. Participants were excluded if any source (i.e., Diagnostic Interview Schedule scores, hospital records, referrals, or personal interviews) indicated that they had one of the following: a history of neurological dysfunction (e.g., major head injury with loss of consciousness longer than 15 min, stroke, epilepsy, or seizures unrelated to alcohol withdrawal); electroconvulsive therapy; major psychiatric disorder (e.g., schizophrenia or primary depression); symptoms of depression within the 6 months before testing; current use of psychoactive medication; history of abuse of drugs besides alcohol; clinical evidence of active hepatic disease; history of serious learning disability or dyslexia; and uncorrected abnormal vision or hearing problem.

All participants were given a structured interview in which they were questioned about their drinking patterns. Information was obtained about length of abstinence and the number of years of heavy drinking (quantified as more than 21 drinks per week). A Quantity-Frequency Index (QFI), which takes into consideration the amount, type, and frequency of use of alcoholic beverages either over the last 6 months (for the nonalcoholics) or over the 6 months preceding cessation of drinking (for the alcoholics), was calculated for each participant (Cahalan et al., 1969). Alcoholic subjects met DSM-IV (American Psychiatric Association, 1994) criteria for alcohol abuse and dependence for at least 5 years, and they had abstained from alcohol use for at least 4 weeks before testing.

The Wechsler Adult Intelligence Scale, Revised edition (WAIS-R) (Wechsler, 1981), the Wechsler Memory Scale, Revised edition (WMS-R) (Wechsler, 1987), and the Hamilton (1960) depression scale also were administered to all participants. Demographic information and other characteristics of the research participants are provided in Table 1.

## Procedures

Five tests were administered to assess several aspects of frontal system functioning (Lezak, 1995; Spreen and Strauss, 1998): Trail Making Test versions A and B (US Army, 1944); Wisconsin Card Sorting Test (WCST) (Berg, 1948; Grant and Berg, 1948); Controlled Oral Word Association Test (FAS test) (Spreen and Strauss, 1998); Ruff Figural Fluency Test (RFFT) (Ruff, 1988); and Progressive Planning Test (PPT) (Kodituwakku et al., 1995). Table 2 lists the five tests, as well as the various measures derived from each of them.

The Trail Making Test A is a test of sequential motor ability that requires individuals to connect an ordered series of numbered circles. The Trail Making Test B adds a cognitive flexibility/mental-tracking component to the task by requiring the subject to alternate between number and letter series (1, *A*, 2, *B*, and so on). The WCST was administered to examine perseverative responding and to measure concept formation. This test was administered manually and was scored with a computer program (Heaton et al., 1993). Verbal and figural fluency were assessed with the FAS test and the RFFT, respectively. The FAS requires subjects to name as many words as they can with the letter *F* (then *A*, and then *S*) within 60 sec. In the RFFT, subjects must connect dots to make as many unique patterns as possible within a specific time period. The fifth test, the PPT, was used as a measure of problem-solving ability. In the PPT, performance was timed, and subjects were required to move three or four beads from an initial position to a new position, with a specified order, while observing two rules: move only one bead at a time, and do not return beads to the original stick once they are removed. There were eight three-trial problems that began simply and became increasingly more difficult.

Of particular interest because of their special putative sensitivity to frontal system dysfunction were the following five measures: time to complete the Trail Making Test B, percentage of perseverative responses on the WCST, percentile score on the FAS test, the number of unique designs on the RFFT, and the total score on the PPT.

## RESULTS

Data were analyzed with StatView and SAS version 8 (SAS Institute, Cary, NC). Linear regression analyses were used to determine whether age or education was significantly related to the outcome variables. Our major interest centered on comparisons involving alcoholics (with and without Korsakoff's syndrome). Therefore, the first regression analyses involved comparisons among the NC and alcoholic groups with and without Korsakoff's syndrome. In cases in which age or education was significantly related to an outcome variable, we determined the significance of the interaction of Age and Education with Group. When there were significant Group × Age or Group × Education interactions, separate linear regression analyses were performed with age and education as predictor variables for each of the groups. The only significant interaction of Group × Age occurred for Picture Arrangement [$F(2,131) = 4.40$; $p = 0.01$], although the percentage of perseverative responses on the WCST approached significance [$F(2,132) = 2.81$; $p = 0.06$]. The only significant interaction of Group × Education occurred for time on Trail Making Test B [$F(2,131) = 4.96$; $p < 0.01$]. No other interactions were significant, and they were removed from the regressions. The analyses were then rerun, controlling for age and education and treating the NCs as the reference group for determining the main effects of Group and Age. Thus, by regressing the resulting age-adjusted (and education-adjusted) scores, we were able to determine the effects of these variables in relation to alcoholism (with and without Korsakoff's syndrome), having taken normal aging (and education) into account. An analogous approach was taken when comparing the Korsakoff and RH groups; no significant Group × Age or Group × Education interactions were observed. In addition to the regression analyses, ANOVAs were performed to compare the Korsakoff and RH groups with subgroups of age- and education-equivalent AL and NC subjects (aged ≥50 years), followed by Scheffé post hoc pairwise comparisons. For significant variables in the results reported below, we provide *F* statistics of the overall models, as well as multiple partial *t* test statistics and *p* values.

### Measures of Prefrontal Functioning

Performance on each of the five tests sensitive to frontal system dysfunction (Trail Making Test, WCST, FAS, RFFT, and PPT; Table 3) will be addressed in turn. As noted previously, of particular interest were the following five measures: time to complete Trail Making Test B, percentage of perseverative responses on the WCST, percentile score on the FAS test, number of unique designs on the RFFT, and total score on the PPT. Results of other measures acquired with the five frontal tasks also are reported when significant effects were observed.

**Trail Making Test—**As noted previously, initial regression analyses revealed a significant interaction between time on Trail Making Test B and education [$F(2,131) = 4.96$; $p < 0.01$].

Subsequent analyses showed that performance by the AL group was significantly related to education ($t = 2.80$; $p < 0.01$). That is, the time on Trail Making Test B decreased as a function of education in the AL group, but this was not significant for the NC, Korsakoff, or RH groups. Group main effects were also significant for time on Trail Making Test B [$F(4,133) = 24.48$; $p = 0.0001$] and on Trail Making Test A [$F$(3,134 = 13.55; $p = 0.0001$]. The Korsakoff group spent the most time on Trail Making Test A and B, with RH patients the next slowest group. The Korsakoff patients were significantly slower than the AL and NC groups on both versions of the test ($t > 4.36$; $p = 0.0001$), and the RH group was significantly slower than the NC group on Trail Making Test B ($p = 0.05$). The difference between the Korsakoff and the RH groups was significant only for Trail Making Test A ($t = 2.62$; $p < 0.05$). Finally, age was found to play a significant role in the performance of both the AL and NC groups on the Trail Making Test, indicating that older subjects responded more slowly (Trail Making Test B, $t = 3.62$, $p < 0.001$; Trail Making Test A, $t = 3.65$, $p < 0.001$).

**WCST—**Although all of the groups performed equivalently on the measure of total correct responses on the WCST, with respect to perseverative response percentiles, there was a significant Group main effect [$F(3,134) = 3.47$; $p < 0.05$]. The Korsakoff group made significantly more perseverative errors overall (reflected as low percentile scores) on the WCST than the AL group ($t = -2.10$; $p < 0.05$), and the RH patients made significantly more perseverative errors (lower percentile scores) than age-equivalent AL and NC subjects ($p = 0.05$). Additionally, the interaction of Group × Age approached significance [$F(2,132) = 2.81$; $p = 0.06$]. Subsequent post hoc analyses suggested that for the AL group, perseverative errors decreased as a function of age (as reflected in increased WCST percentile scores; $t = 4.05$; $p < 0.001$; Fig. 1).

**FAS Test—**On the FAS test, there was a significant Group main effect [$F(4,126) = 11.20$; $p = 0.0001$]. The Korsakoff patients had significantly lower FAS percentile scores than the AL, NC, and RH groups ($t = -5.05$, −5.28, and −3.05, respectively; $p < 0.01$). No other group comparisons were significant.

**RFFT—**There was a significant main effect of Group in the number of RFFT unique designs [$F(4,129) = 9.34$; $p = 0.0001$]. The Korsakoff patients made significantly fewer unique designs than the NC group ($t = -2.51$; $p = 0.01$). The Korsakoff patients also had a significantly higher ratio of unique designs to perseverations when compared with the AL group ($t = 2.39$; $p < 0.05$) and the NC group ($t = 3.37$; $p = 0.001$). No other group differences were statistically significant.

**PPT—**There was a significant Group main effect in the comparisons among the four age-equivalent groups [Korsakoff, non-Korsakoff alcoholics, NCs, and RH; $F(3,39) = 2.84$; $p < 0.05$] on the PPT total score, but post hoc comparisons revealed no specific significant group differences on any of the PPT variables.

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### Measures of Visuospatial Functioning

Subtests of the WAIS-R that have been reported to be sensitive to normal aging and to alcohol-related visuospatial dysfunction are Digit Symbol, Picture Arrangement, Block Design, and Object Assembly (Ellis and Oscar-Berman, 1989; Oscar-Berman and Schendan, 2000; Rourke and Loberg, 1996). As was done for the measures of prefrontal functioning, regression analyses were performed to determine the effects of age and education on the four visuospatial outcome variables for the alcoholic and NC groups, and ANOVA was used to compare age- and education-equivalent subgroups of AL and NC subjects with the Korsakoff and RH groups. We expected the performance by the Korsakoff and AL groups to most resemble that of the RH patients on these tests.

The regression analyses revealed a significant Group × Age interaction for Picture Arrangement [$F(2,131) = 4.40$; $p = 0.01$], but no group comparisons were significant. A significant Group main effect was observed for Digit Symbol [$F(4,133) = 8.00$; $p = 0.0001$]; both the Korsakoff and AL groups performed more poorly than the NC group ($t = -3.65$ and $-2.02$, respectively; $p < 0.05$), and the Korsakoff group performed significantly worse than the AL group ($t = -2.71$; $p < 0.01$). When comparing performance levels by the four age-equivalent groups (Korsakoff, non-Korsakoff alcoholics, NC, and RH), we found that the RH group had the lowest scores overall. There was a significant Group main effect for Digit Symbol [$F(3,48) = 11.85$; $p < 0.0001$] and Picture Arrangement [$F(3,48) = 3.01$; $p < 0.05$], but not for Block Design or Object Assembly. Group differences were significant for Digit Symbol only, as described previously.

### Drinking Variables

The following drinking variables were also investigated: QFI, length of abstinence, and number of years of heavy drinking (>21 drinks per week). The QFI (Cahalan et al., 1969) takes into consideration the amount, type, and frequency of use of alcoholic beverages, either over the last 6 months (for the NC group) or over the 6 months preceding cessation of drinking (for the AL group). The QFI for the NC group ranged from 0 to 1.5; the range for the AL group was 0.4 to 26.7. First, we performed regression analyses to determine whether age was significantly related to QFI, abstinence, and years of heavy drinking. Age was related to length of abstinence ($p < 0.001$) and years of heavy drinking ($p < 0.05$), but not to QFI. Subsequent analyses comparing the AL and NC groups on QFI (controlling for age) indicated a significant Group effect [$F(2,129) = 83.66$; $p < 0.0001$]. The AL group consumed more alcohol than the NC group ($t = 12.93$; $p < 0.0001$).

Next, we compared the performance of 31 AL participants with high alcohol intake scores (QFI ≥5) with that of 25 NC participants of comparable age, education, and Hamilton scores. The AL subgroup was impaired on WAIS-R Digit Symbol [$F(1,54) = 5.05$; $p < 0.05$; Fig. 2] and Trail Making Test B *t* score [$F(1,54) = 3.90$; $p < 0.05$]. Thirteen AL individuals with the highest alcohol intake (QFI of ≥10) also performed more poorly on WMS-R Visual Reproduction II compared with 13 matched NCs [$F(1,24) = 5.78$; $p < 0.05$].

With respect to abstinence, results indicated that short periods of sobriety were associated with lower scores on some tests, whereas long periods of sobriety were not. Thirteen ALs with less than 3 years of sobriety were compared with 13 NCs of equivalent age, education, and Hamilton depression scores (Fig. 2). Significant group differences were found on the WAIS-R Digit Symbol subtest [$F(1,24) = 4.98$; $p < 0.05$], as well as on three memory measures from the WMS-R: General Memory [$F(1,24) = 4.39$; $p < 0.05$], Verbal Memory [$F(1,24) = 4.85$; $p < 0.05$], and Logical Memory I [$F(1,24) = 5.66$; $p < 0.05$]. When ALs with 5 years of sobriety or less were compared with controls of equivalent age, education, and Hamilton scores ($n = 18$ for each group), only WAIS-R Digit Symbol remained significantly lower in the AL group [$F(1,34) = 5.14$; $p < 0.05$]. Up to 9 years of sobriety was associated with no significant group differences.

When considering the duration of heavy drinking, the ALs who reported drinking more than 21 drinks per week for longer than 20 years ($n = 15$) performed more poorly on WAIS-R Picture Arrangement than 14 matched NCs [$F(1,27) = 12.14$; $p < 0.01$]; those who drank more than 21 drinks per week for 10 or fewer years did not differ from the NC group.

## DISCUSSION

The primary purpose of this study was to compare performance by alcoholics with and without Korsakoff's syndrome on tests of neuropsychological functioning, especially on behaviors controlled by frontal brain systems. As expected, memory measures were highly sensitive to the neurological dysfunction found in Korsakoff's syndrome, but the Korsakoff patients were not globally deficient, as demonstrated by intact performance on several IQ subtests (Table 3). Additionally, the Korsakoff patients clearly demonstrated frontal dysfunction on measures derived from four of the five frontal tasks: Trail Making Test, WCST, FAS, and RFFT. That is, compared with the AL and NC groups, the Korsakoff patients took more time to complete Trail Making Tests A and B, their FAS Percentile Scores were lower, and they had a higher ratio of unique designs to perseverations on the RFFT. The Korsakoff group also made significantly more WCST perseverative errors than the AL group and made significantly fewer RFFT unique designs than the NC group.

The findings from this study support those of other studies of Korsakoff patients that have reported clinical and laboratory signs associated with damage to the frontal cortex, such as emotional apathy, disinhibition, and abnormal response perseveration (Kopelman, 1995; Moselhy et al., 2001; Oscar-Berman and Evert, 1997). Research adapting tests highly sensitive to frontal lobe damage in nonhuman primates (comparative neuropsychological tests; Oscar-Berman and Bardenhagen, 1998) also strongly supports the view of frontal system dysfunction in alcoholic Korsakoff's syndrome.

Findings from neuropathologic and neuroimaging studies support the neurobehavioral findings of this study (for reviews, see Oscar-Berman, 2000; Sullivan, 2000). For example, Hunter et al. (1989) measured cerebral blood flow in Korsakoff patients. In comparison to NC subjects, Korsakoff patients showed a trend toward reduced blood flow in frontal regions. The Korsakoff patients showed several significant correlations between the degree of flow reduction in the prefrontal cortex and the degree of impairment on memory and orientation tests (decreased flow corresponded to increased impairments). Hunter (1990) noted that frontal metabolic deficits could mean that a normal tissue mass had reduced neuronal activity or that a reduced tissue mass had normal activity levels—or some of both. Hunter further noted that because some computed tomographic and neuropathologic studies point to structural loss of gray and white matter in the frontal lobes of Korsakoff patients, the metabolic impairment in this region, probably at least in part, reflects reduced tissue mass.

Paller et al. (1997) used positron emission tomography to measure regional cerebral metabolism in Korsakoff patients performing a continuous recognition test. The investigators found severe memory impairment in delayed recognition by the Korsakoff patients, along with widespread decline in glucose metabolism in frontal, parietal, and cingulate regions (but not in the hippocampus), thereby providing further evidence that cortical and neuropsychological abnormalities are related.

Researchers have reported frontal deficiencies in non-Korsakoff alcoholics. For example, in a study of regional cerebral blood flow (Adams et al., 1993), the investigators reported hypometabolism in the medial frontal region of alcoholics. Significant correlations were found (1) between frontal lobe metabolism and errors on a test sensitive to frontal lobe damage and (2) between cerebral metabolism and atrophy of the medial frontal cortex on computed tomographic or magnetic resonance imaging scans. Other studies have validated reports of a correlation between impaired neuropsychological performance on tests of frontal functioning and decreased frontal lobe perfusion or metabolism in alcoholics (Adams et al., 1995; Gansler et al., 2000; Nicolás et al., 1993; Wang et al., 1993). Thus, investigators have observed expected relationships between reduced frontal brain activity and abnormalities in abilities such as executive control skills. The findings collectively support the view that alcoholism results in impaired metabolic and neurobehavioral functions of frontal brain systems (Hoaken et al., 1998; Oscar-Berman, 2000; Sullivan, 2000).

In concert with results of other neuropsychological studies (Oscar-Berman and Bardenhagen, 1998; Oscar-Berman and Hutner, 1993; Ratti et al., 2002), this study also found some evidence of frontal impairment in alcoholics without symptoms of Korsakoff's syndrome. These findings were related to age. That is, with aging, the AL group performed more slowly on Trail Making Test B, but their perseverative errors decreased on the WCST. Whereas the former finding lends some support to the notion that alcoholism and aging are synergistic, the latter finding does not. When patterns of drinking were considered, the results suggested subtle neuropsychological deficits associated with the quantity of alcohol consumed over long periods of time, the length of sobriety before testing, and QFI. Non-Korsakoff alcoholics with long periods of heavy drinking (at least 20 years) performed poorly on the WAIS-R Picture Arrangement subtest; those with l0 or fewer years of drinking heavily did not demonstrate significant differences on any task. Alcoholic participants with fewer than 3 years of sobriety had lower scores on WMS-R General Memory, Verbal Memory, and Logical Memory I and on WAIS-R Digit Symbol than matched controls. Those with fewer than 5 years of abstinence displayed significant differences only on Digit Symbol. Finally, the alcoholics with a QFI of 5 or more were significantly impaired on Digit Symbol and the Trail Making Test B *t* score; those with a QFI greater than 10 had significantly lower scores on WMS-R Visual Reproduction.

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In differentiating non-Korsakoff alcoholics from age-equivalent controls on visuospatial tasks, only the WAIS-R Digit Symbol consistently detected deficits; non-Korsakoff alcoholics and RH patients were equally impaired. The pattern of RH deficits on the visuospatial tasks likely reflects the small sample size and individual differences in the location of the RH lesions. RH patients also demonstrated evidence of frontal impairment and visuospatial difficulties. However, as expected, the overall RH performance profile was not similar to that of the alcoholics. Interestingly, the Digit Symbol subtest differentiated non-Korsakoff alcoholics from Korsakoff patients, with the Korsakoff patients being more impaired. Further, non-Korsakoff alcoholics with high QFI scores and those with three or fewer years of sobriety performed most poorly on the Digit Symbol. The Digit Symbol has been found to be highly sensitive to multiple forms of cognitive dysfunction (Lezak, 1995). Therefore, it is not surprising that this particular measure would yield significant differences across the groups tested. However, the results also suggest a relationship between drinking history and neuropsychological impairment that should be further investigated.

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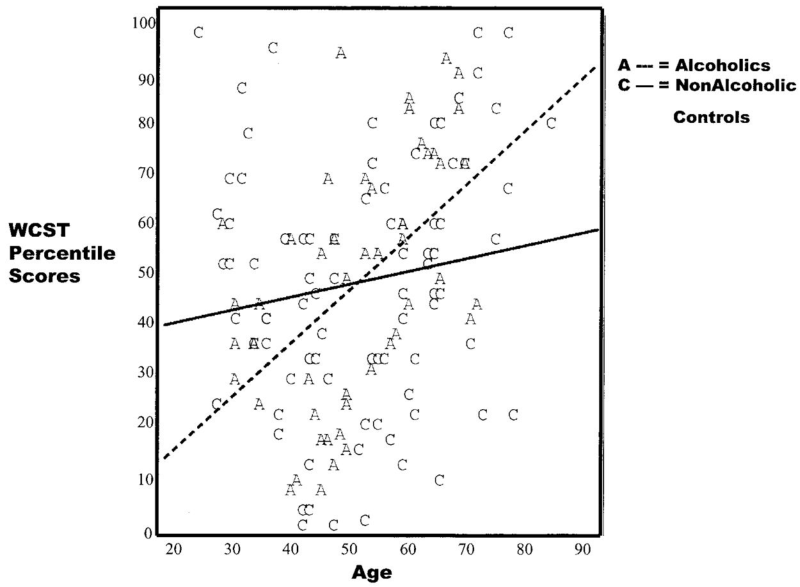


**Fig. 1.**
WCST perseverative responses (percentiles) for the non-Korsakoff alcoholic (A) and nonalcoholic control (C) groups as a function of age.

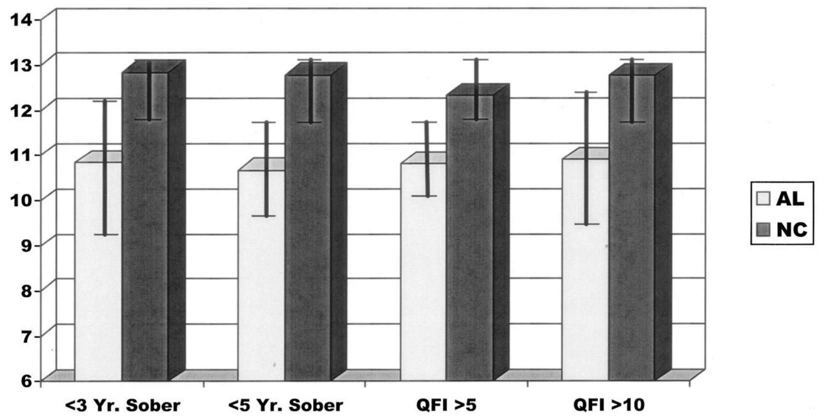


**Fig. 2.**
Digit Symbol performance by non-Korsakoff alcoholic (AL) and matched nonalcoholic control (NC) groups. Scores of the AL participants are related to years of sobriety and QFI (see text for explanation).

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## Table 1

Characteristics of the Research Participants

| Variable | Nonalcoholic controls (NC) (*n* = 82) | Non-Korsakoff alcoholics (AL) (*n* = 50) | Korsakoff patients (K) (*n* = 6) | Right hemisphere patients (RH) (*n* = 6) | Significant group differences |
|---|---|---|---|---|---|
| Age (years) | | | | | |
| Mean (SD) | 52.2 (14.1) | 51.6 (11.3) | 64.5 (7.5) | 62.2 (5.8) | |
| Range | 26–83 | 30–71 | 52–74 | 56–71 | |
| Education (years) | | | | | |
| Mean (SD) | 15.6 (2.2) | 14.6 (2.8) | 10.2 (2.6) | 11.8 (5.7) | K < AL; K < NC; RH < NC |
| Range | 12–21 | 9–23 | 8–14 | 6–22 | |
| WAIS-R Full Scale IQ | | | | | |
| Mean (SD) | 109.8 (11.9) | 108.5 (13.5) | 91.8 (3.7) | 94.8 (16.0) | K < AL; K < NC; RH < NC |
| Range | 81–143 | 83–142 | 87–98 | 79–124 | |
| WAIS-R Verbal IQ | | | | | |
| Mean (SD) | 111.4 (12.2) | 108.7 (12.0) | 89.3 (4.7) | 98.3 (19.0) | K < AL; K < NC |
| Range | 88–150 | 83–135 | 83–97 | 80–133 | |
| WAIS-R Performance IQ | | | | | |
| Mean (SD) | 105.7 (11.0) | 106.0 (13.6) | 98.7 (9.4) | 91.0 (10.0) | RH < NC; RH < AL |
| Range | 75–130 | 76–139 | 84–113 | 80–107 | |
| Hamilton Depression Scale | | | | | |
| Mean (SD) | 1.0 (1.8) | 2.0 (2.4) | 2.8 (3.3) | 1.3 (1.2) | |
| Range | 0–10 | 0–9 | 0–9 | 0–3 | |
| Years of drinking ≥21 drinks per week | | | | | |
| Mean (SD) | N/A | 16.8 (9.6) | ? | N/A | |
| Range | | 5–40 | | | |
| Length of sobriety (years) | | | | | |
| Mean (SD) | N/A | 7.1 (6.6) | ? | N/A | |
| Range | | 0.2–28.8 | | | |
| Quantity Frequency Index | | | | | |
| Mean (SD) | 0.2 (0.3) | 8.2 (5.6) | ? | 0.4 (0.6) | NC < AL; RH < AL |
| Range | 0–1.5 | 0.4–26.7 | | 0–1.4 | |

N/A, not applicable.

**Table 2**

Measures of Frontal System Functioning

| Test | Measure | |
|---|---|---|
| Trail Making Test (parts A and B) | **1** | Time to completion |
| | **2** | Total number of sequencing errors |
| | **3** | Total number of breaks |
| | **4** | Age- and education-corrected *t* score |
| Wisconsin Card Sorting Test | **1** | Total number of correct responses |
| | **2** | Age- and education-corrected percentile ranking for error responses |
| | **3** | Age- and education-corrected percentile ranking for perseverative responses |
| | **4** | Age- and education-corrected percentile ranking for nonperseverative errors |
| | **5** | Age- and education-corrected percentile ranking for conceptual level responses |
| | **6** | Total number of categories completed |
| | **7** | Total number of failures to maintain set |
| Controlled Oral Word Association Test (the FAS test) | **1** | Total words produced for *F*, *A*, and *S* |
| | **2** | Total number of perseverations |
| | **3** | Age- and education-corrected percentile rank |
| Ruff Figural Fluency Test | **1** | Total number of unique designs |
| | **2** | Total number of perseverations |
| | **3** | Error ratio (number of perseverations to unique designs) |
| | **4** | Total number of strategies used |
| Progressive Planning Test | **1** | Highest item achieved |
| | **2** | Planning score |
| | **3** | First trial score |
| | **4** | Average latency over trials |

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## Table 3

Comparisons Among the Groups on the Tests of Prefrontal and Visuospatial Functioning. For Each of the Measures, Significant Effects Are Listed in the Table and Described Further in the Text

| Variable | Nonalcoholic controls (NC; *n* = 82) | Non-Korsakoff alcoholics (AL; *n* = 50) | Korsakoff patients (K; *n* = 6) | hemisphere patients (RH; *n* = 6) | Significant group differences |
|---|---|---|---|---|---|
| Prefrontal functioning | | | | | |
| Trails A time, mean (SD) | 35.28 (16.91) | 35.26 (13.86) | 68.83 (21.31) | 42.50 (18.17) | K < AL; K < NC; K < RH |
| Trails B time, mean (SD) | 65.07 (26.12) | 74.50 (23.33) | 172.17 (97.58) | 162.00 (148.73) | K < AL; K < NC; RH < NC |
| WCST perseverative response percentiles, mean (SD) | 48.81 (25.42) | 48.96 (24.43) | 42.50 (25.07) | 24.67 (24.48) | K < AL; RH < NC; RH < AL |
| FAS percentile score, mean (SD) | 76.71 (22.00)[a] | 71.20 (24.41)[b] | 28.83 (28.87) | 63.33 (32.41) | K < AL; K < NC; K < RH |
| Ruff unique designs, mean (SD) | 80.31 (21.89)[c] | 78.23 (25.86)[c] | 41.00 (8.03) | 53.67 (22.05) | K < NC |
| Ruff ratio: unique designs to preservations, mean (SD) | 0.12 (0.13)[c] | 0.14 (0.19)[c] | 0.44 (0.37) | 0.18 (0.17) | K > AL; K > NC |
| PPT total score, mean (SD) | 34.38 (9.55)[d] | 32.83 (12.92)[e] | 18.83 (9.66) | 23.25 (11.27)[c] | |
| Visuospatial functioning | | | | | |
| WAIS-R Digit Symbol, mean (SD) | 12.23 (2.64) | 11.10 (2.44) | 7.33 (1.75) | 9.00 (2.61) | K < AL < NC |
| WAIS-R Picture Arrangement, mean (SD) | 10.87 (2.38) | 11.80 (2.77) | 9.50 (1.05) | 8.00 (2.61) | |
| WAIS-R Block Design, mean (SD) | 11.09 (2.45) | 10.56 (2.57) | 10.67 (2.16) | 8.33 (1.51) | |
| WAIS-R Object Assembly, mean (SD) | 11.24 (2.73) | 10.42 (2.95) | 11.00 (2.90) | 9.17 (2.14) | |

Trails, Trail Making Test.

[a] Six subjects had missing data.

[b] One subject had missing data.

[c] Two subjects had missing data.

[d] Eleven subjects had missing data.

[e] Four subjects had missing data.