Journal of the International Neuropsychological Society (1999), **5**, 10–19.

Neuropsychological functioning in cocaine abusers with and without alcohol dependence

JANE E. ROBINSON,[1] ROBERT K. HEATON,[2] AND STEPHANIE S. O'MALLEY[1]

[1]Department of Psychiatry, Yale University School of Medicine, New Haven, CT
[2]Department of Psychiatry, University of California, San Diego, La Jolla, CA

(RECEIVED September 8, 1997; REVISED March 25, 1998; ACCEPTED March 30, 1998)

Abstract

Thirty codependent cocaine and alcohol users were compared with age-, education-, race-, and sex-matched cocaine abusers ($N = 30$) and normals ($N = 30$) using an extended Halstead-Reitan Neuropsychological Test Battery to determine whether cocaine abusers with alcohol dependence were more cognitively impaired than singly addicted cocaine abusers. Tests were grouped and analyzed according to 8 major ability areas. Participants who abused both cocaine and alcohol did not differ from normals on the majority of test measures. An unexpected but consistent finding was the poorer performance of the cocaine sample relative to cocaine and alcohol abusers on measures of complex psychomotor and simple motor functioning (ps $< .001$). Pure cocaine abusers, but not abusers of both cocaine and alcohol, also performed more poorly than normals on a measure of global neuropsychological functioning ($p < .01$). These results are consistent with previous reports of generally mild cognitive dysfunction in cocaine abusers. The findings also suggest that cocaine and alcohol abusers of relatively young ages may be less cognitively impaired than demographically comparable cocaine abusers. Evidence from studies of vascular functioning in abusers of cocaine and alcohol alone and in combination is discussed as possible explanation for these findings. (*JINS*, 1999, *5*, 10–19.)

Keywords: Neuropsychological, Cocaine, Alcohol dependence

INTRODUCTION

Cocaine continues to be one of the most widely abused drugs in the United States, and has been associated with serious neuromedical complications including cerebral vasculitis (Bostwick, 1981), stroke (Brust & Richter, 1977; Levine et al., 1987), seizures (Lundberg et al., 1977; Wetli & Wright, 1979), and intracranial hemorrhage (Cahill et al., 1981). In addition, alterations in cerebral blood flow and perfusion defects associated with chronic cocaine abuse have been reported in studies using PET (Volkow et al., 1988) and SPECT scans (Holman et al., 1991).

Reports of morbidity and mortality associated with cocaine abuse are believed to be the result of changing routes of administration and more intensive patterns of use, including the use of cocaine in combination with other drugs (Adams & Kozel, 1985). Treatment-seeking cocaine abusers are frequently dependent on both cocaine and sedative hypnotic substances, usually alcohol (Miller et al., 1990; Rounsaville et al., 1991). Surveys of the cocaine-abusing population suggest that most cocaine abusers use alcohol to alleviate the unpleasant aftereffects of a cocaine binge, primarily paranoia and agitation (Abelson & Miller, 1985; Chitwood, 1985; Kandel et al., 1985). Coadministration of cocaine and alcohol has also been reported to enhance the euphoria or "high" sought from the cocaine experience, and to ameliorate the dysphoric symptoms of acute abstinence.

Despite accruing evidence that a majority of cocaine abusers simultaneously abuse alcohol, the extant research on the neuropsychological consequences of chronic cocaine abuse has generally examined only primary cocaine abusers or has included heterogeneous samples of polysubstance users. The cognitive effects of simultaneous cocaine and alcohol abuse have not been studied systematically, although the neuropsychological findings in primary cocaine abusers and in alcoholics would suggest that the combined abuse of these drugs may significantly compromise cognitive abilities.

One of the earliest and most consistent neuropsychological findings in recently abstinent primary cocaine abusers has been impairments in memory and attention (Ardila

Reprint requests to: Jane E. Robinson, Yale University School of Medicine, 1 Long Wharf, Box 18, New Haven, CT 06511. E-mail: jane.robinson@yale.edu

https://doi.org/10.1017/S1355617799511028 Published online by Cambridge University Press

et al., 1991; Berry et al., 1993; Herning et al., 1990; Melamed & Bleiberg, 1986; Mittenberg & Motta, 1993; O'Malley et al., 1992; Strickland et al., 1993; Volkow et al., 1988).

Some studies have revealed impaired performance on tests of psychomotor speed (Berry et al., 1993), visuomotor tracking (Melamed & Bleiberg, 1986; Mittenberg & Motta, 1993), cognitive flexibility (Melamed & Bleiberg, 1986; Mittenberg & Motta, 1993), nonverbal problem solving (O'Malley et al., 1992), and abstracting ability (Hoff et al., 1991; O'Malley & Gawin, 1990).

A few investigators have examined cocaine abusers who had longer periods of abstinence. Manschreck et al. (1990) tested 33 cocaine addicts who had been abstinent for approximately 2 months, and found impairment on a measure of verbal memory; however, no deficits were found on other verbal or motor tasks in comparison to a matched normal control group. O'Malley et al. (1990) administered the Halstead–Reitan Battery to 25 matched normal controls and cocaine abusers who were abstinent for an average of 4 months. The cocaine abusers performed more poorly on tests of complex psychomotor and simple motor skills, and verbal memory, although comparison with available norms indicated that memory test scores were in the unimpaired range.

Further evidence of neurocognitive dysfunction associated with cocaine abuse derives from studies employing more selective cognitive assessments. Bauer (1993, 1994) and Roberts and Bauer (1993) have studied the reaction time of cocaine dependent subjects after 1, 3, and 12 weeks of abstinence. Compared to non-drug-dependent controls, the cocaine abusers were found to respond more slowly than controls to auditory tones and visual and auditory discrimination tasks across the 12 weeks. In addition, the cocaine dependent individuals exhibited a mild, stable resting hand tremor that persisted across 12 weeks of abstinence.

The cognitive deficits revealed by neuropsychological studies of cocaine abusers appear to be comparatively mild and more restricted than those reported for alcoholics (Grant, 1987). In their review of 15 studies of alcoholics, Parsons and Farr (1981) reported intact verbal abilities but mild-to-moderate impairment in the areas of abstraction–concept formation, visual–spatial and tactual–spatial construction, and visuomotor speed. Losses in both verbal and nonverbal learning have been reported in several investigations of recently sober alcoholics (Brandt et al., 1983; Butters et al., 1977; Cutting, 1978; Guthrie & Ailed, 1980; Miglioli et al., 1979; Ron et al., 1980; Ryan & Butters, 1980). Impairments are most pronounced among samples of older alcoholics with longer histories of heavy drinking (Grant, 1987). On the other hand, longer periods of abstinence are associated with better cognitive functioning (Adams et al., 1980; Brandt et al., 1983; Fabian & Parsons, 1983; Grant et al., 1979, 1984, 1985).

Chronic cocaine abuse appears to adversely affect memory, concentration, and motor functioning although the findings vary across studies. The conflicting evidence likely results from small sample sizes, limited assessment batteries made up of differing test instruments, a lack of appropriate control groups or use of published norms instead of matched normal control participants, different periods of abstinence at time of observation, and failure to control for other substance abuse disorders. The studies by O'Malley and colleagues (1990, 1992) were the only ones to employ matched normal controls, a comprehensive neuropsychological battery, and exclusion of cocaine abusers with comorbid or premorbid dependence on substances other than cocaine.

In light of the magnitude of concurrent alcohol abuse by cocaine abusers, the present study was undertaken to investigate the neuropsychological functioning of a treatment-seeking population of chronic cocaine and alcohol abusers compared to that of singly addicted cocaine abusers, and normal controls matched on age, sex, race, and education. There is an extensive literature linking coexistent alcohol and drug dependence with poorer functioning and greater impairment (Carroll et al., 1993). Furthermore, the combined use of cocaine and alcohol induces the synthesis of cocaethylene, a metabolite of cocaine formed in the presence of ethanol (Jatlow, 1995). Cocaethylene has been associated with increased rates of morbidity and mortality in simultaneous cocaine and alcohol abusers relative to abusers of either drug alone (Andrews, 1997). Given these findings, we hypothesized that cocaine and alcohol abusers would exhibit greater levels of impairment in neuropsychological functioning than demographically matched abusers of cocaine alone, who would perform more poorly than normal controls matched on these variables.

METHODS

Research Participants

All participants in this study had English as their first language and were educated in the United States. With regard to racial composition, all participants were White or African American.

Cocaine and alcohol abusers

Thirty participants who met DSM–III–R criteria for cocaine and alcohol dependence (CA) were recruited from the Substance Abuse Treatment Unit at Yale University School of Medicine, New Haven, Connecticut ($N = 26$) and the Daytop residential program at Fairfield Hills Hospital, Newtown, Connecticut ($N = 4$). Potential participants were excluded if they had a history of (1) DSM–III–R dependence on drugs other than cocaine and alcohol, (2) intravenous drug use, (3) significant head trauma, (4) significant birth or developmental problems, (5) significant learning problems, (6) major medical disorders, (7) a major DSM–III Axis I psychiatric disorder such as bipolar disorder, major depression, or schizophrenia, or (8) current use of a prescription medication that might affect the central nervous system, including neuroleptics, narcotics, sedative hypnotics, or lithium carbonate.

https://doi.org/10.1017/S1355617799511028 Published online by Cambridge University Press

Participants were high intensity cocaine users who, on average, reported using 16.8 g (*SD* = 17.4) of cocaine per month over the course of 5.1 years (*SD* = 2.8). Seventy-seven percent smoked cocaine freebase, and the remainder administered cocaine intranasally. The mean number of days between last cocaine use and the testing session was 95.8 (*SD* = 110.0; range = 3–355). Sixty percent of the sample reported abstinence from cocaine for at least 30 days prior to testing. High intensity alcohol use also characterized the sample. Their reported average consumption was 114.4 drinks (*SD* = 62.9) per month over the course of 8.8 years (*SD* = 4.9). The mean number of days between the last alcohol use and the testing session was 72.9 (*SD* = 95.5; range = 1 to 330). Fifty percent of participants claimed abstinence from alcohol for 1 month or longer at the time of testing. Eight participants reported using an average of five drinks during the week prior to testing.

Cocaine Abusers

An age-, sex-, education-, and race-matched group of 30 cocaine abusers (C) was selected from a larger group that participated in a previously reported study at the Yale University School of Medicine (O'Malley & Gawin, 1990). The participants had been screened using the selection criteria specified for the sample of cocaine abusers with alcohol problems, except that participants were excluded if they met DSM–III–R criteria for alcohol abuse or dependence. These participants reported using an average of 11.9 g (*SD* = 10.9) of cocaine per month over a period of 4.1 years (*SD* = 2.1). Sixty-seven percent smoked cocaine freebase, and the remaining 33% used cocaine intranasally. The mean number of days between last cocaine use and the test session was 146.3 (*SD* = 244.9; range = 3–1095). Forty-seven percent of this group reported abstinence from cocaine for 30 days or longer at the time of testing. More limited data were available on the pattern of alcohol use among the pure cocaine abusers. While no participant in this sample met DSM–III–R criteria for alcohol abuse or dependence, participants reported using alcohol for an average of 5.3 days (*SD* = 6.3) during the month prior to testing, and a lifetime history of alcohol use of 3.8 years (*SD* = 5.7). There were no data available on the amount of recent or lifetime alcohol use among the pure cocaine abusers. To further assess alcoholic symptomatology across the two groups of cocaine abusers, we compared their scores on the MacAndrew Alcoholism Scale from the Minnesota Multiphasic Personality Inventory (MMPI) (Hathaway & McKinley, 1967).

Normal controls

The normal control sample (NC) was composed of 30 individuals matched with the two foregoing groups on age, sex, education, and race. One-half of the participants were selected from a database of 550 normals who had been administered neuropsychological testing in the laboratories at the University of Colorado, University of Wisconsin, and the University of California at San Diego (Heaton et al., 1986). Potential participants in this group were excluded if they reported a history of excessive alcohol use, a history of intramuscular or intravenous drug use, use of solvents, or use of any drug in a recreational manner for 10 or more days in a month in the past year. Additional exclusion criteria included abnormal birth or developmental history, significant learning problems, significant head trauma, any history of psychotic disorder, or any major medical problem or medication use that may affect the central nervous system. Because this available sample of normals was predominantly White, 15 African-American participants were recruited and tested for the normal control sample. These participants were screened according to the selection criteria specified for the White normal controls.

Procedures

As noted above, the majority of volunteers (*N* = 75) were recruited from the New Haven area. Potential participants were interviewed by an examiner to assess their eligibility for the study and to obtain informed consent. Prior to the day of testing, a complete psychiatric history was obtained on the two samples of cocaine users using the Schedule for Affective Disorders and Schizophrenia (SADS; Endicott & Spitzer, 1978). DSM–III–R criteria were used to make drug and alcohol diagnoses. Other psychiatric diagnoses were classified using DSM–III criteria. Depressive and alcoholic symptomatology were further assessed by the Depression and MacAndrew Alcoholism Scales from the MMPI. Cocaine users also completed an inventory about their pattern of substance use, including route of administration, frequency and intensity of use, and length of abstinence. Volunteers who met criteria for participation in the study were screened by self-report and urinalysis to confirm that they had not used drugs within 72 hr prior to testing. All participants were found to be negative for alcohol use when screened by intoximeter on the day of testing.

Fifteen participants recruited for the NC sample were screened using the selection criteria specified for the normal sample tested at the University of Colorado, University of Wisconsin, and University of California at San Diego.

Neuropsychological Assessment

Participants were administered an expanded Halstead–Reitan Neuropsychological Test Battery (Heaton et al., 1991; Reitan & Wolfson, 1985). In addition to the core Halstead–Reitan tests, the battery was augmented with the Wechsler Adult Intelligence Scale–Revised (WAIS–R; Wechsler, 1981), the Grooved Pegboard Test (Kløve, 1963), the Reitan–Kløve Sensory Perceptual Examination (Reitan & Wolfson, 1985), a modified Aphasia Screening Test (Reitan, 1984) and the Story and Figure Memory Tests (Heaton et al., 1991) to provide a more comprehensive assessment of neuropsychological (NP) abilities. All NP measures were administered according to the standard instructions contained in the various test manuals. In addition, the test examiners were

https://doi.org/10.1017/S1355617799511028 Published online by Cambridge University Press

trained in the testing procedures used to collect the normative sample at the University of Colorado, University of Wisconsin, and University of California at San Diego to further ensure standardized test administration across the three samples. Administration time was approximately 7 hr; participants were paid for their time.

To facilitate comparison of cognitive abilities across and within the three groups, all the raw scores on the NP tests were converted to age, education, and sex-corrected *T* scores based on data from large normative samples (Heaton et al., 1991, 1992). For NC participants in the published normative study *T* scores were normally distributed with a mean of 50 and a standard deviation of 10.

To facilitate presentation and interpretation of results the NP tests were grouped according to the ability area measured by the test (Heaton et al., 1994). Eight ability areas were assessed. The tests that contributed to the assessment of each of these eight ability areas included the following:

1. *Verbal*: Aphasia Screening Test–Verbal, WAIS–R Comprehension, WAIS–R Information, WAIS–R Similarities, and WAIS–R Vocabulary
2. *Abstraction and cognitive flexibility*: Category Test and Trails B
3. *Learning and incidental memory*: Figure Memory Test (Learning), Story Memory Test (Learning), Tactual Performance Test–Location, and Tactual Performance Test–Memory
4. *Memory*: Figure Memory (percent retention after 4-hr delay) and Story Memory (percent retention after 4-hr delay)
5. *Attention*: Rhythm Test, Speech Sounds Perception Test, WAIS–R Arithmetic, and WAIS–R Digit Span
6. *Complex perceptual–motor skills*: Aphasia Screening Test–Spatial Relations, Tactual Performance Test–total time, Trails A, WAIS–R Block Design, WAIS–R Digit Symbol, and WAIS–R Object Assembly
7. *Motor skills*: Finger Tapping Test (dominant and nondominant hands), Grooved Pegboard Test (dominant and nondominant hands), and Hand Dynamometer Test (dominant and nondominant hands)
8. *Sensory abilities*: Sensory Perceptual Examination (right and left errors) and Tactile Form Recognition Test (right and left times)

In addition to these eight major ability areas, we considered two standard summary NP variables from this battery: the WAIS–R Full-Scale IQ and the Average Impairment Rating from the Halstead–Reitan Battery. A third summary score, the *global deficit score*, was computed in order to identify individual participants who were "impaired" on the total test battery. To compute deficit scores, the *T* score on each test was assigned a deficit rating based on the following scale: *T* scores equal to or greater than 40 represented *no impairment* (deficit score = 0); 39–35 *mild impairment* (deficit score = 1); 34–30 *mild-to-moderate impairment* (deficit score = 2); 29–25 *moderate impairment* (deficit score = 3); 24–20 *moderate-to-severe impairment* (deficit score = 4); and below 20 *severe impairment* (deficit score = 5). Deficit scores for all of the tests were then averaged to create a *global deficit score* (GDS) for the entire test protocol of each participant. Recent neuropsychological studies using the deficit score approach have demonstrated its validity in detecting clinically significant impairment (Heaton et al., 1994, 1995).

Statistical Analyses

The distribution of each of the continuous demographic, substance abuse, and NP variables was examined to detect violations of normality or homogeneity of variance. Nonnormally distributed data were transformed by using square root, log, or reciprocal (inverse) transformations until parametric assumptions were met. Nonparametric statistics were used to compare the groups on variables that were categorical or ordered, and when normality and/or homogeneity could not be achieved by transformations.

Multivariate analyses of variance were performed to compare the three groups on the eight NP ability areas. If the multivariate analysis of an ability area was statistically significant, univariate analyses were used to compare the three groups on the individual tests of that domain. Tukey HSD *post-hoc* tests were used to probe significant univariate effects. The summary scores of Full-Scale IQ and average impairment rating (AIR) were also compared *via* univariate analyses of variance, with *post-hoc* comparisons when an ANOVA was significant. Chi-square analyses were used to examine whether the groups differed in the percentage of participants who exhibited at least mild impairment according to GDS.

RESULTS

Table 1 summarizes the demographic characteristics of the three groups, and the substance use characteristics of the cocaine abusers. There were no significant group differences on the matching variables of age, sex, race, and education. The cocaine and alcohol abuse (CA) participants had a lower socioeconomic status than normals (NC) and pure cocaine abusers (C). The C and CA groups were similar in duration and intensity of cocaine use, and in length of abstinence from cocaine prior to testing. The substance abuse groups were also comparable in the number of days that they had used alcohol in the past month. As expected, the CA group had a longer duration of alcohol use and higher scores on the MacAndrew Alcoholism Scale than the pure cocaine abusers, who scored in the nonclinical range on this measure. Cocaine and alcohol abusers also scored higher than normal controls on the depression scale of the MMPI, although all of the group means fell in the normal range of functioning. The cocaine only group did not score signifi-

https://doi.org/10.1017/S1355617799511028 Published online by Cambridge University Press

Table 1. Demographic, substance use, and global cognitive characteristics of participants*

Variable	Group NC	Group C	Group CA	p	Group effects
Demographics					
Age	29.0 (6.7)	28.7 (5.6)	30.1 (6.0)	NS[a]	
Education	13.0 (1.5)	13.0 (1.6)	13.0 (1.9)	NS[a]	
Race, % White	43.3	43.3	43.3	NS[b]	
Sex, % male	53.3	53.3	53.3	NS[b]	
SES[d]	3.6 (1.0)	3.9 (0.8)	4.6 (0.9)	.0001	CA > NC = C
Substance Use					
Days since last used cocaine	—	146.3 (244.9)	95.8 (110.0)	NS[c]	
Amount of cocaine used per month (g)	—	11.9 (10.9)	16.8 (17.4)	NS[c]	
Duration of cocaine use (years)	—	4.1 (2.1)	5.1 (2.8)	NS[c]	
Route of administration					
Freebase (%)	—	33.3	23.3	NS[b]	
Intranasal (%)	—	66.7	76.7		
Duration of alcohol use (years)	—	3.8 (5.7)	8.8 (4.9)	.0001[c]	
Days used alcohol past month	—	5.3 (6.3)	5.4 (9.2)	NS[c]	
MAC–*T* score	—	60.1 (16.9)	71.4 (12.5)	.005[a]	
Cognitive					
Depression–*T* score	53.4 (10.9)	58.1 (11.7)	64.7 (11.9)	.001[a]	CA > NC
Full-Scale IQ	95.4 (17.6)	94.6 (14.6)	93.5 (11.4)	NS[a]	
Average Impairment Rating – *T* score	45.1 (11.4)	41.2 (11.4)	41.2 (8.5)	NS[a]	
Global Deficit Score % Impaired	3.3	26.7	6.7	.01[b]	C > NC = CA

*Values are means (*SD*s) or percentages. NC = normal control; C = cocaine only; CA = cocaine and alcohol. *N* = 30 for each group.
[a]*F* test; [b]χ^2; [c]Kruskal–Wallis test; [d]Socioeconomic status according to Hollingshead and Redlich's Two Factor Index of Social Position.

cantly higher than normals or cocaine and alcohol abusers on this scale.

Group comparisons on the summary measures of global cognitive functioning are also represented in Table 1. There were no significant group differences on the WAIS–R Full Scale IQ, or the AIR from the Halstead–Reitan Battery. We compared rates of global impairment for the three groups using two different strategies. In the first, more conservative comparison a cutpoint was identified that yielded a false positive error rate of approximately 3% within the control group (i.e., a 2-*SD* cut-off). This cut-off corresponded to a GDS of 1.0 or greater, or an average of mild impairment across all component test measures. When this criterion was used, a significantly higher percentage of C participants were impaired in comparison to the other two groups. Approximately 27% of the C group was impaired, *versus* 6.7% and 3.3% of the CA and NC groups, respectively. A more traditional comparison in which a 1-*SD* cut-off (Heaton et al., 1995) was used yielded a nonsignificant finding ($p > .22$) in the same direction.

The multivariate analyses of variance revealed significant differences among the three groups in the areas of complex psychomotor skills, simple motor skills, and attention (see Table 2). There were no significant group differences on measures of verbal skills, abstraction and cognitive flexibility, learning and incidental memory, memory, and simple sensory abilities.

Table 3 presents the results of the univariate analyses used to follow up on significant multivariate analyses of the ability areas. In the area of complex psychomotor skills, the two groups of substance abusers performed significantly worse than normal controls on the Digit Symbol subtest of the WAIS–R. C participants also scored significantly lower than NC and CA participants on the Picture Arrangement subtest of the WAIS–R. The average time to complete Trails A was also poorer for the C group than for the NC group. Finally, C participants made more errors on spatial relations than the NC group ($\chi^2 = 11.60$; $df = 2{,}87$; $p < .003$), and their mean *T* score of 34.7 was in the mildly-to-moderately impaired range.

The C group also scored more poorly on some of the measures of simple motor functioning. While NC and CA participants exhibited normal functioning on the Hand Dynamometer test, the C group scored in the mildly impaired range for grip strength of the dominant hand, and was borderline normal with the nondominant hand; with both hands the C group was significantly weaker than the other two groups. There was also a trend ($p < .06$) for the C group to take longer than the NC group to complete the grooved pegboard with the nondominant hand.

On measures of attention, the C group made significantly fewer errors on the Speech Sounds Perception test than the CA group and even the NC group. There were no other differences among the groups on the attention measures.

https://doi.org/10.1017/S1355617799511028 Published online by Cambridge University Press

Table 2. Results of multivariate analyses of ability areas

Ability	Test	F*	p
Verbal skills	Vocabulary Information Comprehension Similarities Aphasia	1.25	.26
Abstraction–cognitive flexibility	Category Errors Trails B	1.95	.11
Attention	Speech Perception Rhythm Digit Span Arithmetic Picture Completion	3.74	.0002
Learning and incidental memory	Figure Learning Story Learning TPT – Location TPT – Memory	.33	.95
Memory	Story Memory Figure Memory	1.49	.21
Psychomotor	TPT Min/Block Digit Symbol Picture Arrangement Object Assembly Block Design Trails A Spatial Relations	3.15	.0005
Simple motor	Finger Tapping Grip Strength Grooved Pegboard	3.48	.0001
Simple sensory	Perceptual Errors	.57	.5

*Multivariate F. $N = 90$; $df = 2,87$ except for Learning and Memory ability areas because 4 participants were missing Story Learning and Memory data, and 5 were missing Figure Learning and Memory data. $Df = 2,82$ for Learning and Memory.

DISCUSSION

The results of this study do not support the hypothesis of greater levels of neuropsychological impairment in abusers of cocaine and alcohol in combination than in abusers of cocaine alone. However, the hypothesis of poorer neuropsychological performance by cocaine abusers relative to normal controls was supported by the results of the global deficit score comparisons. In addition, group mean comparisons on individual neuropsychological tests demonstrate mild but definite impairment in the psychomotor and simple motor functioning of this group. An unexpected but consistent finding was the poorer performance of the C group relative to CA abusers on the majority of tests in these same ability areas. Although differences between the CA group and normals on measures of psychomotor and simple motor functioning were generally not significant, the CA participants performed more poorly on most of these tests.

The C sample's poorer performance on tests of psychomotor and simple motor ability relative to normal controls reflects a number of specific weaknesses. The marginal performance on the Grooved Pegboard and inefficient completion of Trails A observed in the present sample of pure cocaine abusers is consistent with previously reported evidence of psychomotor slowing in cocaine dependent patients (Herning et al., 1990; O'Malley & Gawin, 1990; Roberts & Bauer, 1993). Decrements in Digit Symbol further suggest psychomotor slowing, and in combination with poorer performance on Picture Arrangement and Trails A relative to the other two groups, point to mild deficiency in sequential organization capacities. The C group's impairment on the spatial relations component of the Reitan–Indiana Aphasia Screening Test suggests an additional mild deficit in spatial construction skills. Finally, the finding of mild impairment on strength of grip in the present cocaine sample has not been observed before but may indicate deficient motor strength in cocaine abusers relative to normals.

Unlike previous investigations, the present study failed to detect significant differences between cocaine abusers and normals on measures of verbal memory functioning. O'Malley and Gawin (1990) noted however, that the verbal memory skills of cocaine abusers, while poorer than that of normals, tend to fall within the normal range, and that memory impairments in cocaine abusers are likely to be very subtle. The findings in the current study tend to support this observation. The pattern of group means for delayed recall of information from the Story Memory Test reflects somewhat poorer retention of verbal information for the two groups of substance users relative to normal controls. Specifically, on average the CA abusers failed to recall 19.2% of learned material after the delay ($SD = 11.4$), as compared to 18.2% for the C group ($SD = 15.5$) and only 11.9% ($SD = 9.0$) for the NC group [$F(2,82) = 2.73$, $p = .07$].

An unexpected result was the significantly better attention and speed of information processing in the cocaine abusers, which was found to be entirely due to their better performance on the Speech-Sounds Perception Test. It seems likely that this finding is due to chance. Consistent with this possibility was the fact that the NC group inexplicably scored quite low on this test when compared to the available external norms (see Table 3). Thus, the difference between the C and NC groups on this test appears to be due to the NC's poor results rather than the C group's especially good performance.

The most notable finding of the present study was the demonstration of poorer neuropsychological performance among singly addicted cocaine abusers compared to codependent cocaine and alcohol users. While this unexpected outcome may represent a chance finding, considerable participant selection and screening efforts were made to control for alternative explanations of the observed neuropsychological differences between these groups. Although there are several premorbid and concurrent factors known to influence the neuropsychological performance of substance abusers, all participants were carefully selected to exclude confounding effects attributable to physical, psychiatric or neurological disease, head injuries, medication, family his-

https://doi.org/10.1017/S1355617799511028 Published online by Cambridge University Press

Table 3. Group mean comparisons on neuropsychological measures (*T* scores)

Ability test	Group *M* (*SD*) NC	C	CA	*F*	*p*	Pairwise comparisons[a]
Psychomotor						
TPT Min/Block	47.9 (12.2)	44.5 (8.8)	44.7 (11.0)	.97	.38	
Digit Symbol	52.1 (10.9)	45.9 (10.7)	43.3 (6.8)	6.56	.002	NC > C, CA
Picture Arrangement	48.5 (9.7)	42.5 (9.6)	49.1 (9.1)	4.50	.01	NC , CA > C
Object Assembly	48.0 (10.6)	48.7 (12.2)	48.7 (8.8)	.04	.96	
Block Design	48.4 (9.7)	45.7 (9.3)	47.3 (11.1)	.57	.57	
Trails A	49.5 (12.8)	40.4 (9.1)	44.8 (8.6)	5.80	.004	NC > C
Simple Motor						
Finger Tapping						
DH	53.9 (10.1)	53.2 (7.4)	53.3 (8.2)	.06	.94	
NDH	56.2 (9.0)	53.9 (7.0)	53.8 (9.5)	.72	.49	
Grip Strength						
DH	48.1 (9.0)	38.9 (8.0)	51.5 (8.6)	16.52	.0001	NC, CA > C
NDH	49.8 (8.5)	41.5 (8.2)	53.4 (7.8)	16.74	.0001	NC, CA > C
Grooved Pegboard						
DH	45.2 (11.6)	41.2 (15.5)	43.5 (11.4)	.74	.48	
NDH	45.5 (11.1)	38.4 (13.5)	40.7 (10.4)	2.88	.06	
Attention						
Speech Perception	42.1 (9.3)	53.9 (12.2)	39.7 (7.2)	18.22	.0001	C > NC, CA
Rhythm[b]	3.9 (.25)	3.9 (.17)	3.9 (.26)	.24	.78	
Digit Span	49.1 (12.3)	52.2 (9.2)	48.2 (9.2)	1.25	.29	
Arithmetic	44.6 (11.3)	44.5 (9.4)	42.7 (9.9)	.33	.72	
Picture Completion	46.1 (10.2)	46.8 (8.1)	46.1 (7.2)	.06	.94	

NC = normal control; C = cocaine; CA = cocaine and alcohol.
DH = dominant hand; NDH = nondominant hand.
[a]Significant differences by Tukey-HSD procedure, following significant ANOVA and overall MANOVA.
[b]A square-root transformation was applied to the distribution of this variable.

tory of severe psychiatric problems, or developmental and learning disabilities. In addition, the samples were matched on demographic variables that correlate highly with neuropsychological performance, and there was no difference between the cocaine groups on the MMPI depression scale. Furthermore, the substance abusers were carefully screened by self-report and, when available, treatment records to exclude individuals with a history of dependence on drugs other than those investigated by the study; they also were proven to be abstinent from cocaine, alcohol, opiates, benzodiazepines, sedative hypnotics, and marijuana at the time of testing.

Despite efforts to control for possible confounding factors that could affect neuropsychological performance of substance abusers, the self-reporting of inaccurate or even false data by drug users can never be fully discounted in studies of substance abuse populations. The existing neuropsychological research on cocaine abusers, however, tends to support the pattern of impairments identified in the present singly addicted cocaine sample. Moreover, the nascent literature on the cognitive effects of dual dependence on cocaine and alcohol lends some support for our counterintuitive finding of less cognitive dysfunction in cocaine and alcohol dependent individuals in the present study. Easton and Bauer (1997) have observed impairments in abstraction and total IQ in singly-addicted cocaine dependent patients relative to alcoholics and patients with dual cocaine and alcohol dependence. In addition, Higgins et al. (1993) found that cocaine and alcohol dependent patients reported less difficulty concentrating and fewer seizures than patients dependent on cocaine alone. Recently, Hersh et al. (1997) found greater validity in estimates of drug use provided by combined cocaine and alcohol users relative to abusers of cocaine alone, and suggested that this may reflect a lesser degree of cognitive impairment among the dually addicted cocaine users.

While the mechanism underlying the majority of neurologic defects observed in cocaine abusers is believed to be of a vascular nature (Fischman et al., 1976; Foltin et al., 1988; Jacobs et al., 1989; Kaye & Fainstat, 1987; Levine et al., 1987; Mody et al., 1988; Pascual-Leone et al., 1991; Rezkalla et al., 1992; Tumeh et al., 1990; Volkow et al., 1988), severe vascular sequelae are generally not seen in alcohol abusers of comparable ages (Johnson et al., 1986; Risberg & Berglund, 1987; Shaw, 1987). Speculations of increased risk for cardiovascular complications in combined cocaine and alcohol users have focused on the role of cocaethylene (Farre et al., 1993; McCance-Katz et al., 1993). However, more recent investigations of the effects of coca-

https://doi.org/10.1017/S1355617799511028 Published online by Cambridge University Press

ethylene in clinical populations (Signs et al., 1996), and healthy volunteers who ingested ethanol after cocaine snorting (Perez-Reyes, 1994) have not observed cardiotoxic effects from cocaethylene. In these samples, cocaethylene attained plasma concentrations that were comparable to those observed in the studies by McCance-Katz et al. (1993) and Farre et al. (1993), but did not alter cardiovascular effects of cocaine (Perez-Reyes, 1994) or had no effect on cardiovascular performance (Signs et al., 1996). Variations in the route of cocaine administration, the order and dose of cocaine or alcohol consumption, and the elapsed time since the last dose of either drug are factors that may contribute to contrasting findings on the effects of cocaethylene. Finally, it is possible that cocaethylene may not be associated with greater neuropsychological consequences than cocaine or alcohol alone.

A second potential mechanism for vascular complications associated with cocaine use has been suggested by recent findings of increased platelet aggregation in cocaine abusers (Kugelmass et al., 1993; Rezkalla et al., 1992; Rinder et al., 1994). By contrast, studies of the effect of alcohol on blood platelets have found that alcohol inhibits platelet aggregation (Deykin et al., 1982; Renaud & DeLorgeril, 1992). If the vasodilating properties of alcohol counteract the cerebrovascular action of cocaine, individuals who abuse cocaine and alcohol in combination might be expected to demonstrate a lesser degree of neurologic and cognitive compromise than those who abuse cocaine alone, at least within the first few years of their addiction. Although a few investigators have recently suggested that perfusion defects are more common in patients dependent on cocaine and alcohol than on cocaine alone, these studies have examined very small numbers of individuals, included patients with extensive histories of polydrug abuse, or did not employ a control group (Holman et al., 1991; Kosten et al., 1997).

Additional research using larger sample sizes is needed to further substantiate the effects of cocaine and of combined cocaine and alcohol abuse on cognitive functioning. In addition, the duration of alcohol use in the cocaine and alcohol abusers in this study was relatively brief compared to participants who were impaired in neuropsychological studies of alcoholics. The possibility that cognitive functioning may be more compromised in cocaine abusers with longer periods of alcohol abuse remains to be investigated.

With these limitations in mind, the results of this study suggest that chronic cocaine abusers may exhibit more cognitive dysfunction than cocaine abusers with concurrent alcohol problems and non-drug-dependent individuals. Interestingly, anecdotal reports from cocaine users indicate that concurrent use of alcohol seems to ameliorate some of the unpleasant effects of a cocaine binge, particularly paranoia, agitation, and sleeplessness. While the findings of this study must be considered preliminary and require replication, they suggest that, at least in the short term, concurrent use of cocaine and alcohol may result in fewer adverse effects of cocaine on cognitive functioning.

ACKNOWLEDGMENTS

This research was supported in part by National Institute on Drug Abuse Center Grant P50-04060 (Thomas Kosten, P.I.), and K02-AA-00107 from the National Institute on Alcohol Abuse and Alcoholism (R.K.H.). This paper was presented in part at the 57th Annual Meeting of the College on Problems of Drug Dependence, Scottsdale, June 10–15, 1995.

REFERENCES

Abelson, H.I. & Miller, J.D. (1985). A decade of trends in cocaine use in the household population. In E.H. Adams & N.J. Kozel (Eds.), *Cocaine use in America: Epidemiologic and clinical perspectives* (pp. 35–49). Washington, DC: NIDA.

Adams, E.H. & Kozel, N.J. (1985). Cocaine use in America: Introduction and overview. In E.H. Adams & N.J. Kozel (Eds.), *Cocaine use in America: Epidemiologic and clinical perspectives* (pp. 1–7). Washington, DC: NIDA.

Adams, K.M., Grant, I., & Reed, R. (1980). Neuropsychology in alcoholic men in their late thirties: One year follow-up. *American Journal of Psychiatry*, *137*, 928–931.

Andrews, P. (1997). Cocaethylene toxicity. *Journal of Addictive Disorders*, *16*, 75–84.

Ardila, A., Rosselli, M., & Strumwasser, S. (1991). Neuropsychological deficits in chronic cocaine abusers. *International Journal of Neuroscience*, *57*, 73–79.

Bauer, L.O. (1993). Motoric signs of CNS dysfunction associated with alcohol and cocaine withdrawal. *Psychiatry Research*, *47*, 69–77.

Bauer, L.O. (1994). Vigilance in recovering cocaine-dependent and alcohol-dependent patients: A prospective study. *Addictive Behaviors*, *19*, 599–607.

Berry, J., van Gorp, W.G., Herzberg, D.S., Hinkin, C., Boone, K., Steinman, L., & Wilkins, J.N. (1993). Neuropsychological deficits in abstinent cocaine abusers: Preliminary findings after two weeks of abstinence. *Drug and Alcohol Dependence*, *32*, 231–237.

Bostwick, D.G. (1981). Amphetamine induced cerebral vasculitis. *Human Pathology*, *12*, 1031–1033.

Brandt, J., Butters, N., Ryan, C., & Bayog, R. (1983). Cognitive loss and recovery in chronic alcoholic abusers. *Archives of General Psychiatry*, *40*, 435–442.

Brust, J.C. & Richter, R.W. (1977). Stroke associated with cocaine abuse. *New York State Journal of Medicine*, *77*, 1473–1475.

Butters, N., Cermak, L.S., Montgomery, B.A., & Adinolfi, A. (1977). Some comparisons of the memory and visuoperceptive deficits of chronic alcoholics and patients with Korsakoff's disease. *Alcoholism: Clinical and Experimental Research*, *1*, 245–257.

Cahill, D.W., Knipp, H., & Mosser, J. (1981). Intracranial hemorrhage with amphetamine abuse. *Neurology*, *31*, 1058–1059.

Carroll, K.M., Rounsaville, B.J., & Bryant, K.J. (1993). Alcoholism in treatment-seeking cocaine abusers: Clinical and prognostic significance. *Journal of Studies on Alcohol*, *54*, 199–208.

Chitwood, D.D. (1985). Patterns and consequences of cocaine use. In E.H. Adams & N.H. Kozel (Eds.), *Cocaine use in America: Epidemiologic and clinical perspectives. NIDA research monograph series, No. 61* (pp. 111–129). Rockville, MD: National Institute on Drug Abuse.

Cutting, J. (1978). Specific psychological deficits in alcoholism. *British Journal of Psychiatry*, *133*, 119–122.

Deykin, D., Janson, P., & McMahon, L. (1982). Ethanol potentiation of aspirin-induced prolongation of the bleeding time. *New England Journal of Medicine*, *306*, 852–854.

Easton, C. & Bauer, L. (1997). Neuropsychological differences between cocaine-dependent, alcohol dependent, and dually-dependent patients. *Psychiatry Research*, *71*, 97–103.

Endicott, J. & Spitzer, R.L. (1978). A diagnostic interview: The schedule for affective disorders and schizophrenia. *Archives of General Psychiatry*, *35*, 837–844.

Fabian, M.S. & Parsons, O.A. (1983). Differential improvements of cognitive functions in recovering alcoholic women. *Journal of Abnormal Psychology*, *92*, 81–95.

Farre, M., De la Torre, R., Llorente, M., Lamas, X., Ugena, B., Segura, J., & Cami, J. (1993). Alcohol and cocaine interactions in humans. *Journal of Pharmacology and Experimental Therapeutics*, *266*, 1364–1373.

Fischman, M.W., Schuster, C.R., Resnekov, L., Shick, J.F.E., Krasnegor, N.A., Fennell, W., & Freedman, D.X. (1976). Cardiovascular and subjective effects of intravenous cocaine administration in humans. *Archives of General Psychiatry*, *33*, 983–989.

Foltin, R.W., McEntee, M.A., Capriotti, R.M., Pedroso, J.J., & Fischman, M.W. (1988). Effects of cocaine, alone and in combination with task performance, on heart rate and blood pressure. *Pharmacology, Biochemistry & Behavior*, *31*, 387–391.

Grant, I. (1987). Alcohol and the brain: Neuropsychological correlates. *Journal of Consulting and Clinical Psychology*, *55*, 310–324.

Grant, I., Adams, K.M., & Reed, R. (1979). Normal neuropsychological abilities of alcoholic men in their late thirties. *American Journal of Psychiatry*, *136*, 1263–1269.

Grant, I., Adams, K.M., & Reed, R. (1984). Aging, abstinence, and medical risk factors in the prediction of neuropsychologic deficit among long-term alcoholics. *Archives of General Psychiatry*, *41*, 710–718.

Grant, I., Adams, K.M., & Reed, R. (1985, February). Long-term neuropsychological recovery in alcoholics. In O.A. Parsons (Chair), *Progress on critical issues in the neuropsychology of alcoholism*. Symposium conducted at the 13th Annual Meeting of the International Neuropsychology Society, San Diego, CA.

Guthrie, A. & Ailed, W.A. (1980). The nature and reversibility of cerebral impairment in alcoholism: Treatment implications. *Journal of Studies on Alcohol*, *41*, 147–155.

Hathaway, S.R. & McKinley, J.C. (1967). Minnesota Multiphasic Personality Inventory: Manual for administration and scoring. New York: Psychological Corporation.

Heaton, R.K., Grant, I., & Matthews, C.G. (1986). Differences in neuropsychological test performance associated with age, education, and sex. In I. Grant & K.M. Adams (Eds.), *Neuropsychological assessment of neuropsychiatric disorders* (pp. 100–120). New York: Oxford University Press.

Heaton, R.K., Grant, I., & Matthews, C.G. (1991). *Comprehensive norms for and expanded Halstead–Reitan Battery: Demographic corrections, research findings, and clinical applications*. Odessa, FL: Psychological Assessment Resources, Inc.

Heaton, R.K., Kirson, D., Velin, R.A., Grant, I., & the HNRC Group (1994). The utility of clinical ratings for detecting early cognitive change in HIV infection. In I. Grant & A. Martin (Eds.), *Neuropsychology of HIV infection* (pp. 188–206). New York: Oxford University Press.

Heaton, R.K., Paulsen, J.S., McAdams, L.A., Kuck, J., Zisook, S., Braff, D., Harris, J., & Jeste, D.V. (1994). Neuropsychological deficits in schizophrenics: Relationship to age, chronicity, and dementia. *Archives of General Psychiatry*, *51*, 469–476.

Heaton, R.K., Grant, I., Butters, N., White, D.A., Kirson, D., Atkinson, J.H., McCutchan, J.A., Taylor, M.J., Kelly, M.D., Ellis, R.J., Wolfson, T., Velin, R., Marcotte, T.D., Hesselink, J.R., Jernigan, T.L., Chandler, J., Wallace, M., Abramson, I., & the HNRC Group. (1995). The HNRC 500—Neuropsychology of HIV infection at different disease stages. *Journal of the International Neuropsychological Society*, *1*, 231–251.

Herning, R.I., Glover, B.J., Koeppl, B., Weddington, W., & Jaffe, J.H. (1990). Cognitive deficits in abstaining abusers. In J.W. Spencer & J.J. Boren (Eds.), *Residual effects of abused drugs on behavior. NIDA Research Monograph*, *101*, 167–178.

Hersh, D., Mulgrew, C., & Kranzler, H. (1997). *The validity of the Timeline Follow-back Interview Assessment of cocaine use in two groups of cocaine abusers*. Manuscript submitted for publication.

Higgins, S.T., Rush, C.R., Bickel, W.K., Hughes, J.R., Lynn, M., & Capeless, M.A. (1993). Acute behavioral and cardiac effects of cocaine and alcohol combinations in humans. *Psychopharmacology*, *111*, 285–294.

Hoff, A., Riordan, R., Alpert, R., & Volkow, N.D. (1991). Cognitive function in chronic cocaine abusers. *Journal of Clinical and Experimental Neuropsychology*, *13*, 60–61.

Holman, B.L., Carvalho, P.A., Mendelson, J., Teoh, S.K., Nardin, R., Hollgring, E., Hebben, N., & Johnson, K.A. (1991). Brain perfusion is abnormal in cocaine-dependent polydrug users: A study using technetium-99m-HMPAO and ASPECT. *Journal of Nuclear Medicine*, *32*, 1206–1210.

Jatlow, P. (1995). Cocaethylene. What is it? *American Journal of Clinical Pathology*, *104*, 120–121.

Jacobs, E.G., Roszler, M.H., Kelly, J.K., Klein, M.A., & Kling, G.A. (1989). Cocaine abuse: Neurovascular complications. *Radiology*, *170*, 223–227.

Johnson, R.H., Eisenhofer, G., & Lambie, G.H. (1986). The effects of acute and chronic ingestion of ethanol on the autonomic nervous system. *Drug and Alcohol Dependence*, *18*, 319–328.

Kandel, D.B., Murphy, D., & Karus, D. (1985). Cocaine use in young adulthood: Patterns of use and psychosocial correlates. In E.H. Adams & N.J. Kozel (Eds.), *Cocaine use in America: Epidemiologic and clinical perspectives* (pp. 76–110). Washington, DC: NIDA.

Kaye, B.R. & Fainstat, M. (1987). Cerebral vasculitis associated with cocaine abuse. *Journal of the American Medical Association*, *258*, 2104–2105.

Kløve, H. (1963). Clinical neuropsychology. *Medical Clinics of North America*, *46*, 1647–1658.

Kosten, T.R., Cheeves, C., Palumbo, J., Seibyl, J.P., Price, L.H., & Woods, S.W. (1997). *Regional cerebral blood flow during acute and chronic abstinence from combined cocaine-alcohol abuse*. Manuscript submitted for publication.

Kugelmass, A.D., Oda, A., Monahan, K., Cabral, C., & Ware, J.A. (1993). Activation of human platelets by cocaine. *Circulation*, *88*, 876–883.

Levine, S.R., Washington, J.M., Jefferson, M.F., Keiran, S.N., Moen, M., Feit, H., & Welch, K.M.A. (1987). "Crack" cocaine-associated stroke. *Neurology*, *37*, 1849–1853.

Lundberg, G.D., Garriott, J.C., Reynolds, P.C., Cravey, R.H., &

Shaw, R.F. (1977). Cocaine related death. *Journal of Forensic Sciences*, *22*, 402–408.

Manschreck, T.C., Schneyer, M.L., Weisstein, C.C., Laughery, J., Rosenthal, J., Celada, T., & Berner, J. (1990). Freebase cocaine and memory. *Comprehensive Psychiatry*, *31*, 369–375.

McCance-Katz, E.F., Price, L.H., McDougle, C.J., Kosten, T.R., Black, J.E., & Jatlow, P.I. (1993). Concurrent cocaine-ethanol ingestion in humans: Pharmacology, physiology, behavior, and the role of cocaethylene. *Psychopharmacology*, *111*, 39–46.

Melamed, J.I. & Bleiberg, J. (1986, August). *Neuropsychological deficits in freebase cocaine abusers after cessation of use*. Paper presented at the American Psychological Association, Washington, DC.

Miglioli, M., Buchtel, H.A., Campanini, T., & deRisio, C. (1979). Cerebral hemispheric lateralization of cognitive deficits due to alcoholism. *Journal of Nervous and Mental Disease*, *167*, 212–217.

Miller, N.S., Gold, M.S., & Belkin, B.M. (1990). The diagnosis of alcohol and cannabis dependence in cocaine dependence. *Advances in Alcohol and Substance Abuse*, *8*, 33–42.

Mittenberg, W. & Motta, S. (1993). Effects of chronic cocaine abuse on memory and learning. *Archives of Clinical Neuropsychology*, *8*, 477–483.

Mody, C.K., Miller, B.L., McIntyre, H.B., Cobb, S.K., & Goldberg, M.A. (1988). Neurologic complications of cocaine abuse. *Neurology*, *38*, 1189–1193.

O'Malley, S., Adamse, M., Heaton, R.K., & Gawin, F.H. (1992). Neuropsychological impairment in chronic cocaine abusers. *American Journal of Drug and Alcohol Abuse*, *18*, 131–144.

O'Malley, S. & Gawin, F.H. (1990). Abstinence symptomatology and neuropsychological impairment in chronic cocaine abusers. In J.S. Spencer & J.J. Boren (Eds.), *Residual effects of abused drugs on behavior. NIDA Research Monograph*, *101*, 179–190.

Parsons, O.A. & Farr, S.D. (1981). The neuropsychology of alcohol and drug use. In S.B. Filskov & T.J. Boll (Eds.), *Handbook of clinical neuropsychology* (pp. 320–365). New York: Wiley.

Pascual-Leone, A., Dhuna, A., & Anderson, D.C. (1991). Cerebral atrophy in habitual cocaine abusers: A planimetric CT study. *Neurology*, *4*, 34–38.

Perez-Reyes, M. (1994). The order of drug-discrimination: Its effect on the interaction between cocaine and ethanol. *Life Sciences*, *55*, 541–550.

Reitan, R.M. (1984). *Aphasia and sensory-perceptual deficits in adults*. Tucson, AZ: Neuropsychology Press.

Reitan, R.M. & Wolfson, D. (1985). *The Halstead–Reitan neuropsychological test battery: Theory and clinical interpretation*. Tucson, AZ: Neuropsychology Press.

Renaud, S. & DeLorgeril, M. (1992). Wine, alcohol, platelets, and the French paradox for coronary heart disease. *The Lancet*, *339*, 1523–1526.

Rezkalla, S., Mazza, J.J., Kloner, R.A., Pillema, V., & Chang, S. (1992). The effect of cocaine on human platelets. *Journal of the American College of Cardiology*, *19*, 322A.

Rinder, H.M., Ault, K.A., Jatlow, P.I., Kosten, T.R., & Smith, B.R. (1994). Platelet alpha-granule release in cocaine users. *Circulation*, *90*, 1162–1167.

Risberg, J. & Berglund, M. (1987). Cerebral blood flow and metabolism in alcoholics. In O.A. Parsons, N. Butters, & P.E. Nathan (Eds.), *Neuropsychology of alcoholism: Implications for diagnosis and treatment* (pp. 64–75). New York: Guilford Press.

Roberts, L.A. & Bauer, L.O. (1993). Reaction-time during cocaine versus alcohol withdrawal: Longitudinal measures of visual and auditory suppression. *Psychiatry Research*, *46*, 229–237.

Ron, M.A., Acker, W., & Lishmen, W.A. (1980). Morphological abnormalities in the brains of chronic alcoholics: A clinical, psychological and computerized axial tomographic study. *Acta Psychiatrica Scandinavica*, *62*, 41–46.

Rounsaville, B.J., Foley, S., Carroll, K., Budde, D., Prusoff, B.A., & Gawin, F.H. (1991). Psychiatric diagnosis of treatment seeking cocaine abusers. *Archives of General Psychiatry*, *48*, 43–51.

Ryan, C. & Butters, N. (1980). Learning and memory impairments in young and old alcoholics: Evidence for the premature-aging hypothesis. *Alcoholism: Clinical and Experimental Research*, *4*, 288–293.

Shaw, T.G. (1987). Alcohol and brain function: An appraisal of cerebral blood flow data. In O.A. Parsons, N. Butters, & P.E. Nathan (Eds.), *Neuropsychology of alcoholism: Implications for diagnosis and treatment* (pp. 129–152). New York: Guilford Press.

Signs, S.A., Dickey-White, H.I., Vanek, V.W., Perch, S., Schechter, M.D., & Kulics, A.T. (1996). The formation of cocaethylene and clinical presentation of ED patients testing positive for the use of cocaine and ethanol. *American Journal of Emergency Medicine*, *14*, 665–670.

Strickland, T.L., Mena, I., Villanueva-Meyer, J., Miller, B.L., Cummings, J., Mehringer, C.M., Satz, P., & Myers, H. (1993). Cerebral perfusion and neuropsychological consequences of chronic cocaine use. *Journal of Neuropsychology and Clinical Neuroscience*, *5*, 419–427.

Tumeh, S.S., Nagel, J.S., English, R.J., Moore, M., & Holman, R.L. (1990). Cerebral abnormalities in cocaine abusers: Demonstration by SPECT perfusion brain scintigraphy. *Radiology*, *176*, 821–824.

Volkow, N.D., Mullani, N., Gould, L., Adler, S., & Krajewski, K. (1988). Cerebral blood flow in chronic cocaine users: A study with positron emission tomography. *British Journal of Psychiatry*, *152*, 641–648.

Wechsler, D. (1981). *Wechsler Intelligence Scale for Adults–Revised*. New York: The Psychological Corporation.

Wetli, C.V. & Wright, R.K. (1979). Death caused by recreational cocaine use. *Journal of the American Medical Association*, *241*, 2519–2522.