Effects of Alcohol in Chronic Cocaine Abuse: A Follow Up Study

Abstract
Alcohol is the substance most commonly abused in combination with cocaine. The present study sought to investigate the possible influence of alcohol abuse in memory improvement during abstinence among chronic cocaine users. Forty-eight subjects were selected and grouped as either cocaine only abusers (COC) or cocaine and alcohol abusers (CA). All subjects were undergoing treatment at a south Florida area residential drug rehabilitation program at the time of testing. Participants were tested at the second week of abstinence (early abstinence) and retested at 2 months (late abstinence). Findings demonstrated that cocaine participants exhibited a similar memory recovery profile in short term memory tasks independently of their history of alcohol abuse. However, significant group differences emerged in delayed memory tasks. On the Rey-Osterrieth Complex Figure (ROCF) delayed memory test the CA group performed significantly worse than the COC group with significantly less improvement in scores during abstinence as well. The reduced score enhancement during abstinence in the CA group was also observed in the California Verbal Learning Test (CVLT) delayed memory variables. The present study suggests that the use of alcohol in combination with cocaine may have an effect on memory recovery with specific impact over long-term memory tasks. These findings may have important treatment implications.

Keywords: Cocaine; Alcohol; Abstinence; Memory; Neuropsychology

Introduction
A major setback in examining the primary effects of a particular substance on cognitive function in a drug abusing population is that a significant percentage of these individuals will often abuse several drugs simultaneously. At times this problem may go undetected due to a dependence on self-reported primary drug abuse and the lack of any detailed investigation into an individual's drug history. Other times, even in the presence of a history of significant polydrug abuse, those drugs not the focus of investigation may be understated or deemed irrelevant to the study at hand.

The National Survey on Drug Use and Health (NSDUH) reported that in 2009 approximately 22.5 million people aged 12 or older were classified either as having a substance abuse problem or as being dependent upon a psychoactive drug. Of the 7.1 million individuals classified as abusing or being dependent on illicit drugs, 1.1 million primarily used cocaine (COC) only. It was also reported that 15.4 million abused or were dependent on alcohol only and that 3.2 million were dependent on or abused both alcohol and one or more illicit drugs [1].

Alcohol is the substance most commonly abused in combination with COC. Several studies have found that between 60 and 80% of those persons that abuse COC also abuse alcohol [2-4]. Additionally, Rubio and associates [5] ran a 4-year follow up study that tracked alcohol dependence levels and cocaine use between heavy drinkers that did not abuse cocaine and heavy drinkers that did abuse cocaine. It was found that after four years of concurrent cocaine and alcohol use, cocaine (CA) participants consumed twice the amount of alcohol compared to the alcohol only group and 67.9% of CA participants met diagnostic criteria for alcohol dependence, compared to only 13.6% for alcohol only users. It has also been suggested that between 50 and 80% of individuals who display a pattern of alcohol use disorder also exhibit signs of severe cognitive impairment [6]. Given that such a potential exists for an additive and/or possible associated interaction of
combined cocaine and alcohol (CA) abuse [7], research into the neuropsychological effects of COC in recently abstinent abusers can be severely complicated, resulting in overestimations of the level and extent of COC effects on function, as well as the sequelae of COC abuse and dependence.

It is estimated that 57-65% of individuals that abuse COC show signs of cognitive impairment [8, 9]. However, investigations concerning performance on neuropsychological measures by COC abusers repeatedly tend to be contradictory. Differing results in domains such as executive function, attention and concentration, learning and memory, including verbal memory and recall as well as spatial memory and recall are often seen across studies [8, 10-15].

Kelley et al. [11] examined a group of 12 COC patients during the acute stage of withdrawal to assess the drug’s effects on cognitive flexibility using measures of verbal fluency, verbal and spatial memory, as well as attention, a strong measure of executive function. Their results showed significant impairment in the domains of both verbal fluency and verbal memory on both the Controlled Oral Word Association (COWA) and California Verbal Learning Test (CVLT). However, no deficits were seen in the areas of spatial construction and memory on the Rey-Osterrieth Complex figure test (ROCF). Impairment was noted on the color naming portion of the Stroop, revealing some difficulty in the sustained attention aspect of executive function, while none was seen in color-word portion which calls for the inhibiting of contradicting stimuli, i.e. the color of letters as opposed the actual color the letters spell. In a similar study, Hoff et al. [12] also looked at cognitive function in recovering cocaine abusers. Analysis of results from 38 subjects suggested that chronic COC abuse negatively affected some areas of function while others may have improved. As in the study by Kelley et al. [11], Hoff and his associates found impairment in the area of visual memory using the Benton Visual Retention Test (BVRT) when compared to normal controls; however, none was seen on the immediate and delay portions of the Wechsler Memory Scale (WMS) Visual Reproduction. Furthermore, no deficits were revealed in domain of verbal memory as measured using the CVLT, Logical memory or WMS associate learning subset. On the other hand, results from the COWA showed enhanced performance in the domain of verbal fluency, while results varied across measures of executive/frontal lobe function. They reported that scores were significantly better on the Wisconsin Card Sorting Test (WCST) for the number of correct categories completed, while results were similar to those seen in Kelly, et al. on the word-color portion of the Stroop, suggesting preserved frontal lobe function. Lastly Ardila et al. [15] examined 37 crack cocaine (CC) abusers and found significant deficits in a wide range of functions using the WMS, ROCF and verbal fluency tests. Lower scores were seen in the areas of short-term verbal memory and short-term non-verbal visual memory, as well as attention. Using normative data sets, it was estimated that scores ranged between 1 and 2 standard deviations below normal, suggesting moderate, although significant impairment.

Differing outcomes on measures of neuropsychological function seen across studies could be the result of other various contributing factors rather than concurrent CA abuse. Length and frequency of abuse, in addition to dose size [16], level of education, traumatic brain injury (TBI) or other preexisting neurological disorders are among some of the factors that may possibly contribute to the differences seen in the memory and recall as well as other cognitive functions in COC abuse.

Studies by both Hoff et al. [12] and Ardila et al. [15] examined cocaine’s chronic effects using samples of recovered CC abusers only. Each group had an average length of abstinence of approximately 24 and 30 days respectively. Similar exclusion criteria were used as well, (e.g., no preexisting neurological or psychiatric disorders). In addition, Hoff et al. [12] screened for and excluded those who reported dependence on other substances, including individuals that exhibited more than moderate alcohol use. Ardila et al. [15] however did not screen for alcohol abuse, and all participants had previously been polysubstance abusers (PSA), the abuse of three or more substances concurrently (DSM-IV-TR, 2002), before reporting CC as being their primary substance of abuse. Lastly, Kelley and associates [11] study used a small sample of 12 subjects to examine impairment during the early stages of COC withdrawal. Nonetheless, five of the subjects concurrently used other substances, 1 abused opiate, 1 used marijuana daily, and 3 were heavy alcohol users. Equally problematic, two had histories of bi-polar disorder and one had sustained a head trauma which resulted in loss of consciousness for an unspecified period of time.

Although studies on the effects of cocaine abuse in the area of neuropsychological function are often equivocal with respect to the specific types of deficits observed, which may be or may not be the result of the sensitivity of the instruments used, the vast majority of studies indicate that at some deficits such as attention, learning and memory, and executive function, are commonly reported. A current meta-analysis of the effect size of COC on cognitive abilities found that abusers frequently present a range of deficits, with the greatest impairment seen in the area of attention, followed by spatial memory, verbal fluency and memory, respectively [16, 17]. Jovanovski and associates also included several samples with concurrent diagnoses of alcohol and cocaine abuse, but not dependence, in order to maintain generalizability due to the frequent comorbidity of these substances. Effect size was calculated using 15 studies for a total of 481 cocaine abusers and 586 healthy cocaine naïve controls. Large effects were found in the area of attention, however slightly larger effects were seen in the areas of executive function and visual memory. These later findings in executive function and visual memory may not be unexpected in as much as attention is suspected as being the key element in most domains of cognitive function [18].

The range of deficits seen in chronic alcohol abusers tends to be broad and persistent. Poor learning and memory, problem solving, difficulty in verbal and non-verbal abstractions, visuospatial abilities, impaired executive function as well as slower perceptual motor skills and speed of processing are the most commonly reported persistent cognitive deficits found among chronic alcoholics [19-23], most of which has also been reported in many other studies of illicit psychoactive substances including COC.

Nixon et al. [22] compared the effects of alcohol on both implicit and explicit cueing on memory and recall. A large battery of tests...
which measured various cognitive skills was given to 44 alcoholic subjects as well as to a group of 44 alcohol naive controls. Included in the battery was one test designed to measure associated learning by matching an adjective to a three consonant Tri-gram, as well a degree of learning manipulation meant to control for the problem of environmental context seen in other studies. Analysis demonstrated that alcoholic subjects had significant problems in the areas of learning and memory; they produced more omissions and errors and required more trials to acquire equivalence with controls. Lastly, despite the greater number of trials, the alcoholic groups mean score declined on recall while the controls mean score increased. This decline in mean scores may suggest impairment in the ability to encode and retrieve newly learned information. Likewise, a study of memory and recall conducted by Acheson, Stein, and Swartzwelder [24] had similar results. They found that intoxicated subjects could recall lists of words immediately after they had been presented, but were impaired on recall of these items 20 minutes later. Several other studies have also shown that even a moderate level of alcohol consumption can affect explicit memory tasks, the learning and recall for word lists as well as the learning and recognition of recently presented faces [19, 25].

A study by Leitz and her colleagues [26] also found that memory impairment after acute alcohol use is not only specific to recall, but can also have a deleterious effect on prospective memory. In this study, after 20 participants were administered alcohol, they were given a Virtual Week task that assesses a participant’s ability to remember everyday tasks (i.e., have lunch, go to class, etc.) and irregular tasks, such as, doing laundry by moving a gamepiece on a boardgame with dice. It was found that the alcohol group performed significantly poorer on all of the prospective memory tasks than the control group. These findings indicate a generalized effect of alcohol on memory that is not localized in one type of memory formation.

Some research also suggests a possible long term effect of alcohol abuse on memory formation. Sullivan, Fama, Rosenbloom and Pefferbaum [27] looked at a wide range of neuropsychological function in 43 female alcoholics with a mean sobriety of 3.6 months. Visuospatial and as well as verbal and non-verbal working memory (WM) were the areas most effected; declarative memory and executive function were also affected but only moderately. Medina et al. [28] examined the effects of PSA in 63 women on verbal and visual memory and found a significant problem in the area of verbal learning, but none was seen in visual memory. Their results also indicated a strong relationship between frequent CA abuse and verbal learning, delayed recall and recognition abilities.

Even more telling is a study by Selby and Azrin [29] who examined 355 male prisoners, with a mean of 36 months of abstinence. Participants were classified into four subgroups (three abuse groups): 101 alcohol dependence or abuse, 56 PSA, 60 COC, and a group of 138 substance abuse naïve controls. All were tested on measures of memory, recall and attention. Interestingly results showed that the COC group performed as well as controls. To be more exact, and in contradistinction to many other studies of primary COC abuse, no real impairment was found in this group. Conversely the PSA and A groups performed significantly poorer on most measures of memory and visual skills than either the COC or control group. In addition, those who abused a combination of both cocaine and alcohol performed significantly poorer than those who abused only one of these substances. A correlation between the length of abstinence from drug usage and neuropsychological performance found that the alcohol only group showed greater improvement on individual domains and measures than the PSA or COC groups. However, despite these significant gains, the alcohol group failed to reach parity with either the COC group or controls. Such results as seen in the Selby & Azrin study point to not only greater cognitive dysfunction and poorer recovery among alcoholics, but also greater impairment in those individuals who abuse multiple substances in combination with alcohol.

Not controlling for concurrent substance abuse or dependence, or having not explicitly describing their inclusion or exclusion criteria is seen in other studies as well [3, 11, 14, 30-32]. The frequent use of other neuro-active substances in conjunction with COC can obscure its’ singular effect on neurecognitive function. A major problem, if not the primary in isolating the particular effects of COC, is the widespread concurrent abuse of both cocaine and alcohol.

Interestingly even though the concomitant use of cocaine and alcohol appears to be common, only a small number of studies have investigated the effects of combined CA abuse versus COC only abuse on cognitive function. Horner [32] was one of the first to compare combined CA use to a multiple drug naïve group, in this case a group of “uncomplicated” alcohol abusers, in order to investigate the cognitive sequelae of cocaine abuse in alcoholics. Both groups were tested on several measures of neuropsychological function. Results demonstrated a specific decrement in the areas of immediate and delayed verbal memory in the CA group only; no other group differences were seen. However no follow up testing was performed to assess any possible recovery of function for either group.

On the other hand, Di Sclafani, Tolou-Shams, Price and Fein [33] examined the differential effects of CC and CC plus alcohol (CCA) dependence at 6 weeks and 6 months of abstinence using the computerized MicroCog: Assessment of Cognitive Functioning (MicroCog). A similar effect size for both CC and CCA groups was found on most measures at 6 weeks, with both groups demonstrating similar levels of impairment in most domains compared to controls. Largest effects were seen in the domains of executive function and spatial processing. At six months only a small difference was found in most domains, but remained essentially unchanged. Longitudinal analysis showed improvement in only one domain, immediate verbal memory. However, at six months only 6 of the original 20 CC subjects and 16 of the 37 CCA group were available for retesting to assess the longitude influence of abstinence on functional recovery. This loss was supplemented by recruiting 6 more CC subjects and 12 CCA subjects, unfortunately no pretesting was done on these recruits and no information was given as to the length of abstinence for the supplement participants. Easton and Bauer [23] studied three groups: alcohol only, COC only and CA in the
areas of verbal ability, abstraction and IQ. Significant effects were found for abstraction and IQ; the COC group having the lowest scores. However, no significant differences were found across the three groups on verbal scores. Although Easton and Bauer went to considerable means to test for cocaine and alcohol dependence and to exclude those with major affective or medical disorders, no mention was made of screening for other possible drugs which may affect normal CNS function.

Lastly, in order to confirm the hypothesis that combined CA abuse would result in significantly greater impairment than COC abuse only, Robinson and associates [34] examined 30 COC, 30 CA and 30 controls in 8 areas of function, including verbal skills, cognitive flexibility, attention, learning, and memory. Each area was measured using several tests and the resulting scores were averaged to create a Global Deficit Score (GDS). Multivariate analysis found the COC only group performed better than the CA group and controls on measures of verbal skills, abstraction, cognitive flexibility as well as learning and memory. The COC group did significantly better than the CA group and controls in one area of attention, while no significant difference was detected between the three groups in other areas. Also no significant differences were found in the area of verbal memory between the COC only and controls. Similar results were also found by Lawton-Craddock and colleagues [35] in which they replicated the finding that the CA group performed better than the COC only group in the aforementioned cognitive categories. However, they also found that these differences were present in gross motor speed and grasp strength tasks. Although the researchers carefully selected their subjects to avoid confounding effects such as head injury, medication, family history, and neurological disease, they admit that poorer performance found in the COC only, based on the results previous studies, may be due to chance and small sample size effects.

In summary previous research has suggested that cocaine abusing individuals who also abuse alcohol as well as other substances may be at greater risk for neuropsychological impairment [7-9]. Research also implies that the effects of cocaine alone tend to be mild by comparison to that of alcohol alone [8, 9, 16, 29, 36]. Moreover, these results also suggest a possible additive effect for the dual abuse of cocaine and alcohol compared with COC abuse only. Robinson and associates [34] examined 30 COC, 30 CA and 30 controls in 8 areas of function, including verbal skills, cognitive flexibility, attention, learning, and memory. Each area was measured using several tests and the resulting scores were averaged to create a Global Deficit Score (GDS). Multivariate analysis found the COC only group performed better than the CA group and controls on measures of verbal skills, abstraction, cognitive flexibility as well as learning and memory. The COC group did significantly better than the CA group and controls in one area of attention, while no significant difference was detected between the three groups in other areas. Also no significant differences were found in the area of verbal memory between the COC only and controls. Similar results were also found by Lawton-Craddock and colleagues [35] in which they replicated the finding that the CA group performed better than the COC only group in the aforementioned cognitive categories. However, they also found that these differences were present in gross motor speed and grasp strength tasks. Although the researchers carefully selected their subjects to avoid confounding effects such as head injury, medication, family history, and neurological disease, they admit that poorer performance found in the COC only, based on the results previous studies, may be due to chance and small sample size effects.

This study aims to examine the possible additive effects of alcohol abuse on memory function and recovery in a sample of cocaine dependent individuals at 2 weeks and three months of abstinence. Based on the possible additive and/or interactive effects of dual cocaine and alcohol abuse on functional and structural properties of the CNS suggested by Bond et al. [7], coupled with research that demonstrate relatively mild impairment among individuals who abuse only COC, and the diffuse global cognitive effects in alcohol abusers [16, 21, 36], the following hypotheses were tested: 1) individuals which abuse CA will demonstrate greater impairment in the domains of verbal and visual memory than those individuals that abuse only COC, and 2) CA participants will show poorer recovery in these memory domains after an extended period of abstinence, leading to significant interactions between length of abstinence and substance group favoring those subjects that abuse COC only.

Method

Participants

Forty-eight subjects were selected from a sample of 74 cocaine dependents that had completed both an initial and follow-up assessment in the domains of visual and verbal abilities. All subjects were undergoing treatment at a south Florida area residential drug rehabilitation program at the time of testing. Participants were grouped as either cocaine only abusers (COC) or cocaine and alcohol abusers (CA); see selection and grouping criteria section below. The COC group was comprised of 18 subjects (15 males and 3 females; 9 European Americans, 6 African Americans and 3 Hispanic Americans). The CA group consisted of 30 subjects (25 males and 5 females; 17 European Americans, 12 African Americans and 1 Hispanic American). Age and years of education did not differ significantly between the two groups (Table 1).

Description of the substance history for both groups is presented on Table 2. One-way ANOVA found no significant differences in the age of first drug use for any in category, i.e. alcohol, cocaine, crack or marijuana and in the length of abstinence. There was however a significant divergence in the mean length of alcohol use. Analysis of ordinal categories for alcohol use showed significant differences in alcohol usage patterns for the previous year but no significant group differences were observed for cocaine, crack or marijuana.

Procedures

Prior to collecting individual histories and the initial assessment each potential subject first underwent a preliminary interview to determine eligibility for inclusion. The following inclusion criteria were used: (1) fulfillment of the Diagnostic and Statistical Manual of Mental Disorders IV- text revised (DSM-IV-TR) [37] criteria for cocaine substance dependence; (2) absence of significant neurological or psychiatric antecedents such as brain injury with loss of consciousness for more than 10 minutes, cerebrovascular disease, epilepsy, and psychiatric hospitalizations (different from substance dependence); (3) report of cocaine dependence problems for more than two years. Participants with history of dependence to substances different from cocaine and with
positive HIV history were excluded from the study. Signed consent forms were then collected for all participants that met the preliminary criteria and volunteered to participate in the study. All self-reports were crosschecked with the facility records for consistency. Additionally, participants were given random drug tests by the treatment center, ensuring that none of the participants were abusing drugs at the time of testing (Table 2).

Neuropsychological assessments were carried out by trained research assistants on a one to one basis at the subjects’ respective rehabilitation center. Due to the length of time required to collect individual histories as well as perform testing, approximately 3 hours in total, the interview portion and assessment portion were conducted in two separate ninety minute sessions. Breaks were taken on request. Participants were tested at the second week of abstinence (early abstinence) and retested at 2 months (late abstinence) if they did not relapse. Mean number of days between testing at early abstinence and retesting at late abstinence, for both groups was 106.37 days (SD=37.61).

Selection and grouping criteria

Selection and grouping criteria was based on individual alcohol, cocaine, and crack cocaine usage frequencies for the last one and five years before entering treatment. Subjects were questioned as to the number of times they had used any of the drugs as well as other substances (i.e. opiates, stimulates, barbiturates, lithium or marijuana) in a month, week, and day, or if they never used the substance at all in the previous one and five years before entering treatment. Depending on the subjects’ response, each individuals level of use was coded and recorded using the following rank ordinal scale; 0=never used, 1=only 1-3 times, 2=about 1 time per month, 3=2-3 time per month, 4=about 1 time per week, 5=about 2-6 times per week, 6=1 time per day, 7=about 2-3 times per day and 8=4 or more times per day.

For the COC only group, subjects were selected based on one and/or five-year history of powder cocaine and/or smoked crack cocaine usage frequency of no less than 2-6 times per week and a frequency of alcohol consumption no greater than 1 time per week. For inclusion into the CA group, participants were required to meet the same criteria for cocaine usage as the COC only group and were also required to demonstrate a one and/or five-year history of alcohol consumption of no less than 2-6 times per week. Individuals were excluded if they showed a usage pattern greater than 1 time a week for any other controlled substances. Also, both groups were required to meet the criteria for cocaine dependence, while the CA group must also meet the criteria for alcohol abuse as set forth in the Diagnostic and Statistical Manual of Mental Disorders [37].

Once subject selection was completed, the corresponding groups were compared on factors of age of use, duration of use as well as frequency of substance use in the past one and five years confirm group independence (Table 2).

Despite extensive efforts to exclude other substances from the final samples, it was necessary to include a number of concurrent marijuana users in both groups. Marijuana use on a weekly basis in the previous year before entering rehabilitation accounts for 6 of the COC sample and 10 of the CA sample. None of them, however, met the criteria for Cannabis dependence as described by the DSM-IV-TR [37].

Measures

Visual memory

1) The Rey-Osterrieth Complex Figure test (ROCF) [38, 39] is a widely used measure of long term visual memory that is sensitive to mild neuropsychological impairment [18]. It is frequently used to assess visuospatial processing, memory and executive function in clinical populations. The ROCF is comprised of 18 individual elements that are arranged to form a single complex figure. The test’s format consists of a copy trial, where the subject simply copies the complex figure on to a sheet of paper, and a recall trial which is administrated after a 25-minute interval and giving with no forewarning following the incidental memory paradigm [40, 41]. At recall the subject is required to draw the figure from memory. During the period between trials the participants of the current study were required to perform a verbal fluency task and a trial making task.

The ROCF is scored using the 18 elements which comprise the figure. Each element is scored on scale of 0-2 with, 5 increments; with a total maximum score is 36 points. Inter-rater reliability for the ROCF recall is good, (r=0.91 to 0.98) and test-retest reliability is (r=0.60 to 0.76) [18].

2) The Benton Visual Retention Test (BVRT) [14] is sensitive to visual inattention and provides a measure of immediate visual recall [18]. Participants are presented a series of 10 cards containing various geometric figures. These are presented one at a time for 5 seconds. Immediately after each presentation the subject is required to reproduce the arrangement of figures. The BVRT is scored based the number of correct reproductions as well as the number errors.

The inter-rater reliability for the BVRT number of correct ranges from 0.85 to 0.96 and between 0.93 and 0.97 on error score [18].

Verbal memory

1) The California Verbal Learning Test (CVLT) [42, 43] is designed to measure many aspects of verbal memory ability. Subjects are verbally presented with two “shopping lists” of 16 words each, list “A” and list “B.” Each list contains four semantic categories with four words in each category (e.g. tools, spices & herbs, clothes and fruit). Also the subjects are not made aware of these categories beforehand. Both lists are presented by at a rate of approximately 1 word per second. At the end of each presentation the subject is asked to recall as many words as possible and the results are manually recorded by the examiner.

List “A” is presented 5 times for a total of five trials. After completion of all 5 trials list “B” is presented only once, this more or less acts as a distracter. Immediately after the list “B” task is completed the subject is again asked to recall as many words as possible from list “A,” this is used to evaluate the individuals’ short delay free recall (SDFR). The subject is then asked to recall the words in list “A” using semantic cues representing the four
categories, this portion is called the short delay cued recall (SDCR) and allows the tester to help subjects who failed to do semantic association during the learning trials. After a 25-minute interval, during which the subject is presented with an intervening visual task, their long term memory is assessed using the long delay free recall (LDFR) and long delay cued recall (LDCR) portions of the CVLT. This allows for the gauging of verbal memory consolidation.

Reliability coefficients of 0.77 to 0.86 and of 0.90 for the CLVT have been reported by Delis, Kramer, Fridlund and Kaplan [42] and Lezak et al. [18] respectively.

2) The Digit Forward and Digit Backward subtests of Wechsler Adult Intelligence Scale-Revised (WAIS-R) [44] are commonly used to measure short term verbal memory capacity as well as attention. Both consist of seven two paired sequences of random numbers, with the number of digits increasing with each sequence. Each sequence is read to the subject at a rate of approximately 1 digit per second. The subject is then required to recall the numbers either as presented or in reverse order. Testing is discontinued in each condition, forward condition or backward condition, when the subject fails to recall two sequences in tandem. The effects of practice on Digit span forward is negligible so test-retest reliability ranges from 0.66 to 0.89 and is dependent on the length of the test-retest interval. For all the analyses, the Digit forward and the Digit backward scores were combined into one total Digit span score.

Statistical analysis

Scores of immediate, short and long delay verbal recall as well as immediate and delay visual recall were analyzed using a 2 × 2 mixed factorial ANOVA. Group (CA and COC) was the between subjects factor and is meant to examine the differential effects of dual as opposed to singular substance abuse. Abstinence, the cessation of substance use between trials, was the within subjects factor and was used to assess any differences in improvement of function. Subjects were tested during the early period of abstinence and again after several months of treatment.

All data was analyzed using SPSS software package, with an alpha level of .05 used for all statistical tests. Raw scores were used in all analyses. However, the normative data of each test was used to transform the average mean raw scores into the corresponding percentile scores (Table 3).

Results

Visual memory

Results on the ROCF showed no between group differences in the ability to copy the figure but significant group differences in recalling it (Table 3). The dual cocaine and alcohol abuse group scored significantly lower that the COC alone group. Moreover, a significant interaction demonstrated a medium effect for group X abstinence; while both groups showed improvement in ROCF recall scores from early abstinence to late abstinence; this progress was larger in the COC group than in the CA group (Figure 1). The COC group moved from percentile 10 at early abstinence to percentile 60 at late abstinence. The CA group on the other hand improved from percentile 2 to percentile 10 (Figure 1).

Scores on the BVRT demonstrated a significant within subject’s effect for abstinence in the domain of short term visual memory (Table 3). Participants recalled a significant higher number of geometric figures, and had significant fewer errors the second time they were tested compared to the first one. No significant between group subject effects or interactions were found. It is important to mention that both groups remained at a very low percentile on the BVRT at late abstinence.

Verbal memory

Results show a significant main effect for abstinence (Table 3) in all CVLT measures except for List B. Both groups showed a significant improvement in the total number words recalled on trials 1-5, as well as in the short term and long term CVLT scores. No group effects were significant for any measure on the CVLT. Scores on this memory test were similar between the CA and COC groups. Group × abstinence interactions were significant for both measures of long delay recall with the dual substance abuse group showing less improvement on recovery in the domains of both LDFR (Figure 2) and LDCR (Figure 3). The COC participants scored at the 15th percentile at early abstinence and at the 50th percentile at late abstinence, whereas the CA participants remained at the 15th percentile at late abstinence (Figures 2 and 4).

A significant within subject effect for abstinence and a no significant main group effect were seen on the digit span. In addition, a significant interaction for abstinence and group disclosed that mean scores for the COC group increased while CA means remained equal between first and second abstinence periods (Figure 3).

Discussion

The present study sought to investigate the possible influence of alcohol abuse in memory improvement during abstinence among chronic cocaine users. Findings demonstrated that cocaine participants exhibited a similar memory recovery profile in short term memory tasks independently of their history of alcohol abuse. However, significant group differences emerged in delayed memory tasks. On the ROCFT delayed memory test the CA group performed significantly worse than the COC group with significantly less improvement in scores during abstinence as well. The reduced score enhancement during abstinence in the CA group was also observed in the CVLT delayed memory variables. The present study suggests that the use of alcohol in combination with cocaine may have an effect on memory recovery with specific impact over long-term memory tasks.

Comparison of individual verbal and visual short term memory and learning tests revealed no significant differences between the COC and CA groups. Both group of participants showed similar recovery in BVRT and the CVLT immediate verbal recall and learning tasks. These results are consistent with previous findings [32-34]. Di Scalfani et al. [33] found no differences in immediate verbal and visual memory between crack dependents and crack and alcohol dependents. Moreover, they found that both groups of crack addicted subjects showed the most improvement in immediate memory tasks during an abstinence period of six months. Robinson et al. [34] found no difference
in verbal and non-verbal learning tasks between a group with a single addiction to cocaine and a group of cocaine abusers with alcohol dependence. The negligible influence of cocaine and alcohol combined on immediate memory tasks has also been found when cocaine and alcohol dependents are compared with alcohol dependents only [32].

The most significant finding of the present study is that abstinent cocaine dependent participants without concomitant alcohol abuse had significantly better improvement of ROCF delayed memory scores when compared with cocaine dependent participants with concomitant alcohol use. This same trend of improvement was also observed for the long term delay CVLT scores. Horner [32] found that cocaine and alcohol dependent participants differed from the alcohol dependent ones in the delayed recall of a story but he did not find group differences in the delayed recall of a complex figure. However, Jovanoski et al. [16] found a moderate to large effect sizes for deficits in visual memory tests such as the ROCF that resulted from cocaine use.

The very few longitudinal studies of abstinent cocaine abusers in the literature have found among other cognitive deficits more persistent changes in memory [45, 46]; However, no group differences have been observed over time between cocaine only users and cocaine and alcohol combined users [33]. To date Di Sclafani et al. [33] is the only study to examine the longitudinal effects of abstinence in COC and dual cocaine/alcohol abuse. The Di Sclafani et al’s sample had a very high attrition rate and therefore the sample at followed up was much smaller than the one described in the current study. The small sample size in Di Sclafani et al’s may limit the generalization of their results.

The results from this study suggest that the chronic abuse of alcohol may decrease the consolidation process of new memories in chronic cocaine users. Alcohol has been shown to influence memory and learning in humans and animals [19, 47]. One primary action of alcohol in the CNS is the inhibition.
of the glutamate receptor, *N*-methyl-*D*-aspartate (NMDA) [48, 49]. Glutamate mediated NMDA receptors are involved in long-term potentiation (LTP), a process that is essential in memory formation [48]. Previous research has also shown that the combined use of alcohol and other drugs in particular cocaine has a significant impact over memory tasks [7]. Moreover, recent neuroimaging studies disclose hypo functioning of more brain regions in individuals who abuse alcohol and cocaine compared to cocaine only abusers [50, 51]. This evidence supports the theory of a “global” neurological effect for the combined use of cocaine and alcohol abuse [36] compared to the primarily frontal regional effect of cocaine alone [30]. This greater global brain effect of alcohol may help to explain the differences in memory tasks found between the two cocaine groups of this study.

In summary, this study showed that the abuse of alcohol in chronic cocaine users had an effect on long-term memory recovery but it does not affect short term memory processes. Several limitations in this study need to be addressed. Most apparent is the lack of a substance abuse naive control group. The use of this group would have allowed us to control for the effects of previous exposure to the tests. In fact, one important limitation of this study does not know how much of the improvement during abstinence is due to practice effects. We did not use alternate forms of the tests. A second limitation is the absence of an alcohol only abuse group. The inclusion of an alcohol only group would have allowed for the examination of the relative contribution of alcohol compared to cocaine on cognitive function and recovery as illustrated in Selby and Azrin [29]. The small sample gives limited power to our results and potentially, as participants in the present study were examined after only a brief period of abstinence, the findings do not necessarily reflect cocaine abuser’s long term memory function. Although, the results reflect the memory status of cocaine participants initiating cocaine abuse treatment.

Acknowledgement
Our gratitude to Deven Christopher for her editorial support.

<table>
<thead>
<tr>
<th>Table 1 Demographic information.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>COC</strong></td>
</tr>
<tr>
<td>(n=18)</td>
</tr>
<tr>
<td><strong>M</strong></td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Education</td>
</tr>
<tr>
<td>Gender M:F</td>
</tr>
</tbody>
</table>

COC=Cocaine Group (9 European Americans, 6 African Americans and 3 Hispanic Americans).
CA: Cocaine and Alcohol Group (17 European Americans, 12 African Americans and 1 Hispanic American).

<table>
<thead>
<tr>
<th>Table 2 Age of first use, duration of use, length of abstinence and usage frequency for previous one and five years.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>COC</strong> (n=18)</td>
</tr>
<tr>
<td><strong>M</strong></td>
</tr>
<tr>
<td>Age when first used Alcohol</td>
</tr>
<tr>
<td>Age when first used Cocaine</td>
</tr>
<tr>
<td>Age when first used Crack</td>
</tr>
<tr>
<td>Age when first used Marijuana</td>
</tr>
<tr>
<td>Duration of use (years) Alcohol</td>
</tr>
<tr>
<td>Duration of use (years) Cocaine</td>
</tr>
<tr>
<td>Duration of use (years) Crack</td>
</tr>
<tr>
<td>Duration of use (years) Marijuana</td>
</tr>
<tr>
<td>Length of abstinence in days</td>
</tr>
<tr>
<td>Alcohol use for previous year+</td>
</tr>
<tr>
<td>Alcohol use for previous 5 years+</td>
</tr>
<tr>
<td>Cocaine use for previous year+</td>
</tr>
<tr>
<td>Cocaine use for previous 5 years+</td>
</tr>
<tr>
<td>Crack use for previous year+</td>
</tr>
<tr>
<td>Crack use for previous 5 years+</td>
</tr>
<tr>
<td>Marijuana use for previous year+</td>
</tr>
<tr>
<td>Marijuana use for previous 5 years+</td>
</tr>
</tbody>
</table>

scores/0=never/not used, 1=only 1-3 times, 2=about 1 time per month, 3=about 2-3 times per month, 4=about 1 time per week, 5=about 2-6 times per week, 6=about 1 time per day, 7=about 2-3 times per day, 8=about 4 or more times per day
Table 3 Main effects and interactions (means, standard deviations, percentiles and partial eta square).

<table>
<thead>
<tr>
<th>Neuropsychological Instruments</th>
<th>Test 1</th>
<th>Test 2</th>
<th>Test 1</th>
<th>Test 2</th>
<th>Test/Retest Main Effects</th>
<th>Interactions</th>
<th>Between subjects Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>RocTF copy</td>
<td>31.50</td>
<td>(1.75)</td>
<td>30</td>
<td>31.92</td>
<td>(3.13)</td>
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<td>31.88</td>
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<tr>
<td>RocTF recall</td>
<td>17.68</td>
<td>(7.58)</td>
<td>10</td>
<td>22.17</td>
<td>(5.51)</td>
<td>60</td>
<td>14.83</td>
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<tr>
<td>Benton correct</td>
<td>5.50</td>
<td>(1.46)</td>
<td>5</td>
<td>6.22</td>
<td>(2.34)</td>
<td>15</td>
<td>4.50</td>
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<tr>
<td>Benton errors</td>
<td>7.71</td>
<td>(2.55)</td>
<td>85</td>
<td>5.89</td>
<td>(4.23)</td>
<td>70</td>
<td>8.67</td>
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<tr>
<td>Digit span</td>
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<td>(3.78)</td>
<td>35</td>
<td>17.06</td>
<td>(4.05)</td>
<td>50</td>
<td>14.90</td>
</tr>
<tr>
<td>CvlT 1-5</td>
<td>45.06</td>
<td>(9.05)</td>
<td>31</td>
<td>52.22</td>
<td>(10.36)</td>
<td>50</td>
<td>45.17</td>
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<tr>
<td>CvlT trail 1</td>
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<td>(2.08)</td>
<td>15</td>
<td>7.39</td>
<td>(2.04)</td>
<td>40</td>
<td>6.03</td>
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<td>List B</td>
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<td>(137)</td>
<td>15</td>
<td>5.50</td>
<td>(1.65)</td>
<td>50</td>
<td>6.07</td>
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<tr>
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<td>(2.91)</td>
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<td>15</td>
<td>12.06</td>
<td>(2.44)</td>
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<td>10.00</td>
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<td>15</td>
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<td>(2.56)</td>
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<td>(2.23)</td>
<td>50</td>
<td>10.59</td>
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</tbody>
</table>

*p<0.05, *p<0.01, $\eta^2p$=Partial eta square
+Percentile (mean raw scores were transformed into percentiles using the normative date)
References


39 Osterrieth PA (1944) Le test de copie d’une figure complexe; contribution à l’étude de la perception et de la mémoire. Archives de Psychologie 30: 206-356.


