Effects of Cocaine Use and Withdrawal on Clinical Memory and New Learning.

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Effects of cocaine use and withdrawal on clinical memory and new learning

Uddo-Crane, Madeline, Ph.D.

The Louisiana State University and Agricultural and Mechanical Col., 1989

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EFFECTS OF COCAINE USE AND WITHDRAWAL ON CLINICAL MEMORY AND NEW LEARNING

A Dissertation

Submitted to the Graduate Faculty of the Louisiana State University and Agricultural and Mechanical College in partial fulfillment of the requirements for the degree of Doctor of Philosophy

in

The Department of Psychology

by

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Abstract

This project was conceptualized as an exploratory examination of the neuropsychological sequelae of cocaine abuse, specifically the drug's effect on new learning and memory. The experimental groups were composed of 30 veterans enrolled in a drug treatment program for cocaine abuse. This group was divided equally by route of administration, i.e., group one included 15 individuals whose preferred route of administration was intravenous injection, group two included 15 individuals whose preferred route of administration was smoking. The comparison group consisted of 15 individuals enlisted in the National Guard. The groups were essentially homogeneous, with a mean age of 34.6 (SD=6.6), mean education level of 13.1 (SD=1.7), mean IQ of 98.6 (SD=8.8). On two separate occasions, five widely used memory assessment instruments were administered to measure visual memory, verbal memory, and attention/concentration (Auditory Verbal Learning Test (AVLT), Complex Figure Test, Digit Span, Visual Memory Span, Verbal Fluency Test). Alternate forms of these memory tests were administered during the posttest (four weeks subsequent to the initial testing). Nine univariate analyses of variance (ANOVA) using a 3 x 2 repeated
measures design were employed to analyze the data. Controls performed significantly better than the IV group on two measures of new learning ability: sum of AVLT trials 1-5 $F(2,42) = 5.60, p > .006$ and on the immediate memory score of the Complex Figure Test $F(2,42) = 3.88, p < .028$. Smokers and controls performed significantly better than the IV group on the delayed recall component to the Complex Figure Test $F(2,42) = 4.35, p < .019$. Controls performed significantly better than both experimental groups on trial 7 (delayed recall) of the AVLT $F(2,42) = 6.42, p < .004$. The results of this study indicate that chronic cocaine ingestion has an adverse effect on new learning and recall of both verbal and visually mediated tasks. Additionally, the degree of impairment appears to be correlated with the route of administration, i.e., individuals who reported intravenous injection as their preferred route of administration demonstrated greater impairment than those who chose smoking as their primary route of ingestion. Because IV injection provides the most efficient delivery of the drug to the brain, it is hypothesized that cocaine is a neurotoxin with a dose dependent effect on memory functioning.
Chapter I

Cocaine use and its untoward effects have increased dramatically since the drug's resurgence of popularity over the past two decades. Use of this illicit drug is now approaching epidemic proportions. The most recent National Institute on Drug Abuse (NIDA) epidemiological investigation of cocaine use revealed that the number of Americans who had used the drug at least once increased from 5.4 million in 1974 to 22 million in 1985, and that 5.6 million were current users (i.e., individuals who had used cocaine within the past 30 days), a 29% increase from 1977 to 1985. As a correlate to increased use, the number of cocaine related emergency room admissions, treatment admissions, and deaths has also risen (Adams & Kozel, 1985). Additionally, this survey estimated that in 1985, 3 million people were dependent on the drug.

A recent assessment of demographic trends in cocaine use is provided by a survey conducted via the National Cocaine Hotline, 800-COCaine, which receives an average of 1400 calls per day (Herridge & Gold, 1986). Compared to 1983, survey respondents in 1987 were younger (average age=27), had fewer years of education, lower incomes,
higher rates of unemployment, were more likely to be male, and chose smoking as the preferred route of administration. Results of this survey suggest that cocaine is being used by a larger, more diverse sample of the population.

History of Cocaine Abuse

Cocaine, derived from the leaves of the Erythroxylum coca plant, is found predominantly at high altitudes in Peru, Bolivia, and Columbia. From 0.6-1.8 percent of the alkaloid cocaine is contained in the small leaves (Ritchie & Greene, 1985), which are harvested on an average of three times per year. It is estimated that 400,000 acres of South American highlands are utilized to cultivate cocaine and that approximately 200 tons of illicit cocaine are imported into the United States annually, half of the total exports (White, 1988).

Despite its dangers, many diverse cultures have used cocaine for its psychotropic properties for thousands of years. Archaeological evidence suggests that South American cocaine use may date to 3,000 B.C. (Van Dyke & Byck, 1982). However, the Incas were the first to document its use and hence are often cited as the first to self-administer cocaine for its psychotropic effects. Coca leaf chewing is well described as an integral part of early Inca civilization, where it was known as the “gift of the Sun.”
God" (Kleber, 1986). Members of this culture believed the coca plant was
the divine providence of the God Inti, who sent it to alloy unhappiness and
satisfy basic needs (Allen, 1987a). Following Pizarro's conquest in the
early 1500's, coca leaf chewing was banned by the Spaniards, until it was
found that the Incas were more productive while under the influence of
the drug. As a result of this discovery, King Philip II endorsed cocaine as
beneficial to the Indian people and the Catholic church became the major
South American supplier of coca to the indigenous Indian people
(Peterson, 1977).

In spite of initial impediments, cocaine was soon introduced to
Europe. Early attempts by the Spaniards to introduce the stimulant to
their homeland were fruitless because the leaves lost their potency
during the voyage from South America (Allen, 1987a). Hence, the drug did
not become known in Europe until the alkaloid cocaine was extracted from
the coca leaf. Although Friedrich Gaedecke, a German chemist, was the
first to successfully execute this procedure in 1855, the product of
extraction was not named "cocaine" until 1859 by Albert Niemann, a
professor at the University of Gottingen in West Germany (Allen, 1987a).
Niemann observed that his discovery had an unpleasant taste and caused
his tongue to become numb (Ritchie & Greene, 1985). Following these discoveries, cocaine assimilated into European society.

Because early reports presented cocaine as a wonder drug, it soon became a popular ingredient of beverages and elixirs. In 1659, Pablo Mantegazzo published an essay which praised the new drug as a cure for fatigue, weakness, and decreased libido. Attendant to the publication of Mantegazzo's research, cocaine was added to many over-the-counter preparations (Kleber, 1988). During the mid 1860's, Angelo Mariani, a Corsican entrepreneur, developed one such mixture of cocaine and wine called Vin Mariani. Well received as a stimulant and digestive aid, it was endorsed (in exchange for a free case) and used by turn of the century leaders of society, e.g., Pope Leo XIII, Robert Louis Stevenson, Henrik Ibsen, Thomas Edison, President William McKinley, Sarah Bernhardt (Allen, 1987a; Kleber, 1988). In the spirit of competition, John Styth Pemberton of Georgia introduced Coca-Cola, a non-alcoholic product containing coca syrup and caffeine, to the United States in 1886. Cocaine remained a major ingredient of this new product, which was marketed as "the intellectual and temperance beverage," until 1903 (Allen, 1987a).

While the general public was enjoying the stimulant effects of cocaine in beverages, a Russian physician and professor was
experimenting with the clinical properties of the drug. In 1880, Vassili finding that his skin was numbed to a pin puncture following a cocaine von Anrep documented the anesthetic properties of the compound after injection (Ritchie & Greene, 1965). Cocaine was the first local anesthetic to be discovered and has since been employed in this capacity, primarily in the fields of ophthalmology, dentistry and facial surgery. Currently local anesthesia is the only medically indicated use for cocaine.

Contemporaneously with von Anrep's discovery, other investigations into the drug's psychotropic qualities were being conducted by Sigmund Freud, who became interested in the central nervous system effects of cocaine while employed in neurology at a Vienna hospital. Following personal experimentation, he endorsed its use in treating a vast array of unrelated ailments, such as alcohol and drug abuse, gastrointestinal disorders, venereal disease, asthma, fatigue, impotence, depression, hysteria, and altitude sickness (Kleber, 1988). As Freud extolled the virtues of the drug in his 1884 book entitled Uber Coca, the head of the American Medical Profession made collateral laudatory testimony. Such endorsements lead to prevalent cocaine use in both Europe and America (Allen, 1987). It is estimated that in 1907, 1.5 million pounds of cocaine entered the United States and that Americans consumed equivalent
amounts of the drug in 1906 and 1976, even though the population had increased two fold by the later date (Allen, 1987a).

Although originally deemed safe, disillusionment and sanctions began as the untoward effects of cocaine (e.g., addiction, death) became evident. Cocaine was made illegal by the Harrison Narcotics Act of 1914 (Kleber, 1988). Such restrictions on the use, sale, and distribution of cocaine elicited concomitant increases in price and decreases in availability and popularity. Between the end of this first, turn of the century, epidemic and the beginning of the second, cocaine was primarily recreation for the elite and avant-garde.

As drug experimentation increased during the late 1960's and early 1970's, cocaine was rediscovered; currently, because of greater potency and availability, the use of this drug is approaching epidemic proportions. The initial resurgence of cocaine's popularity may be partially attributable to the widespread belief that, relative to other illicit drugs, cocaine was safe and not physically addicting. This tenet was put forth by credible sources including the Comprehensive Handbook of Psychiatry (Kaplan, Freedman, & Sadock, 1980), the Diagnostic and Statistical Manual of Mental Disorders-Third Edition (DSM-III, 1980), the National Commission on Marihuana and Drug
Abuse (National Commission, 1973) and the Strategy Council on Drug
(Strategy Council, 1973). Originally, cocaine was deemed psychologically,
but not physically addicting because it did not produce tolerance or
withdrawal. However, Gawin and Kleber (1986) have described a cocaine
withdrawal syndrome which is characterized by sleep and appetite
disturbances, fatigue, depression, and irritability. While this withdrawal
symptomatology is not life threatening or as debilitating as syndromes
common to withdrawal from central nervous system depressants, it does
represent a well-defined syndrome experienced following cessation of
prolonged cocaine use. In addition, a tolerance phenomenon is described
by individuals who abuse the drug over extended periods of time, i.e.,
chronic users report an inability to attain levels of intoxication
comparable to those experienced during the early stages of cocaine use,
despite drastic increases in the quantity consumed (Jones, 1987).
Additionally, several theorists have begun conceptualizing cocaine as
physically addicting based on the findings that chronic ingestion of
cocaine alters neurochemistry which results in cravings to continue
cocaine use.

The most compelling evidence that cocaine use can lead to dependence
is seen within animal research paradigms and in the effects of the drug
on individuals who abuse it. Animal studies which have examined the reinforcing properties of cocaine provide cogent illustrations of the unparalleled addiction potential of cocaine. These studies which have examined the consequences of allowing rats and monkeys unlimited, continuous access to self-administered intravenous injections of cocaine have consistently shown that within days these animals will compulsively ingest cocaine to the point of death (Aigner & Bolster, 1978, Bozarth & Wise, 1965; Deneau, Yanagita, Seevers, 1969; Johanson, Balster, Bonese, 1976). Likewise, animals will go to great lengths to obtain cocaine. For example, Yanagita (1973) found that rats would bar press over 12,000 times in order to receive a cocaine injection, studies with comparable results were conducted by Bedford, Baily, & Wilson (1978), Griffiths, Brady, & Shell (1978), and Griffiths, Findley, Brady, Dolan-Gutcher, & Robinson (1975). Similarly, it was demonstrated that monkeys continued to self-administer cocaine even when the infusion was accompanied by an electric shock (Bergman & Johanson, 1981; Grove & Schuster, 1974) Furthermore, Johanson (1977) found that monkeys preferred infusion of a high dose of cocaine given in tandem with an electric shock to half that dose with no shock.

Examples of similar compulsive behavior in humans, i.e., endurance of
severe punishment in order to obtain and use cocaine, maintenance of cocaine use despite adverse consequences and to the exclusion of other pleasurable activities and basic sustenance are replete in the cocaine literature and mass media. Additionally, there has been an escalation in cocaine-related treatment admissions, emergency room admissions, and deaths during recent years. Although the image of cocaine as a benign, nonaddicting drug persisted until the beginning of the present decade, it has become apparent that this conceptualization was erroneous. It appears that cocaine may be psychologically addicting because of its highly reinforcing effects, and physically addicting because of its effect on neurotransmitter systems. The revision of the DSM III (DSM-III-R, 1987) has added cocaine dependence to its list of psychoactive substance abuse disorders and in recent years cocaine has become regarded as a powerful drug with high addiction liability.

During the early stages of its rebirth, the high price of the drug was both a deterrent and an enticement; that is, the high cost made it a status symbol. Although cocaine use continued to escalate into the early 1980's, the expense and limited supply prevented widespread abuse (Julien, 1988). However, new trends in cocaine use have emerged, partially as a result of basic economic principles: new cocaine marketing
strategies have effectively increased the supply, therefore decreasing price and increasing availability, while higher potency has boosted the demand. As a consequence of increased potency and decreased price, abuse liability of the drug has greatly increased and use has spread to a wider range of social strata, age, and educational level (Roehrich, Gold, & Lonoff, 1960).

**Pharmacology.**

Both the pharmacological properties of cocaine and the hedonistic qualities of living organisms are major factors in the drug's high addiction liability. A rapid alternation between pleasant and unpleasant states occurs in the cocaine use cycle; that is, ingestion of cocaine induces euphoria of short duration followed by a state of craving to re-experience the "high" (Washton, Stone, & Hendrickson, 1988). This pattern is intensified when smoking and injection are used as ingestion routes, making these routes of administration more prone to abuse. Latency to addiction is shorter and severity of addiction is more profound in individuals employing these highly efficient methods of administration (Verebey & Gold, 1988).

The most widely held pharmacological theory of this local anesthetic and central nervous system stimulant is that reinforcing properties
result from dopamine reuptake inhibition and consequent increase of
dopamine in the synaptic cleft (Dockis & Gold, 1988; Wise, 1984; Wyatt,
Karoum, Suddath, & Hitri, 1988). Psychological effects are attributed to
its sensitization of the dopamine reward pathways of the brain. Support
for the dopamine hypothesis is provided by animal research which
suggests amelioration of the reinforcing properties of cocaine with the
administration of dopamine antagonists (Wise, 1984). In addition,
Bromocriptine, a dopamine agonist, has been found to decrease cocaine
 cravings in human subjects (Dockis & Gold, 1985). Although evidence
suggests that the major actions of cocaine likely result from effects on
the dopaminergic pathways, other, less understood, neurotransmitter
(e.g., norepinephrine, serotonin) and possibly neuroendocrine effects may
contribute to its actions. In fact, while acknowledging the central role of
dopamine, the most current NIDA research concludes that the
pharmacological mechanisms of cocaine are likely more complex than
previously hypothesized. That is, more recent investigations suggest that
effects within the dopaminergic system, and between dopamine, other
neurotransmitters, and peptides are likely more extensive than suggested
by earlier research (Dunwiddie, 1988).
Routes of Administration

Routes of administration are important in determining the efficacy of drug delivery to the brain, and hence the potential for addiction (Verebey & Gold, 1988). Recent trends indicate that smoking and parenteral routes of administration are replacing intranasal use (Malow, 1989). A partial explanation for the increased abuse of cocaine is the increased popularity of these more efficient modes of ingestion. Although cited as a form of cocaine administration in the United States for over a decade, statistics indicate a drastic increase in cocaine smoking (Cohen, 1987). A survey conducted via the Cocaine Hotline reported that 56% of the callers employed the smoking route of ingestion in 1987, up from 21% in 1983 (Roehrich, Gold, & Lonoff, 1988).

Purified cocaine is smoked in either the form of "crack" (50-95% pure) or freebase (90-100% pure). While pharmacologically similar, crack and freebase are differentiated by method of preparation and presentation. Freebase is produced by adding a volatile substance (e.g., ether) and heat to cocaine hydrochloride and crack is formed by treating the drug with an alkaloid, e.g., sodium bicarbonate (baking soda) or sodium hydroxide (Julien, 1988). The latter process yields a mass of pure cocaine which is then divided into chips, or "rocks," and smoked, most commonly, in a
water pipe or cigarette. These preparations have a lower melting point than cocaine hydrochloride, and as a result, potent concentrations of the drug are delivered to the brain when smoked (Arif, 1987). The major distinction between crack and freebase is packaging freebase preparation is the responsibility of the consumer, while crack is purchased in a "ready to smoke" form (Gawin & Ellinwood, 1986). Additionally, this marketing strategy makes it cost effective to sell small quantities at low prices, which are affordable to adolescents and individual of lower socio-economic status (Cohen, 1987). Smoking is an efficient method of administration because very high concentrations of pure cocaine are delivered from the lungs to the brain within seconds, however, duration of the extremely reinforcing effects is only 5 to 10 minutes (Verebey & Gold, 1986).

Although cocaine smoking is relatively new to the United States, coca paste smoking is an established method of use in the South American countries which cultivate the drug (Cohen, 1987). Coca paste is an intermediate product in the preparation of cocaine hydrochloride, with 40-85% purity. This off-white semi-solid extraction is the product of ground coca leaves and a solvent, e.g., gasoline, kerosene, or sulfuric acid. The paste is added to a tobacco or marijuana cigarette and smoked
Although similar to freebase in effects, this method delivers lower concentrations to the brain and adverse physical reactions may result from ingestion of the solvents used in the extraction process (Seigel, 1982).

When treated with hydrochloric acid, coca paste becomes the white powder known as cocaine, the preparation which is used for intranasal and intravenous modes of administration. Intranasal use, or "snorting," gained popularity during the early 1970's, and while addicting, the expense and less efficient delivery to the brain likely prevented the epidemic that crack smoking has become. The powder is absorbed into the nasal mucous membranes when inhaled. Routinely diluted with a variety of other substances (e.g., amphetamine, sugar, caffeine, laxatives, powdered milk) to increase profits, purity of cocaine hydrochloride varies from 20% to 80%. The drug takes effect within two to three minutes and the "high" lasts from 30 to 40 minutes. Complications of this method include nasal bleeding and sores, sinus irritation and congestion, in addition to septum damage (Verebey & Gold, 1988).

Cocaine hydrochloride produces a powerful, rapid response when it is dissolved in water and injected into a vein (Fischman, 1988). The drug exerts its effect on the brain within 30 to 45 seconds following
injection, producing feelings of intense euphoria which subside within 10 to 20 minutes. This is a highly efficient method of absorption with nearly 100% bioavailability. A cogent contraindication of intravenous injection of cocaine is the risk of contracting Acquired Immune Deficiency Syndrome (AIDS) by sharing a needle with an individual who is infected with the Human Immunodeficiency Virus (HIV). Other, less fatal, health risks associated with this route of administration include phlebitis and hepatitis (Allen, 1987b).

Oral administration, via coca leaf chewing or ingestion of cocaine hydrochloride, is the least effective mode of administration (Verebey & Gold, 1988). A malleable substance made of toasted coca leaves and an alkaline, e.g., lime or ash, is chewed or stored between the cheek and gum to produce mild feelings of well-being, anorexia, and energy which last for up to one and a half hours. Coca leaf purity is 0.5 to 1.8% (Arif, 1987). This is the most popular type of ingestion in South America. Cocaine hydrochloride may be swallowed to achieve a slow-acting effect with absorption rates similar to intranasal use (Verebey & Gold, 1988). Although nausea may occur, this method appears to be devoid of serious physical or psychological side effects.
Neuropsychology and Substance Abuse

Effects of Specific Drugs on Memory

Alcohol. Memory impairment is an integral part of the constellation of neuropsychological impairments common among alcoholics (Tarter & Edwards, 1985). Until the hypothesis—that low ceiling effects on standard memory assessment instruments preclude manifestation of alcohol induced deficits—was tested and upheld by Butters, Cermak, Montgomery, & Adinolfi (1977), memory impairments were not consistently found in alcoholics (Jonsson, Cronholm, & Izikowitz, 1962; Parsons & Prigatano, 1977; Weingartner, FaUlice, & Markley, 1971). Since more sensitive measures have been developed and administered, deficits have been identified in several areas, e.g., storage, encoding and retrieval of verbal (Brandt, Butters, Ryan, Bayog, 1983; Ryan, 1980; Ryan & Butters, 1980) and nonverbal (Cutting, 1978; Miglioli, Buchtel, Campanini, & DeRisio, 1979; Parsons & Farr, 1981) material. Additionally, most evidence suggests that new learning and recent memory are more compromised than remote memory (Albert, Butters, Brandt, 1980; Tarter Edwards, 1985).

Length of abstinence has proven to be an important variable in assessing memory functions in alcohol abusers; that is, the most obvious
dysfunctions are evidenced during the first week of abstinence, after which significant, but incomplete, recovery of function occurs, and continues until approximately 6 weeks following cessation of alcohol ingestion (Ryan & Butters, 1986). Data suggest that following this initial period of recovery, mnestic impairments remain relatively stable over time, i.e., persistent memory dysfunctions have been reported following one year (Ryan, DiDario, Butters, & Adinolfi, 1980, Yaman, Parsons, Leber, 1985) and 7 years of sobriety (Brandt, Butters, Ryan, & Bayog, 1983).

Marijuana Results of neuropsychological studies of the effect of marijuana on memory are inconsistent (Hartman, 1988). While some researchers have found short-term memory impairments in chronic marijuana users (Casswell & Marks, 1973; Melges, Tinklenberg, Hollister, Gillespie, 1970), others report no memory dysfunction (Grant, Rochford, Fleming, & Stunkard, 1973; Mendelson & Meyer, 1972; Schaeffer, Andrysiak, & Ungerleider, 1981,).

Opioids Although one study reported that heroin addicts performed in the impaired range on the memory score of the Tactual Performance Test (Hill & Mikhail, 1979), most evidence suggests that abuse of heroin and other opioids does not adversely affect neuropsychological functioning (Fields & Fullerton, 1975, Press, 1983, Rounsaville, Jones, Novelty, &
Polydrug Abuse. It is estimated that 50% of individuals belonging to this classification experience neuropsychological deficits (Tarter & Edwards, 1985). Studies of cognitive functioning in individuals who abuse multiple substances have not focused on memory functions specifically, but general neuropsychological dysfunction is evident in investigations employing the Halstead-Reitan Battery (Grant, Mohns, Miller, Reitan, 1976; Grant & Judd, 1976; Grant, Adams, Carlin, Rennick, Judd, Schooff, Reed, 1978).

Cocaine. While investigation of neuropsychological sequelae of abused substances has received modest attention in general, such investigations regarding cocaine abuse are virtually nonexistent. While lacking rigorous empirical investigation, allusions have been made to the possibility of cognitive dysfunctions attendant to cocaine abuse, for example, 20 percent of chronic cocaine freebase users surveyed, reported memory problems and 37.5 percent reported concentration problems (Verebey & Gold, 1986). Fifty-seven percent of the target population endorsed memory problems in a survey conducted by Washton and Gold (1984). Additionally, items relating to memory and concentration problems are included in the newly developed Cocaine Abuse Assessment
Profile (Washton, Stone, & Henrickson, 1988).

Empirical investigation of mnestic effects of cocaine is sparse. Current studies include a doctoral dissertation (Press, 1983) which investigated neuropsychological functioning in opiate and cocaine users using the Luria-Nebraska Neuropsychological Battery. Participants in the cocaine group either smoked freebase or snorted cocaine hydrochloride, however, of the 16 subjects, the exact number using each of the administration methods was not reported. While cocaine users, as a group, evidenced no significant memory impairment, a similar pattern of memory deficits was identified in two freebase users, leading Press to hypothesize that route of administration differentially effected memory functions, that is, freebase users may be more likely than intranasal users to evidence memory impairment.

Two studies have examined the effect of cocaine intoxication on memory, that is, subjects were assessed while under the influence of the drug. Resnick (1978) found after insufflation of cocaine, individuals made more errors on a verbal learning task than did controls. Additionally, a study by Fischman (1984) found that the number of errors made on a test of new learning increased as a function of route of administration, and consequently, cocaine plasma levels; that is, subjects
who received intravenous injections as opposed to intranasal administration performed more poorly.

Withdrawal Effects

Both alcohol and heroin have well described physical withdrawal syndromes, however, such symptoms are not inherent to abrupt cessation of cocaine use. The revision of the Diagnostic and Statistical Manual of Mental Disorders—Third Edition (DSM-III-R) includes a classification for cocaine withdrawal comprised of specific depressive symptomology (e.g., fatigue, sleep disturbance, psychomotor agitation) which must be present for more than one day in order to warrant diagnosis.

In contrast to the unidimensional syndrome identified by DSM-III-R, Gawin and Kleber (1986) have developed a more elaborate explication of withdrawal which differentiates three distinct phases. Phase 1, referred to as the "crash," ensues when the cocaine supply is depleted. Intense cravings for the drug are followed by depressive symptomology (e.g., anhedonia, insomnia, irritability) lasting from 1 to 40 hours. The following 8 to 50 hours are marked by extreme fatigue and increased appetite. Phase 2, or withdrawal, begins with a 1 to 5 day period of normal mood which shortly deteriorates into a pervasive anhedonic state. It is at this point that relapse is highly likely; however, if the individual
remains abstinent, symptoms will abate within 6 to 18 weeks. With the cessation of anhedonic symptoms, phase 3 begins. Periodic drug cravings, typically triggered by environmental cues, are the hallmark of this final phase. Extinction occurs during this phase if the abstinent individual does not succumb to the cravings. While Gawin and Kleber's examination of the affective and biological aspects of cocaine withdrawal demonstrates considerable treatment validity, equally cogent investigations of concurrent neuropsychological functioning are needed.

Rationale

Research examining the neuropsychological sequelae of cocaine abuse and withdrawal is conspicuously absent from the burgeoning cocaine literature. This topic is of particular importance considering the epidemic proportions of cocaine use and the paucity of data on the neuropsychological concomitants of the drug in general, and specifically in relation to the new, more effective, routes of administration currently in vogue. Furthermore, evidence suggests that cognitive functioning is correlated with treatment outcome in alcohol abusers, hence investigation of neuropsychological integrity within abstinent cocaine abusers may be of considerable treatment validity. For example, in a study conducted by Guthrie & Elliot (1980) patients who actively
participated in an aftercare regime were significantly more likely than their counterparts who did not attend aftercare to remain abstinent, however, alcohol abusers who exhibited neuropsychological impairments at the beginning of the treatment program were significantly less likely to attend aftercare and hence less likely to remain abstinent. Similarly, results of a study conducted by Walker, Donovan, Kivlahan, & O'Leary (1983) indicate that participants in an alcohol treatment program who evidenced cortical dysfunction during the first week of treatment were less likely to have remained abstinent nine months following discharge. Additionally, current treatment approaches in the field of substance abuse, e.g., relapse prevention, include a significant educational component. If neuropsychological deficits (e.g., impairments in new learning and memory) exist, then educational material, which is presented in both visual and verbal form, may not be assimilated. Therefore, it is of significant practical importance for this construct to be explored.

Furthermore, identification of deficits in consolidation of new memories may help to localize the pathophysiology of cocaine. That is, if cocaine abusers demonstrate impairments in learning and retention of new information, then it may be hypothesized, for example, that the temporal lobes are affected by chronic cocaine ingestion.
The present study was conducted to examine the effects of cocaine on learning and memory. Given the paucity of data examining the neuropsychological effects of cocaine abuse, the nature of the present study was deemed exploratory. Memory test scores were utilized to evaluate the following empirical questions:

1. Is there a difference between cocaine abusers and controls?

2. Is there a difference between those who inject cocaine intravenously and those who smoke cocaine?

3. Does length of abstinence correlate with degree of impairment?
Chapter II
Method

Subjects.

A total of 45 subjects participated in this study. The experimental group consisted of 30 individuals consecutively admitted to the Drug Dependence Treatment Unit (DDTU) at the New Orleans Veterans Administration Medical Center (VAMC) who met the following criteria: 1) fulfillment of DSM-III-R criteria for cocaine dependence as assessed by the Structured Clinical Interview for DSM III-R (SCID; Spitzer & Williams, 1986), 2) Stated preferred route of cocaine administration of either intravenous injection, IV, (n=15) or cocaine freebase, or "crack", smoking (n=15). Individuals employing intranasal ingestion rarely present for treatment at the DDTU of the New Orleans VAMC and hence were not be studied; 3) estimated I.Q not less than 1 standard deviation below the mean, i.e., 85 or below, as measured by the Shipley Institute of Living Scale (Shipley, 1967); 4) 6 months or longer duration of cocaine use. Patients who reported a history of neurological impairment, including loss of consciousness due to head trauma, were excluded.

Data suggest that chronic alcohol abuse may cause neuropsychological
imperior, hence participants with a history of severe alcohol abuse were excluded. Because previous research has indicated that a high proportion of individuals addicted to cocaine also meet criteria for alcohol dependence (Miller & Gold, 1988), it was concluded that to exclude all individuals who met minimum criteria for alcohol dependence would drastically decrease the number of potential subjects and more importantly, that such a sampling procedure may have yielded a sample which was not representative of the population of interest. Responses to the SCID criteria for alcohol dependence were utilized to assess level of severity, i.e., individuals who endorsed seven or more of the nine items were classified in the severe range and thus were excluded from the study.

Likewise, polydrug abuse has been found to cause neuropsychological compromise, hence individuals who met the threshold for current addiction to more than one illicit drug other than cocaine were excluded. Additionally, the Minnesota Multiphasic Personality Inventory (MMPI; Hathaway and McKinley, 1954) F scale was employed to screen for individuals who potentially were unwilling or unable to participate due to various reasons, e.g., illiteracy, psychosis, malingering. That is, individuals whose MMPI F scale T-score was greater than 90 were
excluded from participation in the study. This protocol was completed routinely by all DDTU residents as a component of ongoing psychological assessment on the unit.

In addition to the exclusionary criteria described above, potential control subjects who had ever smoked or injected cocaine, had used cocaine via the intranasal route more than twice, or met minimum criteria for alcohol dependence were excluded from the control group. The SCID was utilized to assess alcohol dependence.

**Group 1 (Intravenous Injection):**

Members of this cohort included 15 males between the ages of 27 and 46 ($\mu = 37.86, SD = 4.76$). Mean number of years of education completed was 13.30 ($SD = 1.73$). All participants in this group were male, predominately black (86.67%), with mean estimated WAIS-R IQ of 97.73 ($SD = 7.42$).

**Group 2 (Smokers):**

This group was comprised of 15 individuals (2 females) ranging in age from 27 to 48 years ($\mu = 33.20, SD = 5.32$). Ninety-three percent were black, mean number of years of formal education reported was 13.00 ($SD = 1.45$), and mean estimated IQ equaled 95.20 ($SD = 7.88$).

The percentage of blacks versus whites and males versus females within these groups is representative of the population characteristics of
individuals treated on the DDTU.

**Group 3 (Control).**

The control group consisted of 15 individuals (2 females) enlisted in the Army National Guard who ranged in age from 20 to 42 years old and reported a mean level of education of 13.17 years ($SD = 1.78$). This sample was predominately black (80%) and attained an estimated mean IQ of 102.80 ($SD = 9.23$). A summary of demographic variables for each group is presented in Table 1.

Insert Table 1 about here

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**Materials**

The following screening instruments were administered to all new DDTU admissions who reported cocaine as their drug of choice and employed either smoking or intravenous injection as their primary route of administration.

1) Minnesota Multiphasic Personality Inventory (MMPI): This is a 566 item criterion-keyed instrument designed to assess psychological status. This measure is the most widely used personality assessment instrument and has been employed in over 6000 studies (Graham, 1987). The test
yields T-scores on ten clinical scales, three validity scales, and a Cannot Say scale

2) Structured Clinical Interview for DSM-III-R (SCID; Spitzer & Williams, 1986): Cocaine abuse was assessed using this instrument. Subject responses to questions assessing Diagnostic and Statistical Manual of Mental Disorders Third Edition - Revised (DSM-III-R) criteria for the disorder are rated as absent, subthreshold, or threshold. The SCID has received support as an objective approach to diagnosis and for its reliability and validity (Mackinnon & Yudofsky, 1986; Riskind, Beck, Berchick, Brown, & Steer, 1987) Only individuals with 3 or more criteria scored at threshold level for cocaine abuse were included in the experimental group. Abuse of other illicit drugs and alcohol was also assessed using this structured interview. The total number of criteria scored at the threshold level provided a measure of the severity of addiction, i.e., 3/9 = minimum severity, 9/9 = maximum severity.

3) Shipley Institute of Living Scale (Shipley, 1967). This self-administered intelligence screening test consists of two subtests: the vocabulary subtest which is comprised of 40 multiple-choice word definition items and the abstraction subtest, comprised of 20 items which
assess ability to determine the next logical item in a pre-established pattern or sequence. The number of words correctly defined is the vocabulary score, the number of correct answers multiplied by 2 is the abstraction score. An estimated Wechsler Adult Intelligence Scale-Revised (WAIS-R) I.Q. may be derived from the sum of scores on the two subtests (Zachary, Crumpton, & Spiegel, 1985). A .67 correlation was achieved between the WAIS-R and the Shipley using the conversion outlined by Zachary, et al. (1985). Estimates of intellectual functioning were attained using this method.

4) Background Information Questionnaire (BIQ): Demographic information were elicited via this brief questionnaire which is currently in use at the VAMC-New Orleans.

Individuals who met pre-established criteria were chosen as subjects and received alternate forms of several tests of verbal and non-verbal memory on two separate occasions during their treatment on the DDTU. Data suggests that more challenging tests are required in order to detect subtle deficits in substance abusing populations. Therefore, when selecting this battery, neuropsychological tests deemed sensitive to subtle cortical deficits were included (i.e., AVLT and Complex Figure Test) in addition to less demanding tests of word generation (i.e., Verbal...
Fluency) and attention/concentration (i.e., Digit Span and Visual Memory Span). All tests are frequently employed to measure memory. Administration time for this battery was approximately 1/2 hour.

A Verbal Memory

1) Verbal Fluency Test (VFLU): This test, which is frequently included in batteries which assess mental status, requires subjects to generate words that begin with a specified letter of the alphabet. One minute is allowed for each letter. The letters C, F, and L were used during the pretest and P, R, and W were used during the posttest. Norms adjusted for age, sex and education are available for these letters (Benton & Hamsher, 1976). Scores equal total number of correct responses given within the allotted time. Although this instrument is commonly employed as a measure of frontal lobe integrity, it may also measure memory functioning, specifically left hemisphere integrity, since the subject is required to remember the task demands in addition to retrieving appropriate words.

2) Auditory-Verbal Learning Test (AVLT; Rey, cited in Lezak, 1983): This demanding test measures immediate memory, learning over repeated trials, and delayed recall. It consists of 5 administrations of a 15-word list, in addition to an interference trial (a second list of equal length).
which is followed by a sixth trial of the original list. Following each presentation of the first list, the individual was asked to recall as many words from the list as possible. The same procedure was followed for the second list, after which the subject was instructed to once again recall the first list (trial 6). A 30-minute delayed recall of the original list was included. This instrument yields several scores: number of words correctly recalled for each trial, the number recalled during trial 6, and the number of words recalled following the 30-minute delay. An alternate list is available and was administered at follow-up in order to control for practice effects. Norms are available for this measure which is likely more sensitive to left hemisphere compromise.

3) Digit Span The first presentation of this measure of attention/concentration for verbal stimuli consisted of the Wechsler Memory Scale-Revised (WMS-R, Wechsler, 1987) Digit Span subtest. Number sequences used in the Digit Span subtest from the Wechsler Adult Intelligence Scale-Revised (WAIS-R, Wechsler, 1981) were given during the posttest. Initially, subjects were asked to repeat a series of numbers, beginning with 3 numbers and increasing by 1 number (to a maximum of 7) each time one or both of the trials is correctly repeated. Testing was
discontinued when both trials of any given series were failed. Following completion of "digits forward," the subject was asked to repeat a different set of number series in the reverse order from its presentation. Testing began with 2 digits and proceeds, in a fashion similar to digits forward, to a maximum of 8 digits. One point was given for each correct repetition trial. Test-retest reliability coefficients for this test range from .82-.89. Difficulty with this task is generally regarded as a possible indicator of difficulties in attention/concentration.

This test is sensitive to diffuse and or left hemisphere dysfunction.

B. Non-Verbal Memory

1) Complex Figure Test (CFT; Taylor, cited in Lezak, 1983) This challenging test of visual-spatial constructional ability provides a measure of visual memory (immediate and delayed). Subjects were presented with a drawing of a complex geometric design and asked to copy the design on a blank sheet of paper. Upon completion of this task, the original drawing and copy was removed, and the subject was asked to draw the design from memory on another blank sheet, constituting a measure of immediate memory. Approximately 30 minutes later, he was again asked to reconstruct the figure from memory, constituting a measure of delayed
recall Figures were scored via a unit scoring method devised and normed by Osterrieth (cited in Lezak, 1983). Alternate forms, objective scoring criteria, and adult norms are available for this assessment tool. Following the immediate recall task of both the pretest and posttest, individuals were informed of the delayed recall measure. This measure of visual memory is deemed more sensitive to right hemisphere dysfunction.

2) Visual Memory Span (VMS). This subtest from the WMS-R, which requires the examinee to touch colored boxes printed on a card in the same or reversed order as presented by the examiner, was employed to measure attention/concentration for visual stimuli. The “tapping forward” subtest required the subject to touch boxes in the same order as touched by the examiner (beginning with 2 boxes, to a maximum of 8). Two trials of each length were given. Testing was discontinued when both trials of any length were failed. “Tapping backward” followed a similar procedure, however, at this time the subject was directed to tap boxes in the reverse order of presentation. Tapping backward began with 2 taps and has a maximum of 7 taps. One point was earned for each correct sequence. The total raw score for tapping forward and tapping backward is converted to a standard score, for which norms are available. Test-retest reliability for this
test is between .83 and .88. Because this test requires organization and memory of visually-mediated stimuli, it is deemed more sensitive to right hemisphere dysfunction.

**Procedure**

Phase I of the DDTU program consisted of a 21 day inpatient treatment. Upon discharge from this phase, residents began Phase II, a 14 day outpatient stay in a residential treatment facility. During this phase, participants in the program are required to attend 4 meetings per week on the DDTU. Initial memory testing was conducted 7-10 days following admission into Phase I in order to permit adequate time for detoxification (Sheehy, 1987). The posttest was administered at the end of Phase II of treatment, i.e., 30-35 following admission. Routine drug testing is mandatory during this phase of treatment, hence only individuals who remained sober during Phase II received the posttest. It was assumed that conducting the posttest while subjects were still actively participating in treatment would bolster compliance. Screening was conducted approximately one week following admission to the DDTU. The SCID was administered by the examiner, the Shipley was then completed by the subject while supervised by the examiner. The subject completed the MMPI unsupervised.
Subjects who met criteria for participation in the study then received the battery of memory tests. During all sessions, in order to promote standardization, these tests were given in the following sequence: 1) Auditory Verbal Learning Test; 2) Complex Figure Test; 3) Digit Span; 4) Visual Memory Span; 5) Verbal Fluency. The post-test was conducted approximately 4 weeks subsequent to the initial testing.

The same procedure was utilized in testing the control group. A brief interview was conducted with potential subjects in which the study was explained and demographic information was obtained. A consent form summarizing the study and the risks and benefits of participation was signed by those who agreed to participate (see Appendix). These subjects then completed the MMPI and Shipley. During the second session, the SCID for alcohol dependence was administered. The memory battery was then administered if all criteria for participation were met. The posttest memory battery was re-administered in a single session four weeks subsequent to the initial testing.
Chapter III

Results

The control group and experimental groups which were examined in this study were essentially homogeneous. No differences were found among groups on demographic variables which may affect performance on memory tests, e.g., IQ, age, race, and education, hence an analysis of covariance was not conducted.

Significant differences were found between individuals with a history of cocaine abuse and controls on performance of demanding tasks designed to measure the ability to learn and recall new information presented in both non-verbal and verbal form. Furthermore, individuals who employ intravenous injection as their usual route of administration evidenced greater deficits in performance than those who smoke cocaine. No significant differences were found on verbal and non-verbal measures of attention/concentration or verbal fluency. No significant differences among groups in changes in performance were observed as a function of the time factor, i.e., there was no significant difference in performance between the control group and the experimental groups between initial and follow-up memory test scores. Table 2 presents means and
standard deviations of scores achieved by the three groups on each dependent variable during pretest and posttest assessments.

Insert Table 2 about here

Nine univariate analysis of variance (ANOVA) tests using a repeated measures design with factors of 3 (groups) x 2 (time) were employed to compare performance on measures of memory functioning, i.e., three scores form the Auditory Verbal Learning Test (sum of words recalled over trials 1-5, total number of words recalled on trial 6 [trial following the interference trial], total number of words recalled on trial 7 [30 minute delayed recall]); three scores from the Complex Figure Test (copy score, immediate memory score, 30 minute delayed recall); Digit Span-Total; Visual Memory Span-Total; Verbal Fluency-Total. A summary of the results from the Analyses of Variance are presented in Table 3.

Insert Table 3 about here

Using a univariate analysis of variance, a group main effect was found on two measures of learning of new material: the sum of AVLT trials 1-5,
$F(2, 42) = 5.68, p < .006$ and on the immediate memory score of the Complex Figure Test, $F(2,42) = 3.88, p < .028$. In order to control the Type I experimentwise error rate, Tukey's Studentized Range Test was performed and indicated that controls scored significantly higher than the IV cocaine group on both variables. While in the expected direction, the difference in performance between controls and smokers on these two measures was not significant. Significant differences were also found between the control group and both experimental groups on the AVLT measure of delayed recall (trial 7) $F(2, 42) = 6.42, p < .004$. Tukey's Test indicated that controls recalled a significantly greater number of AVLT words following a 30 minute delay than either the IV group or the smoker group. A group effect was also evidenced on delayed recall of the Complex Figure Test, $F(2, 42) = 4.35, p < .019$. Tukey's Test revealed significantly better performance by the control group than by the IV group, as well as significantly better performance by smokers than by the IV group, on this measure. Controls scored slightly higher than smokers on the delayed recall component of the Complex Figure Test, however, the difference between these two groups was not significant.

Univariate analysis of variance revealed a significant main effect for time of administration on AVLT trial 6, $F(1, 42) = 5.04, p < .030$ and trial
$F(1,42) = 12.39, p < .001$. Tukey's Test indicated that posttest scores for all three groups were lower than pretest scores on both tasks. Differences were also found between testing administrations on immediate memory, $F(1,42) = 32.92, p < .0001$ and delayed recall, $F(1,42) = 46.82, p < .0001$ of the Complex Figure Test. Tukey's Test indicated that for all three groups, posttest scores were higher than pretest scores on these two measures.

Univariate analysis of variance yielded no significant main effects or interactions among the three groups on Digit Span-Total, Visual Memory Span-Total, or Verbal Fluency-Total. No significant interaction effects were found on the Complex Figure Test or AVLT.

The strength of association between the independent and dependent variables was measured using eta square. Table 4 lists eta square values for each dependent and independent variable.

Insert Table 4 about here
Chapter IV

Discussion

The current project was conceptualized as an exploratory examination of the neuropsychological sequelae of cocaine abuse, specifically the drug’s effect on new learning and clinical memory. The results of this study indicate that chronic ingestion of cocaine has an adverse effect on learning and recall of both verbally and non-verbally mediated tasks. Additionally, the degree of impairment appears related to the route of administration employed to ingest the drug, i.e., individuals who reported intravenous injection as their preferred route of administration demonstrated greater deficits than their counterparts who chose smoking as their primary route of ingestion.

A major difference between intravenous and intrapulmonary routes of administration is bioavailability, or the percent of the drug which is absorbed. Intravenous ingestion is the most efficient route of administration with 100% bioavailability. When heat is applied to cocaine preparations which are smoked, a significant amount of its active ingredient is lost, therefore, the bioavailability of crack or freebase cocaine, in comparison, is only 6-32% (Verebey & Gold, 1988). In light of
this inherent difference in rate of absorption, it may be hypothesized that cocaine is a neurotoxin with a dose dependent effect on memory functioning. That is, the degree of impairment may be conceptualized on a continuum, with degree of memory impairment dependent upon the amount of cocaine delivered to the brain. The current data support this hypothesis, i.e., mnestic dysfunction is less pronounced in those employing the less efficient intrapulmonary route, while greater impairment is manifested in those employing the more efficient IV route.

Additionally, it may be hypothesized that there is a connection between severity of addiction and route of administration, i.e., those using the more invasive mode of ingestion, IV injection, may manifest a more severe addiction and hence demonstrate greater impairment. It is likely that individuals with a more severe addiction have used the drug over a longer period of time and have consumed a higher total volume, therefore incurring greater toxic effects to the brain. It has been stated that "in the progression of obsessive self-destructive cocaine dependence, intravenous cocaine abuse follows intranasal use" (Verebey & Gold, 1988, p. 515), however, the current review of the literature failed to discover a systematic investigation of correlations between route of administration and severity of cocaine addiction. Future research which assesses this
correlation is warranted

Purity is another factor to be considered when addressing the differences between the two routes of administration of interest. As opposed to crack and freebase, which are purified forms of cocaine, the preparation which is injected typically contains a variety of adulterants, e.g., amphetamine, manitol. Perhaps these unstudied substances exert discrete neurotoxic effects either alone or in interaction with one another. This area merits further examination.

Significant improvement in neuropsychological performance occurs in abstinent alcohol abusers during the initial weeks of sobriety (Ryan & Butters, 1986), however, such recovery of function was not noted in cocaine abusers who participated in this study. The experimental groups did not demonstrate any unique, significant improvements in performance during the posttest. In fact, performance of all three groups was less proficient during retesting on AVLT trials 6 and 7. Motivational factors, fatigue, or boredom with the task may have contributed to the consistent decrements in performance exhibited across all three groups. This task may be considered monotonous by some, hence scores on the posttest may have been lowered because of boredom. The novelty of the task during the initial testing may have contributed to motivation. However, this measure
is rather demanding and requires active attention for a sustained period of
time; therefore, during the posttest, subjects may have recalled the
arduous nature of the task and may have been less motivated to exert a
similar effort during the second testing. Additionally, members of the
experimental groups were in a significantly different phase of treatment
at the time of the posttest. That is, during the initial testing, these
individuals were enrolled in Phase I of treatment (21 day inpatient stay).
During this facet of treatment, residents are reasonably sheltered from
outside stresses. The posttest was conducted during the final days of
Phase II (14 day stay in a residential treatment facility). Upon completion
of this phase of treatment, these individuals return to the community and
its attendant stressors, e.g., returning to drug infested environments,
unemployment, interpersonal and financial difficulties. While all
participants were highly cooperative with the testing protocol, it is
conceivable that with such weighty issues to consider, optimal levels of
motivation may not have been demonstrated when asked to perform a
demanding and repetitious task with little perceived reward. In addition
to motivational factors, because of their involvement with the National
Guard, members of the control group had been required to work extended
hours prior to the posttest, therefore, decreased performance by this
cohort may have been due to fatigue. Lastly, although presumed parallel, psychometric data to support the equivalency of the AVLT alternate list is unavailable, hence the list which was employed during the follow-up testing may have been inherently more difficult than the list used during the initial testing.

The only other significant change from pretest to posttest was noted on the Complex Figure Test: all three groups received higher posttest scores on the immediate memory and delayed recall measures of this test. This may be attributed to practice effects or perhaps, again, to unequivalent alternate forms of the test, i.e., the stimuli employed for the posttest may have been inherently simpler. Because similar, stable time effects were seen across all three groups, these discrepancies in performance cannot be attributed to the effect of cocaine on the brain.

The findings of the current study are consistent with previous research in regard to the relationship between level of difficulty of memory assessment instruments and manifestation of deficits. That is, prior research has concluded that mnestic impairments were not demonstrated in alcohol abusers until more sensitive measures were employed (Albert, Butters, & Brandt, 1980; Ryan, 1980). Ryan & Butters (1986) state that in order for subtle memory dysfunction to be identified in substance abusers,
the tasks utilized to assess memory integrity must "require subjects to process a great deal of unfamiliar information...in a short period of time" (p.390). Both instruments which yielded significant differences among groups (i.e., AVLT and Complex Figure Test) meet these requirements, while the tests which did not yield differences are generally regarded as conceptually simpler tasks (i.e., Digit Span, Visual Memory Span, Verbal Fluency).

A final explanation of the significant differences found among groups on the AVLT and Complex Figure Test is that these findings may have been a chance happening or an artifact of the assessment instruments which were employed. While these tests are widely used, and endorsed by individuals who are prominent in the field of general neuropsychological assessment (Lezak, 1983) and the specific area of neuropsychological toxicology (Hartman, 1988), the psychometric properties of these tests have not been rigorously investigated. Therefore, it could be hypothesized that significant results may be attributable to a lack of integrity of these instruments, and hence that similar results may not be replicable or that the construct being measured was something other than memory.

Limitations of the Study

The practice of utilizing esoteric measures to assess memory
functioning has received considerable criticism because performance on these measures does not generalize to behaviors which are integral to practical, everyday functioning (Crook, 1986; Erickson & Scott, 1977). Based on previous research which concluded that memory deficits in substance abusing population are only apparent on performance of demanding tasks (Ryan & Butters, 1966), it was assumed that typical measures of everyday memory would be unsuccessful in eliciting more subtle memory impairments. However, ecological validity of future research in this area may be bolstered by devising such measures which would be appropriate in studying substance abusing populations. For example, a test designed to measure assimilation of concepts presented during treatment would provide a more meaningful assessment of memory. For instance, if a treatment program employed the relapse prevention model of substance abuse, then a test of relapse prevention concepts which were presented during treatment would measure a construct deemed integral to the individuals' sobriety. While appealing in theory, such a measure is not without its difficulties as this approach may be measuring constructs besides memory, e.g., motivation, test taking ability.

Another limitation of this study is that severity of addiction, amount consumed, and duration of abuse were not systematically investigated
Examination of these constructs is fraught with methodological difficulties since it would be necessary to rely upon self report data to obtain this information. Nevertheless, future research which rigorously examines these dimensions of addiction would be a significant contribution to the literature.

**Clinical Implications**

Results of this study may guide future investigations of the pathophysiology of cocaine. While it appears that cocaine's effect on the brain is likely diffuse, from a grossly oversimplified view of localization of brain dysfunction, decreased performance by cocaine abusers on tasks requiring learning of new information presented in both verbal and visual form implies temporal lobe involvement of the left and right hemispheres.

Data suggest that individuals enrolled in alcohol treatment programs who exhibit neuropsychological impairments are less likely to remain sober than their unimpaired counterparts (Guthrie & Elliot, 1980, Walker, et al.) Results of the present study suggest that individuals enrolled in treatment for cocaine abuse exhibit neuropsychological impairments; specifically, those who inject cocaine demonstrate difficulty learning verbal and non-verbal material. Additionally, data indicate that this group experiences difficulty recalling visually mediated stimuli following a
period of delay. Those who smoke as well as those who inject cocaine
evidence difficulty recalling newly acquired verbal information following
a period of delay. These preliminary findings may be clinically salient in
regard to treatment outcome. For example, treatment outcome may be
adversely effected in cocaine rehabilitation programs which rely heavily
upon an educational component since a substantial number of cocaine
abusers may evidence difficulty assimilating material presented in both
visual and verbal form. If further research supports these finding,
treatment outcome may be enhanced by incorporating methods of
improving retention of this material into the treatment program, e.g.,
repetition, more individualized modes of presentation. Future research
which assesses the relationship between neuropsychological impairment
in cocaine abusers and treatment outcome is indicated.

As the neuropsychological concomitants of cocaine abuse are better
understood, efforts to discourage use of the drug may be bolstered by
providing the public with actual descriptions of the adverse consequences
of chronic use on brain functioning. Such an approach would add a more
empirical, fact-based component to the more emotionally based anti-drug
campaigns currently in vogue (e.g., comparing the effect of drugs on the
brain to an egg in a frying pan). A broad spectrum approach incorporating
both factual and sensational presentations of the adverse consequences of cocaine abuse may access a greater proportion of the population.

Conclusion

Impairments in performance of cocaine abusers relative to controls on challenging tests designed to measure new learning and delayed recall of both verbal and visually mediated tasks suggest that chronic cocaine administration adversely affects mnemonic integrity. Furthermore, the degree of impairment appears to be related to the route of administration employed to ingest the drug, i.e., the IV group evidenced greater impairment than the smoker group. No significant differences were noted among groups on measures of attention/concentration and verbal fluency. While it is not prudent to conclude that an unequivocal cause and effect relationship exists, these preliminary results suggest the possibility of a dose dependent neurotoxic relationship between cocaine and brain functioning and that further research examining this construct is indicated.
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Table 1

Mean Subject Demographic Characteristics

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Table 1 (con't)

Mean Subject Demographic Characteristics

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### Table 2

Mean Scores on Memory Tests for Each Group

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* Controls significantly better than IV group ($p < .05$)

** Controls significantly better than IV and Smoker group ($p < .05$)

*** Controls and Smokers significantly better than IV group ($p < .05$)
Table 2 (cont’d)

**Mean Scores on Memory Tests for Each Group**

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<td></td>
<td>x</td>
<td>SD</td>
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<td>SD</td>
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<tr>
<td>AVLT 1-5 *</td>
<td>39.1</td>
<td>7.1</td>
<td>43.0</td>
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<tr>
<td>AVLT 6</td>
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<td>8.6</td>
<td>2.6</td>
</tr>
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<td>AVLT 7 **</td>
<td>5.5</td>
<td>1.8</td>
<td>6.8</td>
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</tr>
<tr>
<td>CFT-Copy</td>
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<td>3.5</td>
<td>34.8</td>
<td>1.0</td>
</tr>
<tr>
<td>CFT-IM *</td>
<td>25.0</td>
<td>6.4</td>
<td>29.5</td>
<td>5.9</td>
</tr>
<tr>
<td>CFT-DR ***</td>
<td>24.8</td>
<td>6.5</td>
<td>29.8</td>
<td>5.1</td>
</tr>
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<td>Digit Span-Total</td>
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<td>3.2</td>
<td>14.5</td>
<td>3.3</td>
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<tr>
<td>VMS-Total</td>
<td>14.6</td>
<td>3.5</td>
<td>16.1</td>
<td>3.4</td>
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<tr>
<td>VFLU-Total</td>
<td>41.4</td>
<td>9.5</td>
<td>44.6</td>
<td>11.0</td>
</tr>
</tbody>
</table>

* Controls significantly better than IV group (p < .05)

** Controls significantly better than IV and Smoker group (p < .05)

*** Controls and Smokers significantly better than IV group (p < .05)
Table 3

Summary of Results from the Analyses of Variance

<table>
<thead>
<tr>
<th>Variable</th>
<th>F Ratio (2,42)</th>
<th>F Probability Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVLT 1-5</td>
<td>5.68</td>
<td>.0066</td>
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<td>AVLT 6</td>
<td>2.94</td>
<td>.0639</td>
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<td>Complex Figure Test-Copy</td>
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<td>.0476</td>
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<td>Complex Figure Test-DR</td>
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<td>Digit Span-Total</td>
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<tr>
<td>Visual Memory Span-Total</td>
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<tr>
<td>Verbal Fluency-Total</td>
<td>0.94</td>
<td>.3995</td>
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</table>
Table 3 (cont)

<table>
<thead>
<tr>
<th>Variable</th>
<th>F Ratio (1,42)</th>
<th>F Probability Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVLT 1-5</td>
<td>2.13</td>
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<td>.0011</td>
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<td>Complex Figure Test-IM</td>
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<tr>
<td>Visual Memory Span-Total</td>
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<tr>
<td>Verbal Fluency-Total</td>
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<td>.1371</td>
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</table>
### Table 3 (cont)

<table>
<thead>
<tr>
<th>Variable</th>
<th>F Ratio (2,42)</th>
<th>F Probability Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVLT 1-5</td>
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<td>.1730</td>
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<tr>
<td>AVLT 6</td>
<td>2.43</td>
<td>.1266</td>
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<tr>
<td>AVLT 7</td>
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<td>Digit Span-Total</td>
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<td>Visual Memory Span-Total</td>
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<td>.3459</td>
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<tr>
<td>Verbal Fluency-Total</td>
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<td>.5583</td>
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</table>
Table 4

Summary of eta square values

<table>
<thead>
<tr>
<th>Dependent Variable</th>
<th>Group</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVLT 1-5</td>
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<td>.01</td>
</tr>
<tr>
<td>AVLT 6</td>
<td>.09</td>
<td>.03</td>
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<tr>
<td>AVLT 7</td>
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<td>.05</td>
</tr>
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<td>.01</td>
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<td>CFT-IM</td>
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</tr>
<tr>
<td>CFT-DP</td>
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<td>.19</td>
</tr>
<tr>
<td>Digit Span-Total</td>
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<td>.01</td>
</tr>
<tr>
<td>VMS-Total</td>
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<td>.01</td>
</tr>
<tr>
<td>VFLU-Total</td>
<td>.03</td>
<td>.01</td>
</tr>
</tbody>
</table>
1. I understand that I have been asked to participate in a research investigation designed to study memory. I have been informed that the project may not benefit me directly but that it is hoped that it will increase our understanding of the effects of cocaine abuse on neuropsychological functioning.

2. Madeline Uddo Crane has explained the details and procedures involved in my participation in this study. I am aware that I will be asked to divulge personal information regarding my physical and mental health and my drug and alcohol consumption. I have been informed that all information received from me will be kept confidential and at no time will my replies or responses be associated with my name. Further, I have been informed that the following coding system will be employed to assure confidentiality:

   Each participant will be assigned a subject number which will be recorded on the Informed Consent Agreements. All records will be identified and filed by number only. Informed Consent Agreements and identifying information will be stored and locked in a separate master file. The master file will be located in a different site from the working file which will contain non-personal information.

3. There are minimal risks/discomforts associated with the collection of memory data. I understand that possible anxiety related to revealing personal information and/or frustration from lack of success on tests of memory may occur.

4. I understand that my participation in this research study is voluntary and that I may withdraw whenever I might choose. I further understand that a decision to withdraw would in no way adversely affect me.
Page 2, Informed Consent Agreement
Effects of Cocaine Use and Withdrawal on Clinical Memory and New Learning

5 If I have any questions regarding this study or the procedures required of me, I may address my questions to Madeline Uddo Crane, Psychology Service, New Orleans VAMC, telephone (504) 589-5235. I also understand that I may contact Ms. Crane at the above number in the event of a study-related emergency.

6 In case of any adverse effect or physical injury resulting from this study, it is my understanding that eligible veterans are entitled to medical care and treatment. Compensation may be payable under 38 USC 351 or in some instances under the Federal Torts Claims Act. Non-eligible veterans or nonveterans are entitled to medical emergency care and treatment on a humanitarian basis. Compensation would be controlled by the provisions of the Federal Torts Claims Act.

7 Before giving consent by signing this form, I have been sufficiently informed of the purpose of the study, of the nature of the procedures and interviews I will undergo, and the inconveniences, hazards, or adverse effects that might result from the procedures and interviews.

8 Having read and understood the information stated above, I sign this consent form willingly and keep a copy for my records.

Signature of Participant ___________________________ Date _______

Signature of Witness ___________________________ Date _______
CURRICULUM VITAE

PERSONAL DATA

Nome: Madeline Uddo Crane  
Title: Psychology intern  
Birthdate: November 9, 1960  
Place of Birth: New Orleans, LA  
Social Security: 433-23-9672  
Marital Status: Married  
Home Address: 5926 St. Roch Avenue New Orleans, LA 70122  
Home Phone: 504-282-2815

EDUCATION

8/1989-Expected Ph.D.  
Louisiana State University  
Baton Rouge, Louisiana  
Major: Clinical Psychology

12/1987 M.S.  
University of Southwestern Louisiana  
Lafayette, Louisiana  
Major: Experimental Psychology

5/1982 B.A.  
Loyola University  
New Orleans, Louisiana  
Major: Psychology

AWARDS and HONORS

1979-1985 Member, Psi Chi National Honor Society.

1962 Graduated cum laude

CLINICAL INTERNSHIP

Veterans Administration Medical Center  
New Orleans, Louisiana

Drug Dependence Treatment Program
- comprehensive psychological assessment, individual and group psychotherapy with inpatient and outpatient populations, discharge planning, relapse prevention.

Surgery and Medicine Consultation
- assessment and treatment of medically-related psychological problems, including control and adaptation to chronic hemodialysis, training in biofeedback, progressive relaxation, stress management, and cognitive restructuring therapies.
Neuropsychology Specialty
  Geriatric Neuropsychology
  - comprehensive neuropsychological and personality
    assessment of former Prisoners of War of World War II and
    the Korean conflict; oral and written clinical description of
    results.

  Neuropsychology Consultation
  - will be completed June-August, 1989.

Research
  - ongoing assessment of neuropsychological sequelae of cocaine
    abuse

PROFESSIONAL EXPERIENCE

  Veterans Administration Medical Center
  New Orleans, Louisiana

  Louisiana State University
  Baton Rouge, Louisiana
  Supervisor: W. Drew Gouvier, Ph.D.

1/1986-1/1988 Clinical Psychology Practicum
  Louisiana State University
  Baton Rouge, Louisiana
  Supervisors: William F. Waters, Ph.D. and
  Johnny L. Matson, Ph.D.

  Louisiana State University
  Professors: W. Drew Gouvier, Ph.D. and
  John Junginger, Ph.D.

  Louisiana State School for the Deaf
  Baton Rouge, Louisiana
  Supervisor Phyllis Stevens, M.S.

PROFESSIONAL AFFILIATIONS

  Student Affiliate, American Psychological Association

  Student Member, American Psychological Society

  Student Member, Society of Psychologists in Addictive Behaviors
PRESENTATIONS


Mendoza, J. E., Moore, J. N., & Uddo-Crone, M. A qualitative scoring approach for the Rey-Osterrieth Complex Figure. Poster accepted for presentation at the annual convention of the American Psychological Association, New Orleans, Louisiana, August 1989.

PUBLICATIONS


RESEARCH/PROFESSIONAL INTERESTS

Neuropsychology
Substance Abuse
DOCTORAL EXAMINATION AND DISSERTATION REPORT

Candidate: Madeline Uddo Crane

Major Field: Psychology

Title of Dissertation: Effects of Cocaine Use and Withdrawal on Clinical Memory and New Learning

Approved:

N. D. Green
Major Professor and Chairman

Dean of the Graduate School

EXAMINING COMMITTEE

Colette Streitfeld
Frederick Streitfeld
J. G. Johnson
Edward S. Shirey

Date of Examination: July 24, 1989