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The Effects of Personality Disorders on Treatment Response and Outcome among Cocaine-Dependent Out-Patients

by
Madeline Rhum

A dissertation submitted to the Graduate Faculty
in Psychology in partial fulfillment of
the requirements for the degree of Doctor of Philosophy,
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Abstract

The Effects of Personality Disorders on
Treatment Response and Outcome
Among Cocaine-Dependent Out-Patients

by

Madeline Rhum

Adviser: Professor Steven Tuber

This study examined the effects of comorbid Axis II personality disorders on the treatment response and outcome of treatment-seeking cocaine-dependent outpatients who were enrolled in controlled clinical trials at the New York State Psychiatric Institute in New York City. The subjects were 51 patients some of whom were diagnosed with the comorbid Axis I disorders of attention deficit hyperactivity disorder (ADHD; n = 17) or depression ("dep"; n = 19), and a group who were not diagnosed with any additional non-substance related Axis I disorder (N/C; n = 15). It was hypothesized that Axis II diagnoses would be evenly distributed among the three subgroups of study patients. It was also hypothesized that each subgroup of patients would be differently effected by the presence of any Axis II comorbidity. Specifically, it was hypothesized that the ADHD subgroup would not be negatively effected by any Axis II comorbidity; and, that the treatment response and outcome of the "dep" and N/C subgroups would be adversely effected by Axis II comorbidity. Furthermore, it was hypothesized that any patients whose only comorbid diagnosis in addition to cocaine dependence was antisocial personality disorder (ASP), would do less well in treatment than patients who were diagnosed with ASP and any additional Axis I (i. e. ADHD or depression) and/or any additional Axis II diagnoses.

Patients were treated with either an active medication or placebo, and an individual cognitive-behavioral intervention, Relapse Prevention (RP), which focused directly on thoughts, feelings and behaviors associated with the patients' drug use. Patients' Axis II diagnoses were determined using the Millon Clinical Multiaxial Inventory, third edition

(MCMI-III; Millon 1994). Treatment response and outcome were measured through several means including: urine toxicology screens for evidence of cocaine; changes in self-reports of cocaine craving; changes on scores of the drug and psychological severity scales of the Addiction Severity Index, fifth edition (McLellen et al. 1992); and, length of time subject remained in treatment.

No statistically significant results were found between those patients who had a comorbid personality disorder and those who did not. Several factors may have contributed to these findings including: the lack of diagnostic precision of the MCMI-III with this population; and, the effectiveness of the psychotherapeutic intervention (RP) in ameliorating pathological aspects of patients' Axis II disorders.

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I learned many important things through carrying out this research project. Foremost among them was that I simply could not have done it without the support, guidance and encouragement of quite a few people. I am indebted to Drs. Frances Levin and Edward Nunes for allowing me to utilize data from their ongoing treatment studies at the New York State Psychiatric Institute. I am grateful for and amazed by the patience, and consistent, quiet urging and nudging of my advisor Dr. Steven Tuber. I am deeply appreciative of the wise and incisive comments and questions I received from Drs. Paul Wachtel, Diana Diamond, and Denise Hien, the other members of the examination committee. There are four extraordinary women, Melissa Ritter, Mabel Quinones, Toni Andrews, and Linda Jacobs, friends in the truest sense of the word, who believed in my ability to complete this work despite all the evidence I presented them to the contrary. Finally, I would like to honor my classmates Jonathan Brydon and Dennis Twiggs who courageously undertook this enormous life-bending project of becoming a clinical psychologist in the face of overwhelming odds. I dedicate this dissertation to their memories.

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Introduction

Substance Abuse

Substance abuse is one of the most serious problems facing the public today. The impact of substance abuse touches every sector of society and adversly affects individuals, families and whole communities. Current epidemiological data from several sources indicate that while there has been some leveling off or even decrease of certain psychoactive substances within some segments of the population, the prevalence of substance abuse remains unacceptably high. The National Household Survey on Drug Abuse (HSDA) is an annual survey conducted by the federal government which is often cited as an important source of information about current epidemiological trends (United States Department of Health and Human Services, 1997). Results from the 1996 survey indicate that an estimated 13 million Americans had used an illicit drug within the past month during the previous year. The 1996 HSDA found that 73% of all current illicit drug users were employed, but it also found that over 12% of unemployed adults were current users of illicit drugs whereas 6.2% of full-time employed adults had used illicit drugs in the past month, suggesting that a substance abuse problem may contribute to an inability to hold down a job.

Another important source for national epidemiological data on substance abuse comes from the Drug Abuse Warning Network (DAWN; National Institute of Drug Abuse, 1996). Since the 1970's DAWN has reported the estimated number of hospital emergency department episodes that were directly related to some form of illicit substance use. It's most current data is from 1995 when there were over half a million drug related hospital emergency room visits. From 1978 to 1995 the number of drug related episodes increased by 65% while during this same period overall emergency department visits rose by only 24%. They also report that the rate of drug related episodes per 100,000 population increased 37% between 1990 and 1995.

The financial cost to society of alcohol abuse and illegal drug use is enormous. The United States spends approximately $200 billion a year in medical services, law enforcement, lost productivity, property damage, and insurance claims directly related to alcohol and drug abuse . Roughly 25% of the $200 billion is spent on prevention and treatment according to one source (Missouri Department of Mental Health, Division of Alcohol and Drug Abuse, 1994).

Cocaine Abuse: epidemiological data

Cocaine use accounts for the most dramatic increase of all illegal drug use in the 1980s and 1990s with an estimated 1.7 million Americans considered current cocaine users in 1996. According to the DAWN survey, cocaine sent more people to the emergency room from 1985 through 1995 than any other drug. Between 1978 and 1995, cocaine related incidents rose from representing only 1% of all drug related emergency room visits to 27%. Although the rate of emergency room visits related to cocaine use remained stable from 1994-1995, they remain at their highest level since these statistics have been collected. The overall number of people who report using cocaine in the past month is no where near the level it was at its peak in 1985, although a slight increase is evident from 1995 to 1996 according to the HSDA. In 1985 there were an estimated 5.7 million current cocaine users, which declined to 1.4 million in 1992 and there have not been any significant changes since then.

Cocaine Abuse: changes in attitudes

Cocaine has certainly been popular at other times in history and in the late 1800's and into the early part of this century it was enjoyed by many people (e.g., it was an ingredient in Coca Cola until 1903) and respected by medical authorities. Its stimulating properties have made it attractive to many people. Freud's enthusiasm for cocaine for a period of time was well known, for instance. Cocaine made its first appearance in the

United States about the turn of the century and problems associated with cocaine abuse became apparent within a few years. The New York Times reported in 1908 about "The growing menace of the use of cocaine" facing young people in the Bowery. At that time a dire pessimism was expressed about the possibility of helping those who abused cocaine. A neurologist is quoted in the article as saying, "There is nothing we can do for the confirmed user of the drug. The best thing for the cocaine fiend is to let him die." (New York Times, 1908) During the early decades of this century a series of changes in federal laws regulating controlled substances and also changes in social mores (such as the temperance movement) lead to a decrease in the availability of cocaine and its use almost completely disappeared until the 1970s.

Professional and public beliefs about cocaine were very different in the late 1970s when it was just starting to grow again in popularity. In the 70's and into the early 80's cocaine was associated with glamour and prestige. During this period cocaine was widely used by people from all across the socioeconomic spectrum. The perception in the 1970's of cocaine among users and even some mental health professionals was that it was a relatively safe and nonaddictive drug. This point of view appeared within the popular and professional literature. Some of the positive features of cocaine were noted in the Comprehensive Textbook of Psychiatry published in 1980 where the authors wrote: "Used no more than two or three times a week, cocaine creates no serious problems. In daily and fairly large amounts it can produce minor psychological disturbances. Chronic cocaine abuse does not appear as a medical problem" (Grinspoon, L., Bakalar, J. B. 1980). It was not long, however, before the negative consequences associated with cocaine abuse started to become apparent.

Cocaine abusers began showing up in large numbers for treatment in the 1980s. Programs that previously had treated opiate users and alcoholics had to adjust to this new population of substance abusers, and had much to learn about the ways that cocaine

affected abusers on biological and psychological levels (Wallace 1992). Substance abuse research in both the lab and in clinical trials in the treatment setting has contributed a great deal to our understanding of how cocaine acts on the brain and also of the psychological factors which can lead to the cycle of chronic relapsing so often found among cocaine abusers (Kosten & Kleber, 1992). As research progressed, the definitions of cocaine disorders (abuse and dependence) evolved within the standardized diagnostic system of the Diagnostic and Statistical Manual of Mental Disorders (DSM, versions III, III-R and IV) which has been the diagnostic system most widely used in research and clinical settings (American Psychiatric Association 1980, 1987, 1994; Gawin and Kleber 1992). In this study I will use the terms "substance abuse" or "cocaine abuse" when referring generally to problems stemming from the use of drugs and/or cocaine unless otherwise specified; I will use the term "cocaine dependence" when referring specifically to the DSM-defined disorder. A diagnosis of cocaine dependence can be made according to the DSM-IV when:

DSM-IV criteria for a diagnosis of cocaine dependence

a maladaptive pattern of cocaine use, leading to clinically significant impairment or distress, as manifested by three (or more) of the following, occurring at any time in the same 12-month period:

(1) tolerance, as defined by either of the following:
  (a) a need for markedly increased amounts of the substance to achieve intoxication or desired effect
  (b) markedly diminished effect with the continued use of the same amount of the substance
(2) withdrawal, as manifested by either of the following:
  (a) the characteristic withdrawal syndrome for the substance
  (b) the same (or closely related) substance is taken to relieve or avoid withdrawal symptoms
(3) the substance is often taken in larger amounts or over a longer period than was intended
(4) there is a persistent desire or unsuccessful efforts to cut down or control substance use
(5) a great deal of time is spent in activities necessary to obtain the substance (e.g., driving long distances), use the substance, or recover from its effects
(6) important social, occupational, or recreational activities are given up or reduced because of substance use
(7) the substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance (e.g., current cocaine use despite recognition of cocaine-induced depression).

(American Psychiatric Association, 1994)

Cocaine Abuse: Comorbidity

Substance abusing patients with a wide range of psychiatric and emotional problems are frequently seen in treatment, and as a result there has been a growing interest in understanding the relationship between the comorbidity of psychopathology and addictive disorders. The co-occurrence of non-substance induced psychopathology among alcoholics, opioid users and, most recently, cocaine users has been widely investigated (Hesselbrock et al., 1985; Khantzian & Treece 1985; Kleinman et al., 1990). As the picture of what constitutes a cocaine-related disorder has become clearer, clinicians and researchers have become better able to distinguish symptoms caused by cocaine abuse from those stemming from comorbid disorders.

Distinguishing substance related from non-substance related disorders is not a simple task, however, insofar as the interaction of psychopathology and a substance abuse disorder is extremely complex. Diagnosing and treatment planning are complicated by the various ways addictive disorders and psychopathology can interact. Making accurate diagnoses is especially difficult because the effects of psychoactive substance use or the symptoms caused by withdrawal can appear similar to symptoms characteristic of non-substance related disorders such as depression and bipolar disorders. Despite the difficulties in assessing these patients, numerous investigations into the prevalence of comorbid disorders have found high rates of Axis I (clinical syndromes) and Axis II (personality) disorders. For example, between 30%-50% of treatment seeking cocaine abusers also had an Axis I affective disorder (Weiss et al., 1986; Weiss et al., 1988) and attention deficit-hyperactivity disorder (ADHD) was diagnosed in 10% a cohort of treatment seeking cocaine abusers (Levin et al., in press). Prevalence rates of Axis II personality disorders among cocaine abusers have ranged from 50%-90% (Halikas et al., 1994; Kleinman et al., 1990; Malow et al., 1989; Nace et al., 1991; Weiss et al., 1993).

The high rate of psychiatric comorbidity demonstrated by numerous prevalence studies has lead to further investigations into the development of treatments which address

the range of patients' psychological and psychiatric problems. The aim of treating individuals' substance abuse problems and co-existing psychopathology concurrently marks a departure from more traditional approaches to treatment where each problem was addressed separately. For example, chemical dependency treatment programs typically do not address any co-occurring psychopathology, and other the other side, many mental health providers, both clinics and private practitioners, will not treat a patient with a substance abuse problem, but instead will refer the patient to a chemical dependency program. The complex interaction of addictive disorders and additional psychopathology, however, suggests that there may be significant benefit to treating these problems simultaneously (Miller & Brown 1997; Ziedonis 1992).

Comorbidity: theoretical/conceptual concerns

The relationship between a substance use disorder and additional psychopathology can take a number of different forms . Meyer (1986) lays out some possibilities:

> There are five possible relationships (and one non-relationship) between addictive behavior and coexisting psychopathology:
> 1. Axis I and II psychopathology may serve as a risk factor for addictive disorders.
> 2. Psychopathology may modify the course of an addictive disorder in terms of rapidity of course, response to treatment, symptom picture and long-term outcome.
> 3. Psychiatric symptoms may develop in the course of chronic intoxications
> 4. Some psychiatric disorders emerge as a consequence of use and persist into the period of remission.
> 5. Substance-using behavior and psychopathological symptoms (whether antecedent or consequent) will become meaningfully linked over the course of time.
> 6. Some psychopathological conditions occur in addicted individuals with no greater frequency than in the general population, suggesting that the psychiatric disorder and the addictive disorder are not specifically related.
> (p. 7)

The need to provide appropriate treatment for dually-diagnosed cocaine abusing patients has been the focus of several treatment studies which either implicitly or explicitly adhere to certain of the possible relationships outlined by Meyer in the above passage (Arndt et al., 1992; Carroll et. al., 1995; Levin et al., in press). A number of such studies are currently ongoing at the New York Psychiatric Institute (NYSPI) where investigators are running controlled clinical trials for the treatment of cocaine dependent individuals with the

comorbid Axis I disorders of depression and attention deficit-hyperactivity disorder (ADHD). The relationship between cocaine dependence and the comorbid Axis I psychopathology of these patients seems to correspond to several of Meyer's points. It is thought, for example, that individuals who are depressed may be vulnerable to developing a cocaine problem because the euphoric effects of cocaine temporarily alleviate their dysphoria (Nunes et al. 1989). Likewise, individuals with ADHD may be at risk for developing a cocaine problem due, in part, to their impulsivity and tendency to be risk-takers, which are characteristic of those with this disorder (Levin & Kleber, 1995). Meyer's first point is illustrated by both of these cases: That Axis I psychopathology may act as a risk factor for addictive disorders. In his second point he suggests that the development of an addictive disorder and the pattern of substance use may be effected by comorbid psychopathology. For these individuals, who experience an improvement in the symptoms of their Axis I disorder when using cocaine, there appears to be a tendency to use cocaine more frequently and intensely than those without additional non-substance related disorders. Meyer suggests that the course of treatment may differ for multiply diagnosed patients, and preliminary data from these treatment studies at NYSPI seems to support this. There is some evidence that those cocaine dependent individuals diagnosed with additional Axis I disorders do stay in treatment longer and have a better response to treatment than those without additional Axis I diagnoses although the reasons for this remain unclear.

While the complex relationship between any substance use disorder, in this case cocaine, and comorbid psychopathology cannot be reduced to a simple explanatory model, the notion of using psychoactive substances in an effort at "self-medication" is one hypothesis that has gained wide acceptance. According to this hypothesis, certain individuals use cocaine in an attempt to neutralize painful affect states, such as depression, or enhance poor self-esteem (Khantzian 1985). For example, individuals who abuse cocaine who also have ADHD, have reported that cocaine initially ameliorates symptoms

such as impulsivity, distractibility, poor concentration, and inattentiveness which interfere with daily functioning (Khantzian 1983; Weiss et al. 1986).

Treatment Studies

One researcher and clinician who has investigated various aspects of this treatment seeking population noted that "Appropriate treatment of both drug- and nondrug-related illness greatly improves their prognosis. As in other areas of medicine, monolithic theories about etiology, coupled with simplistic approaches to treatment, spells disaster for patients with complicated problems" (Mirin et al., 1988). Both psychological approaches such as Relapse Prevention (RP; Marlatt & Gordon, 1985) and Interpersonal Psychotherapy (IPT; Rounsaville et al., 1985), and pharmacological treatments have been either developed or adapted and tested in clinical trials with the aim of treating both cocaine abuse as well as comorbid Axis I disorders. Pharmacological and psychosocial treatment components have been used together in many of the treatment studies, although it is most often only the pharmacological intervention which has been systematically evaluated. The results of these clinical trials have been mixed. Medications have been shown to diminish symptoms of comorbid Axis I disorders (such as depression) among cocaine users, but have been generally less effective in reducing cocaine cravings or use among depressed cocaine abusers (Arndt et al., 1992; Kosten et al., 1992). Those who were treated for ADHD and cocaine dependence with methylphenidate improved with regard to both their cocaine use and their ADHD symptoms (Levin et al., in press).

Treatment Outcome

Questions about the relationship between substance abuse disorders and additional psychopathology have led to studies of the relationship between psychopathology and treatment outcome in substance abusers (Kosten et al., 1987). These studies have generally found that greater psychopathology leads to poorer treatment outcome (McLellan

et al., 1983; Rounsaville et al., 1986). The focus in these studies is usually on Axis I psychopathology (such as mood and psychotic disorders), antisocial personality disorder, or "psychiatric severity" as measured by the Addiction Severity Index (ASI; McLellan et al., 1980). Most of this research has looked at methadone-maintained opiate abusers or alcoholics, and found not only poorer treatment outcome, but also more severe problems in other areas of functioning such as employment, medical health, family relationships and alcohol and drug abuse (Alterman et al., 1993). In a report on one year treatment follow-up with cocaine abusers, Carroll et al. (1993) found that three types of variables (severity of initial drug use, presence or severity of concurrent alcoholism and severity of psychological symptoms) were consistent predictors of treatment outcome.

Comorbid Axis II Disorders

Despite the extremely high rates of personality disorders among cocaine abusers indicated by numerous prevalence studies, there appears to be little research examining the relationship of personality pathology or Axis II personality disorders to treatment retention and treatment outcome. Nor are there any reports in the literature indicating that clinical trials have been designed to address specifically comorbid personality disorders among cocaine abusers. The literature examining the effect of comorbid Axis II personality disorders on treatment outcome across the spectrum of Axis I diagnoses indicates that the presence of an Axis II personality disorder typically leads to poorer treatment outcome (Reich & Vasile, 1993). The probable negative impact of comorbid personality disorders on the treatment of cocaine abusers has frequently been observed, and has led researchers to make statements such as the following: "In terms of treatment implications, the present study supports previous work in showing that large proportions of cocaine abusers are suffering from both depressive disorders and axis II disorders. Whatever the treatment modality, treatment providers need to be prepared to address their clients' psychopathology as well as their cocaine abuse." (Kleinman et al., 1990). There appears to be very little,

however, in the way of carefully conducted studies where Axis II psychopathology has been either investigated or targeted specifically by the design of treatment studies.

A variety of factors may have contributed to this omission in the design and implementation of treatment research for substance abuse.

1. As the biological aspects of behavior have become increasingly the focus of research, the emphasis in treatment has been on developing novel medication approaches to treating a wide range of disorders. Psychiatric medications treat relatively unambiguous symptoms which are more easily identifiable in Axis I than in Axis II disorders. Personality abnormalities are often more difficult to distinguish precisely than the signs and symptoms of Axis I disorders (Grove & Tellegen, 1991).

2. The relationship of personality disorders to Axis I disorders remains a topic of debate. On the one hand, some would argue that much of Axis I symptomotology reflects a disturbance of personality, and as aspects of personality dysfunction are ameliorated, then a reduction of Axis I-type symptoms will likely abate. On the other hand, the opposite position, that once the Axis I disorder is effectively treated, then much of the pathological personality features will also diminish significantly, has many proponents, especially within psychiatry (Zimmerman, 1994).

3. Personality pathology is difficult to define clearly and not only are Axis II diagnoses continuing to be re-evaluated, but so, too, are notions of what constitutes normal versus abnormal personality features (Strack & Lorr, 1997). This has obvious implications for the difficulty in making diagnostic judgments about personality disorders.

4. Previous investigations into the relationship between personality dysfunction and substance abuse focused on the task of determining specific features of an "addictive personality". This exploration, undertaken through a variety of approaches, proved unsuccessful (Sutker & Allain, 1988). The failure of this line of investigation may have discouraged researchers from exploring personality characteristics of substance abusers (Butcher, 1988).

5. The notion of "personality"-- enduring characteristics which are influenced by a range of factors-- environmental and internal, including unconscious processes-- has been a psychoanalytic object of inquiry. This intellectual paradigm has fallen out of favor in psychological and psychiatric research generally and within the field of substance abuse specifically. A biopsychosocial model guides much of the research and treatment within substance abuse where social-learning and classical conditioning theories comprise the psychological paradigms (Sutker & Allain, 1988).

Although these and other important questions regarding various facets of the construct "personality disorder" remain unresolved, inquiry into the relationship between personality disorders and treatment outcome can, nonetheless, be conducted with the means currently available. If we can understand something more about this relationship, we will be in a better position to design and deliver effective treatments.

The Purpose of the Present Study

Part of what the research on comorbidity in substance abusers tells us is that this is a heterogeneous population in many respects. The treatment studies which have targeted the Axis I comorbidity with medication present one way of trying to address a broader range of these patients' needs. Even within identified Axis I subgroups of substance abusers, however, significant differences in terms of character pathology may be present and these Axis II disorders may exert some influence on treatment course and outcome. By its very definition, personality pathology can influence all aspects of internal and external experience--how one concieves of a sense of self, how one interprets events and interpersonal interactions, how one views one's capacity for making personal changes and where the locus of responsibility for change lies-- to name just a few. These are questions that everyone struggles with at one time or another in his or her life. The specfic personality diagnosis which corresponds to a particular approach in answering those

questions matters less than the degree to which the personality pathology results in an inability to solve these "life challenges". Character pathology often prevents a person from coping with day-to-day dillemas, and finding some measure of satisfaction in life. It was assumed in this study that it would influence the degree to which a person with a cocaine use problem can benefit from treatment.

In this study I compared the Axis II/character pathology diagnoses of three subgroups of cocaine dependent individuals who were enrolled in out-patient treatment. The subgroupings were based on the presence or absence of comorbid Axis I diagnosis, namely depression, ADHD, or no comorbidity. Study participants received a study medication or placebo for their Axis I diagnosis and attended individual Relapse Prevention (RP; Marlatt & Gordon 1985) psychotherapy. RP is a cognitive-behavioral approach which includes coping skill training and strategies for helping the individual to maintain abstinence from cocaine. I determined their personality disorder diagnoses using the MCMI-III (Millon 1994), a widely accepted self-report measure which evaluates both transitory Axis I disorders as well as enduring character pathology. One goal of this comparison was to determine the relative homogeneity versus heterogeneity of these Axis I-based subgroups with respect to personality disorder diagnosis. A second aim of this study was to examine the impact that personality disorders have on treatment response and treatment outcome. Measures such as length of stay in treatment, psychiatric and drug severity as measured by the Addiction Severity Index (ASI), self reports of cocaine use and craving and results of urine toxicology reports were used to ascertain this information.

Literature Review

COMORBIDITY

The Issue in General

Substance abuse researchers and clinicians have been working to understand better the various psychological and psychiatric facets of people who develop a cocaine problem in order to improve treatment. Conceptualizations of substance use disorders and of psychopathology in general have gone through many changes over time, and reflect differing cultural ideas about sickness and health; substance use and abuse; even the nature of free will and its relationship to the prevailing moral ethos (Sutker & Allain 1988; Westermeyer, 1991). What's more, at any given point in time there are differing conceptualizations of psychopathology and addictive disorders, depending on the researcher's/clinician's theoretical orientation which will, in turn, have implications for diagnosis and treatment. For example, the psychiatric disease model of the DSMs differs tremendously from a psychoanalytic viewpoint with respect to etiology, treatment, and even the conceptualization of the construct of "disorder". As is well known, the psychiatric model has emerged as the dominant one in determining diagnoses via established sets of symptom criteria, and the DSM diagnostic system, although continuously evolving, comprises one of the most widely accepted set of diagnostic definitions of psychiatric research. This diagnostic system has provided a tool for many of the prevalence studies which have found high rates of comorbidity among substance abusers.

One such study, published in 1988, investigated psychopathology in a heterogeneous treatment seeking substance abusing population. Beginning in 1980. Mirin, Weiss, Michael, & Griffin, (1988) assessed 160 patients who were consecutively admitted to their Alcohol and Drug Abuse Treatment Center. These patients reported problems primarily with either opiates, cocaine or central nervous system depressants.

Psychopathology was assessed with several self-report rating scales (Beck Depression Inventory, BDI; Symptom Distress Checklist, SCL-90), structured interview rating scale for depression (Hamilton Depression Rating Scale, HDRS). Diagnoses were also made by two ward psychiatrists based on clinical interviews. Family history data was collected with all available first-degree relatives using a structured interview. Laboratory tests were conducted on those thought to have an affective disorder. The results indicated psychopathology in a significant minority of the patients: 42.5% were found to have either alcohol abuse or dependence in addition to their primary substance abuse diagnosis; 20.6% were diagnosed with major/atypical depression; 8.1% were diagnosed with bipolar/cyclothymic disorder; 11.25% were diagnosed with some other Axis I disorder. A total of 40% of the combined three groups had a non-drug Axis I diagnoses. The family history data revealed that the lifetime rate of affective disorders in first degree relatives of substance abusers with affective disorders was three times that of the family histories of substance abusers without an affective disorder (18.9% *vs.* 5.9%). Mirin et al., interpreted this as an important indicator that the affective illnesses of substance abusers were not due simply to the biological or pharmacological effects of substance use and withdrawal, nor to the psychosocial consequences (such as shame, guilt, job loss, etc.) of having a substance use disorder, but rather that they were distinct disorders which were frequently found in this population.

Studies have examined the association between substance abuse disorders and personality disorders as well. In one such study, Johnson, Hyler, Skodol, Bornstein, & Sherman, (1995) found that adolescents who were diagnosed with personality disorders were ten times as likely as those without personality disorders to be identified as depressed and were more than twice as likely as those without personality disorders to be heavy users of alcohol and marijuana.

There have been numerous studies like those mentioned above where the high rate of psychopathology in a population of heterogeneous substance abusers has been

demonstrated. As cocaine abuse became more prevalent and of greater concern to the mental health community, studies have been conducted which focused on cocaine abusers specifically.

Cocaine and Comorbid Psychopathology

The DSM system of diagnosis first recognized cocaine dependence as a disorder in DSM-III-R published in 1987 (American Psychiatric Association, 1987). Around the same time that the definitions of cocaine abuse and dependence were coming into focus, investigations into the co-occurrence of additional psychopathology were already under way. Large scale epidemiological studies such as the National Institute of Mental Health's Epidemiologic Catchment Area study (ECA; National Institute on Drug Abuse) and studies focused exclusively on the psychiatric diagnoses of cocaine users (e.g., the New Haven Cocaine Diagnostic Study, Rounsaville et al., 1991) have uniformly demonstrated that there is a much higher rate of psychopathology among cocaine users than among the general population. Epidemiological studies have also found high rates of cocaine abuse in psychiatric patients (Reiger et al., 1990).

The ECA study evaluated the prevalence of rates of mental disorders, alcohol disorders, and psychoactive substance use disorders by interviewing 20,291 people with a structured interview using DSM-III diagnostic criteria. The estimated lifetime prevalence rates were 13.5% for alcohol use disorders, and 6.1% for other drug use disorders, with only 0.2% having a cocaine use disorder. Of those who were found to have a cocaine use disorder, 76.1% had another psychiatric disorder. This is 11.3 times greater than the general population. In the ECA study cocaine use disorders were associated with schizophrenia (16.7%), affective disorders (34.7%), anxiety disorders (33%) and DSM-III antisocial personality disorder (42.7%) (Regier et al, 1990; Ziedonis, 1992).

Individuals diagnosed with cocaine dependence and comorbid unipolar depressive disorders comprise one of the subgroups of subjects in this study, I will, therefore, review

a few of the studies that have investigated the comorbidity of depressive disorders in cocaine users. I will then present similar data on attention deficit hyperactivity disorder (ADHD), which is the other Axis I comorbid diagnosis treated in this study of cocaine users. Before discussing the comorbidity of ADHD and cocaine, I will also present some of the literature regarding the diagnosis of ADHD in adults, since this is a relatively new and less well known diagnosis in adults.

Comorbid Axis I

Depression

A group of investigators at McLean Hospital have published several studies specifically about psychopathology in cocaine abusers. Weiss, Mirin, Griffen, Michel, & Sollogub, (1986) reported that in a group of 30 hospitalized cocaine abusers 63% met DSM-III criteria for an Axis I diagnosis other than substance abuse. Fifty-three per cent of these patients had an affective disorder. The cocaine abusing patients were compared with opiate and depressant abusers and were found to have a significantly higher prevalence rate of affective disorders than these other groups of substance abusing patients.

Two years later Weiss, Mirin, Griffen, & Michel, (1988) published a report on the changing trends of psychopathology in cocaine abusers as a follow up to the one mentioned above. The patients in the first study had been admitted to the hospital between 1980-1982 which was a time when cocaine was not as widely used as later in the decade. For example, cocaine related emergency room visits quadrupled between 1982 and 1986 according to the National Institute on Drug Abuse (NIDA). The follow up study examined the comorbid psychopathology in an expanded sample of cocaine abusers admitted to inpatient treatment between 1982-1986 in order to answer two questions: 1. had the prevalence rate of affective disorders in chronic cocaine abusers remained stable; and 2. had the changes in the epidemiology of cocaine use resulted in any changes in the characteristics of treatment seeking cocaine abusers. As in the previous study, the results of the cocaine

abusers were compared with opiate and depressant abusers as well. In terms of comparison among the three groups of substance abusers, cocaine abusers continued to have more affective disorder diagnoses although only slightly (26.8% *vs.* 20.1%). They did find a significantly higher rate of cyclothymic disorder (11.4% *vs.* 2.7%). However, overall rates of affective disorders in cocaine abusers had changed a great deal between the two studies. The rate of affective disorders decreased from 50% to 21%. Similar changes were not seen in the opioid and depressant abusers. From these results they concluded that although a significant proportion of cocaine abusers had an affective disorder, having a premorbid affective disorder was a less important risk factor for the development of chronic cocaine abuse since cocaine use had become more widespread.

Nunes, Quitkin, & Klein, (1989) reported on the comorbid Axis I diagnosis in 30 cocaine abusers consecutively admitted to out-patient substance abuse treatment. Patients were diagnosed with the Structured Clinical Interview for DSM-III (SCID; Spitzer & Williams, 1985). Only disorders that predated the onset of any substance dependence disorder were diagnosed. They found that most cocaine abusers had one or more additional Axis I diagnosis. Sixty-three per cent met lifetime criteria for an affective disorder with onset preceding any substance dependencies, of these 33% were unipolar and 30% of the sample met criteria for bipolar spectrum (includes cyclothymic) disorders. Based on the analyses of their data, these researchers proposed subdividing these cocaine abusers into two subgroups: 1) those with a primary affective disorder which can then be further divided into either unipolar vs. bipolar or those with severe vs. mild depression, and 2) those with other drug dependencies. They found that those with affective disorders used a smaller amount of cocaine than those without such disorders, and they suggested two possible explanations for this. The first is that individuals with an affective disorder may be more sensitive to the effects of cocaine or, alternatively, they may be self-medicating depression and, therefore, using the minimum amount needed. Twenty-three per cent of their sample did not have any comorbid affective disorder but did have

additional drug dependencies. They cautioned that this may be a more difficult group to treat than indiviuals without an affective disorder because they generally have begun their cocaine use at an earlier age, use larger amounts of cocaine, are often involved in drug dealing and tend either to smoke or inject cocaine resulting in a more potent effect than when used intranasally.

Kleinman et al., (1990) reported on their study of 76 cocaine and crack abusers entering outpatient treatment in 1987. Patients were assessed according to DSM-III-R criteria using the SCID for DSM-III-R & SCID-II for Axis I and Axis II diagnoses. Patients also completed self-report measures (Symptom Check List-90;SCL-90 & Beck Depression Inventory; BDI). They were also interviewed with a structured interview, the "Addiction Severity Index" (ASI; McLellen, Luborsky, Woody, O'Brien, 1980) which assessed the impact of substance abuse on a number of dimensions including severity of psychopathology, psychosocial functioning and severity of substance use. They found that 28% of the clients were diagnosed as having a current (within the last 30 days) major depressive syndrome, and that 6% were dysthymic. Overall, a total of 47% of clients suffered from some type of depressive illness.

Halikas, Crosby, Pearson, Nugent, & Carlson, (1994) examined psychiatric comorbidity in 207 treatment seeking cocaine abusers. The patients were diagnosed with a structured clinical interview, the Diagnostic Interview Schedule (DIS). They found high rates of comorbidity: 62% met diagnostic criteria for a current psychiatric disorder and nearly 3/4 (73%) met lifetime criteria for at least one psychiatric disorder other than substance abuse. Three disorders, Antisocial personality disorder, affective disorders and anxiety disorders, accounted for most of the diagnosed comorbidity. They note that a special feature of this study was the large sample size relative to other studies of this kind. Their findings replicated those of earlier studies which have shown high rates of comorbid psychopathology in general and of affective disorders specifically among cocaine abusers.

Attention Deficit Hyperactivity Disorder: Background

Attention deficit hyperactivity disorder (ADHD) is thought to be a biological-neurological condition with concomitant psychological and social factors which strongly influence its development and expression (Weinstein, 1994). Individuals with problems of inattention and distractibility and/or hyperactivity and impulsivity may be diagnosed with ADHD, and individuals with problems of inattention without hyperactivity/impulsivity are diagnosed with ADD. It was previously thought that ADHD/ADD was a childhood disorder that was outgrown by adolescence. As a result of several long-term follow up studies, however, it is now considered to be a disorder which begins in childhood and, in 30% to 75% of the cases, persists throughout the person's lifetime (Biederman et al., 1993; Shekim, Asarnow, Hess, Zaucha, & Wheeler, 1990; Weiss and Hechtman, 1986). Wender, who has researched adult ADD/ADHD for over twenty years, estimates that between 1%-6% of the general adult population has the disorder. So, like other neurobiological disorders, ADD/ADHD is now thought to originate in childhood and continue, for a significant number of people, in some form during adolescence and adulthood even if the individual does not seek help or receive the diagnosis until adulthood.

Current epidemiological studies estimate that ADHD effects between 2.0% and 6.3% and ADD effects between 2.2% and 12.6% of all children (Szatmari, 1992). Although it is difficult to predict the long-term outcome of children with ADHD, many researchers and clinicians have argued for greater recognition of this disorder in adults (Mannuzza & Klein, 1992; Silver, 1992; Spencer, Biederman, Wilens, & Faraone, 1994). Often some of the symptoms of hyperactivity and impulsivity have been toned down by adulthood due to the individual's greater maturity and increased sense of the negative interpersonal impact of certain behaviors. For many adults the primary difficulty caused by ADD/ADHD is distractibility (Silver, 1992) This can be manifested, for example, by an inability to keep one's mind on conversations, by being easily distracted due to an inability

to filter out extraneous stimuli, or by frequent forgetfulness to name just a few of the common symptom pictures (Wender, 1996).

Studies have shown that many adults with ADD/ADHD suffer from persistent symptoms which prove very destructive in daily life. Often a concomitant depression develops as a result of the years of frustration and poor achievement in love and work. For example, a study of adults who had been referred for diagnostic work up and treatment for adult hyperactivity found that the only significant differences in comorbidity between those adults who had previously been diagnosed with ADHD as children and those who had not was that this latter group had a higher rate of dysthymia (Shekim et al., 1990). Adults with this disorder tend to report feeling very badly about themselves and often to blame themselves for the lack of success in their lives. A study done at the University of Massachusetts ADHD clinic (Kane et al., 1990) identified the most frequent presenting complaints of adults being evaluated for ADHD:

* difficulty in finding and keeping jobs
* performance on the job below level of competence
* inability to perform up to intellectual level in school
* inability to concentrate
* lack of organization
* inability to establish and maintain a routine
* poor discipline
* depression, low self-esteem
* confusion, trouble thinking clearly

Given the difficulties often experienced by those with ADD/ADHD, one can hypothesize that these individuals would be at risk for developing a substance abuse problem insofar as they may be seeking some kind of escape from frequent humiliations and feelings of inadequacy (Levin & Kleber, 1995). The research in this area seems to indicate that this vulnerability does indeed result in people with ADHD developing a substance use disorder at higher rates than in the general population. The issue becomes further complicated, however, due to the inflated prevalence of psychiatric comorbidity of people with ADHD as

compared to normal adults. Some of the studies investigating comorbidity of ADD/ADHD with other psychiatric disorders including substance use disorders will be presented below.

ADD/ADHD and Comorbidity with Other Psychiatric Disorders

The problems of individuals who have ADD/ADHD extend beyond this disorder alone. There have been numerous studies that have investigated the rates of psychiatric comorbidity among children, adolescents and adults with ADD/ADHD. The findings of these investigations consistently report that the majority of the individuals studied have more than one diagnosis. Some of the research has found that there are two distinct groups of individuals with ADD/ADHD: those that, as adults, exhibit relatively little impairment and psychopathology and have managed to cope well with the impingement associated with ADD/ADHD; and a second group who are at serious risk for destructive behavior and who typically have several comorbid diagnoses, notably antisocial personality disorder and substance abuse disorders (Greenfield, Hechtman, & Weiss 1988).

Comorbidity of ADHD with a variety of additional psychiatric disorders has been investigated both in child and adult samples (Beiderman, Newcorn, & Sprich 1991; Beiderman et al. 1993; Shekim et al. 1990). Prospective follow-up studies of young adults diagnosed with ADHD as children have also been conducted (Mannuzza, Klein, Addalli 1991; Weiss et al. 1985). In all cases, the findings are consistent with regard to the high prevalence of comorbidity.

Shekim et al. (1990) conducted a study of adults referred for diagnosis and treatment of adult hyperactivity. Of the 56 adults who participated they found that 91% met the criteria for ADD/ADHD, but that only seven had the ADHD diagnosis alone. They found that 53% of the sample met DSM-III-R criteria for generalized anxiety disorder, 34% for alcohol abuse or dependence, 30% for drug abuse (sic), 25% for dysthymic disorder and 25% for cyclothymic disorder.

Beiderman et al. (1993) reported that adults with ADD/ADHD have significantly higher rates of other psychiatric disorders when compared to a control sample of normals. This group studied 84 adults who had been referred for treatment of ADHD, each of whom had childhood onset ADHD which was confirmed by a structured interview. They found differences between the controls and target group on several dimensions including: significantly lower scores on Global Assessment of Functioning Scale for the adults with ADHD; adults with the disorder had significantly higher rates of repeated grades and other indicators of poor academic performance as compared with the normals; and, adults with ADHD had significantly lower full scale and freedom from distractibility IQs (as measured by the WAIS-R). The psychiatric diagnoses of the two groups differed as well. The rate of antisocial personality disorder among adults with ADD/ADHD was 12%-18% whereas it is 3% for normals. Major depressive disorder was diagnosed in 31% of the adults with ADHD and only 5% in the comparison group. Rates of substance abuse disorders were also significantly disparate for the two groups: for the adults with ADD/ADHD the rates of substance abuse and dependence disorders (nonspecified) were 17%-20% and for the normals the rate was 6%.

ADD/ADHD in Adults & Substance Abuse:

There is some controversy in the literature about the relationship between ADD/ADHD and vulnerability for substance abuse. The issue concerns the role of conduct disorder in children and antisocial personality disorder (ASPD) in adults, and whether the relationship truly exists between ADD/ADHD and substance abuse or, if instead, the relationship is between ASPD and substance abuse (Kaminer 1992).

Biederman et al. (1995) investigated the association between ADHD and psychoactive substance abuse. They hypothesized that adults with ADHD and other comorbid psychiatric disorders, such as mood, anxiety and antisocial personality disorder would be at a higher risk for also having a substance abuse problem. They compared 120

adults with ADHD to 268 adults without ADHD and found that adults with ADHD had a significantly higher lifetime risk for substance abuse than the controls: 52% *vs.* 27%. They also found that the adults with ADHD were at significantly greater risk for substance use disorder independently of psychiatric comorbidity. Antisocial disorders were found to increase the risk for substance use disorders independently of ADHD status.

Studies of Substance Abusers and Comorbid Psychopathology

These and other studies strongly suggest that adults with ADD/ADHD are vulnerable to developing a destructive substance abuse problem. Due to the relative novelty of this diagnosis in adults, clinicians may fail to pick it up in individuals who seek treatment for substance abuse problems. This has lead some researchers to hypothesize that among adults seeking treatment for substance abuse problems, there may be an underlying, undiagnosed case of ADD/ADHD.

In the Weiss et al. studies (1986 & 1988) discussed above with reference to comorbid affective disorders in cocaine abusers, they also noted that some of their sample had ADHD. In their 1986 study of 30 hospitalized cocaine abusers they found that two patients had a childhood history of ADHD. Both of these patients reported that cocaine originally made them feel more organized and less impulsive. In the 1988 study of 149 inpatient cocaine abusers, seven subjects were reported to have ADHD. Again, the authors noted that these patients reported improvement in their symptoms of impulsivity and inattentiveness when they first began using cocaine.

Rounsaville et al. (1991) found that of 298 treatment seeking cocaine abusers, a lifetime diagnosis of ADHD was present in 34.9%.

Carroll and Rounsaville (1993) used this same sample of treatment seeking cocaine abusers and compared it to a sample of non-treatment seeking cocaine abusers from the community (n= 100). They hypothesized that the presence of ADHD would lead to greater problems associated with cocaine use and would, therefore, be more prevalent among

treatment seekers. They tested several other hypotheses as well. including: that cocaine abusers with a history of ADHD would use cocaine in a pattern consistent with an attempt at self-medicating, i.e., using small amounts on a daily basis. Among the 238 treatment seeking individuals they assessed, 35% met diagnostic criteria for ADHD. The community sample had a 23.8% rate of ADHD, a significant difference. They found that having a diagnosis of ADHD was clinically significant in several ways. Subjects with ADHD began using and abusing cocaine at an earlier age; used cocaine more frequently and intensely; had higher rates of alcoholism; more severe polysubstance abuse; greater involvement with treatment, and a poorer treatment outcome. In addition, patients with ADHD were younger when they initiated treatment and they reported more severe substance use. They also made the point that these characteristics were **not** strongly associated with sociopathy, insofar as the differences tended to be greater in the subsample of subjects with ADHD who did not have ASPD than for those with ASPD. They interpret this finding as evidence that cocaine abusers with ADHD use it as a means of self-medicating functional difficulties. These findings suggest that there may be more adults with a history of ADHD than has been recognized previously, and that these individuals may differ clinically in important ways from other treatment seekers without a history of ADHD.

Levin and Kleber (1995) suggested that there is a clinically significant relationship between ADHD and substance abuse. They reviewed two types of studies. The first type, prospective studies which followed hyperactive children and normal controls into adulthood, consistently reported that adults with ADHD were more likely than normal controls to have had a substance abuse problem. The second type, studies of comorbidity in the substance abuse literature, have recently suggested that individuals with a substance use disorder, particularly a cocaine use disorder were more likely to have had a history of childhood ADHD than the general population (Levin and Kleber 1995).

Levin et al. (in press) have recently completed an epidemiological study of treatment-seeking cocaine users in order to determine the prevalence of ADHD in this population. Their assessments found that roughly 10% of those interviewed met criteria for ADHD, and another 5% had subthreshold ADHD.

Axis II/Personality Disorders:

The General Issues: Definitions and Diagnosis

Personality

The influence of personality factors on the development of a cocaine problem, have not been investigated or speculated on to the same extent as has that of the Axis I disorders. Research on the possible etiological factors of addictions have focused on biological and sociological factors, and psychological investigations have relied on learning and conditioning models. The theoretical position within behavioral and social learning psychology to interpret behaviors as situation/context driven and resulting from a socially derived mental set has guided much of the research on the behavior and psychological factors of substance abusers. The notion of an underlying personality (particularly where unconscious process plays a role) does not have a place within a strictly cognitive, social learning, or behavioral framework (Marlatt et al 1988). The pre-eminence of behavioral psychologists in determining the accepted research paradigm has relegated to the sidelines much of the knowledge and insights of clinicians and researchers from other points of view (Meyer 1986; Sutker & Allain 1988).

Psychoanalytic Ideas

Psychoanalytic theorists have proposed a number of accounts regarding personality or underlying characteristics which would potentially predispose a person to initiate, develop and maintain a substance abuse problem. Psychoanalytic theories, however, usually omit the physiological (biological, pharmacological), sociological and additional

environmental factors, and instead focus exclusively on the psychogenic roots of the substance abuser's problems. Psychoanalytic theorists have been criticized for not taking the multidimensionality of this complex problem into account (Morgenstern & Leeds 1993).

Certain ideas from within a psychoanalytic framework, however, have been adopted by clinicians and researchers from other points of view, such as biological psychiatry. One psychoanalytic hypothesis that has gained wide acceptance within the field of addiction research is the notion of "self-medication" developed by Khantzian. He has written extensively on the psychodynamics of substance abuse generally, and cocaine abuse specifically, including numerous articles on the "self-medication" hypothesis as it relates to cocaine abusers intolerance of dysphoric affects (1980, 1985, 1986, 1990, 1991, 1992). In his own work with cocaine users and the research of others, Khantzian found that these patients often suffer from a coincident affective disorder (Gawin & Kleber 1986; Mirin et al. 1988; Nunes et al. 1989; Weiss et al. 1986). Individuals who use cocaine, he reports, find that in the short term they are able to "medicate" effectively a range of psychiatric problems and dysphoric affect states. Their use of street drugs helps them to cope with "distressful subjective states and an external reality otherwise experienced as unmanageable or overwhelming" (Khantzian 1985). He criticizes earlier formulations that emphasized peer pressure, escape, euphoria or self-destructive themes (Khantzian 1985). He proposed the hypothesis of "self-medication" as an alternative understanding. This hypothesis has been an oft cited rationale for pharmacological treatments of cocaine with various comorbid Axis I disorders such as depression and ADHD.

Personality Studies

There were attempts in the past decades to identify a so-called "addictive personality" (Butcher 1988; Meyer 1986; Sutker & Allain 1988) that is, a personality profile which includes characteristics common to all individuals with some sort of addiction

and also which implies specific predisposing personality features which lead to addiction, but these investigations proved unsuccessful. These studies used measures, such as the Minnesota Multiphasic Personality Inventory (MMPI) (and less frequently other self-report measures such as the Millon Clinical Multiaxial Inventory, the NEO Personality Inventory). There have also been studies using the Rorschach where salient personality features were suggested (Blatt et al. 1984). The failure of these studies to determine the profile of the "addictive personality" lead to criticism of this type of inquiry. These critiques themselves have been criticized in how they oversimplify the attempt to discover important personality features of substance abusers (Platt 1986; Sutker & Allain 1988). Contributing to the poor reception given these studies was the prevailing debate within psychology which pit personality against environmental variables in accounting for addictive behaviors. Personality features of substance abusers has become an area of greater interest in recent years, however, and has taken the form of research into the co-occurrence of DSM Axis II personality disorder diagnoses among substance abusers. These studies will be discussed below.

During the 1980's and 1990's there has been a growing in the interest in personality disorders which has been reflected by an increase in the amount and quality of the research in this area (Grove & Tellegen 1991). The definitions of, and criteria for personality disorder diagnoses both broadly and specifically have evolved with the subsequent versions of the DSMs. The enduring quality of the personality traits associated with these disorders, however, has remained an important feature which demarcates these disorders (known as Axis II) from most Axis I disorders. The current guidelines for diagnosing a personality disorder from DSM IV require:

> A. An enduring pattern of inner experience and behavior that deviates markedly from the expectations of the individual's culture. This pattern is manifested in two (or more) of the following areas:
>
> (1) cognition (i.e. ways of perceiving and interpreting self, other people and events)

(2) affectivity (i.e., the range intensity, lability, and appropriateness of emotional response
(3) interpersonal functioning
(4) impulse control

B. The enduring pattern is inflexible and pervasive across a broad range of personal and social situations.

C. The enduring pattern leads to clinically significant distress or impairment in social, occupational, or other important areas of functioning.

D. The pattern is stable and of long duration and its onset can be traced back at least to adolescence or early adulthood.

E. The enduring pattern is not better accounted for as a manifestation or consequences of another mental disorder.

F. The enduring pattern is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., head trauma).
(American Psychiatric Association 1994)

Many researchers and clinicians have emphasized the importance of diagnosing and treating personality disorders whether or not there is a comorbid Axis I diagnosis (Reich & Vasile 1993; Ruegg & Frances 1995). Investigators studying the prevalence and the clinical significance of personality disorders among various populations have used a variety of methods for diagnosing personality disorders including self-report measures (e.g., Millon Clinical Multiaxial Inventory: MCMI-I; -II, -III; and Personality Diagnostic Questionnaire-Revised: PDQ-R), clinical interviews, hospital chart reviews and structured interviews (e.g., Structured Clinical Interview for DSM-III, -III-R, -IV Personality Disorders: SCID-II). Concerns for more rigorous consistency in diagnosis across methods has lead to some in the field to call for a re-evaluation of these various diagnostic measures (c.f., Perry, 1992).

Changes and/or inconsistencies in diagnostic criteria have occurred both within diagnostic systems (e.g., changes from one version of DSM to the next) as well as across systems (e.g., comparing the DSM criteria to the Research Diagnostic Criteria, which has somewhat more stringent criteria, for ASPD; Carroll, Ball, & Rounsaville 1993). In the

former case, of changes within the DSM system, some researchers in this area have written theoretical papers suggesting that there are problems with the current DSM approach for conceptualizing and diagnosing ASPD. The current definition relies on examples of socially deviant behavior whereas in previous versions underlying sociopathic personality features were required in making an ASPD diagnosis (Alterman & Cacciola 1991; Gerstly, Alterman, McLellan, & Woody 1990; Strain 1995). A debate has ensued about the specificity of symptoms or characteristics which should be included in the given definition of specific diagnoses and investigations of heterogeneity, or presence of subtypes, within a particular diagnostic group (e. g., all substance abusers with ASPD are not antisocial in the same way and differ along measurable personality dimensions) (Brooner, Herbst, Schimdt, Bigelow, & Costa 1993; Cottler, Price, Compton & Mager 1995; Grove & Tellegen 1991; Ruegg & Frances 1995).

A particularly relevant example in the latter case, that of inconsistencies across diagnostic systems, involves a brief exchange of commentaries discussing the comparability of DSM Axis II diagnoses and MCMI diagnoses, an argument which appeared in the literature in the mid-80s (Millon 1985; Millon 1986; Widiger, Williams, Spitzer & Frances 1985; Widiger et al. 1986). That debate is especially germane to this study since the MCMI-III is the measure being used to assess personality disorders of our patient/subject population. The major points of this series of exchanges will be presented below as a preface to a review of the studies which have used the MCMI to diagnose personality disorders among substance abusers.

Empirical Studies of Personality Disorders among Substance Abusers

There have been numerous studies which indicate that individuals with personality disorders are at greater risk for developing a substance abuse problem than those without a personality disorder and, conversely, that a large percentage of individuals with a substance abuse problem are likely to have a comorbid personality disorder. Many of these

investigations suggest that substance abusers with a personality disorder vary in their response to treatment from those without, and that the needs of these patients are special (Barber et al., 1996; Butler et al., 1991; Carroll et al., 1993; Dougherty et al., 1989; 1993; Flynn et al., 1996; Halikas et al., 1994; Johnson et al., 1995; Kleinman et al., 1990; Koenigsberg et al., 1985; Kranzler, et al. 1994; Leal et al., 1994; Links et al., 1995; Miller et al., 1993; Nace et al., 1991; Strain 1995; Weiss et al., 1993). They suggest, furthermore, that the presence of a comorbid personality disorder affects the course and outcome of substance abuse treatment. The importance of recognizing and treating the underlying psychopathology of the personality disorder, in addition to the substance abuse problem, is strongly endorsed by these investigators as a result of their findings. The assessment of Axis II personality disorders allows for the possibility of addressing aspects of personality which influence the thoughts, feelings and behaviors of substance abusers in treatment.

Studies of the comorbidity of substance abuse and personality disorders will be reviewed. Some of these studies reported on the prevalence of the comorbidity of these two types of disorders while others of them pursued further questions, such as the impact on psychosocial functioning due to the comorbidity of Axis I substance abuse disorders and Axis II personality disorders. In addition, some of these investigators examined the relevance of identifying the heterogeneity of individuals similarly diagnosed according to the DSM system particularly as this occurs with substance abusers who are also diagnosed with ASPD.

The studies of personality disorders and substance abuse will be discussed in two sections, and grouped with respect to the method used to assess personality disorders. The first section will include studies where structured interviews, such as the SCID II, and/or chart reviews were used to make DSM Axis II personality disorder diagnoses. The second section will review studies where the MCMI was used for assessing personality disorders. In both cases additional measures, (e.g., the Addiction Severity Index; ASI) may have

been used to assess other areas of psychological or psychosocial functioning. These additional findings will be discussed only when relevant to the present study.

In a large scale study of the relationship of Axis I and Axis II disorders, Koenigsberg, Kaplan, Gilmore, & Cooper (1985) examined the charts of 2,462 in- and out- patients. Among their findings were that while a total of 36% of all the patients' charts reviewed led to an Axis II diagnosis, the distribution of these diagnoses were not evenly distributed among Axis I disorders. Patients who were diagnosed with a substance use disorder on Axis I were the most likely of all the patients to also have an Axis II personality disorder. Sixty-one percent of all patients with a non-alcohol substance use disorder had a comorbid personality disorder. The most common Axis II diagnoses that these patients received were: borderline (43%), antisocial (21%) and mixed-atypical-other (17%). These authors conjectured that there were likely to be several reasons for this strong association between substance use disorders and personality disorders. They hypothesized that the high rates of comorbidity were probably due to the patients' attempt at seeking some relief through substance abuse. These patients, who in addition to having a tendency to behave impulsively, also experienced feelings of emptiness, extreme swings of affect and dysfunctional interpersonal relationships.

Inaman, Bascue, & Skoloda (1985) looked at the presence specifically of borderline personality disorder (BPD) among inpatients being treated for substance abuse. They studied 50 male inpatients and found that 56% of these patients met criteria for BPD while 44% did not. They found that those diagnosed with BPD had greater levels of pathology as measured by the structured personality inventory, the Minnesota Multiphasic Personality Inventory (MMPI) specifically in the areas of depression, antisocial tendencies, inadequate reality testing and poor impulse control. They also found that the patients with BPD tended to leave treatment more rapidly than non-BPD patients.

In a study of psychopathology among cocaine abusers specifically, Kleinman et al. (1990) looked at 76 cocaine and crack users who entered treatment in 1987. They found that 40% had two or more Axis II disorders, while 42% were diagnosed as not having any Axis II diagnosis. The most common Axis II diagnoses were: antisocial (21%), passive-aggressive (21%), borderline (18%) and self-defeating (18%). Some of these patients had concurrent Axis I disorders in addition to their cocaine problem, mostly some form of depressive illness (47%). Of those patients who did not have any other Axis I diagnosis, 25% were diagnosed with an Axis II disorder. In their discussion, these investigators stated that regardless of treatment modality, the comorbid psychopathology of these patients must be addressed along with their cocaine problem.

Nace, Davis, & Gaspari (1991) studied the comorbidity of Axis II diagnoses among 100 inpatients being treated for substance abuse problems. They found that 57% had a personality disorder while 43% did not. Those with an Axis II diagnosis differed from those without in several key areas including more extensive substance abuse, specifically greater lifetime use of marijuana, amphetamines, cocaine, LSD and opiates. These authors noted that a standard approach to treatment for substance abuse patients may be inadequate due to the significantly poorer levels of functioning among patients who also have a personality disorder. They, therefore, recommended individualizing treatment for these patients.

Butler, Gaulier, & Haller (1991) investigated Axis II personality disorders among female substance abusers and found that in their sample of 16 women, 79%-88% were diagnosed with a personality disorder depending on the diagnostic instrument used. The most frequently made diagnoses were antisocial, borderline, histrionic, passive-aggressive, self-defeating and dependent. They recommended that this "dual-diagnosis" deserves attention in treatment because of the potential negative impact of personality disorders on treatment outcome.

Weiss et al. (1993) who had previously examined psychopathology in general among cocaine abusers, published a report specifically on personality disorders in this population. They assessed 50 in-patients who were hospitalized for cocaine dependence. They found that 74% received at least one Axis II diagnosis and of these 69% had a diagnosis during periods of both active drug use as well as during abstinence. They inferred from this that personality disorders remain stable despite current drug use patterns and therefore, recommend that clinicians address maladaptive personality traits as part of treatment. They added that improvement in a patient's drug using behaviors does not necessarily imply improvement in other areas of functioning which are affected by underlying personality disorders. Treatment, therefore, should attempt to address and change problematic personality characteristics, such as impulsivity or poor frustration tolerance, since these could lead to relapse.

DeJong, van den Brink, Harteveld, & van der Wielden (1993) studied personality disorders in substance abusers and alcoholics. They assessed 178 alcoholics and 86 polydrug abusers admitted to an inpatient treatment facility. In the polydrug group, 91% of the patients were diagnosed with at least one personality disorder, and the average number of personality disorder diagnoses per patient was four. Eighty per cent met criteria for at least two personality disorders. The most common Axis II diagnoses were: borderline (65%), histrionic (64%), passive-aggressive (49%), antisocial (48%), schizotypal (41%) and dependent (35%).

Randolph and Yates (1993) looked at the effects of gender on antisocial personality in alcohol and drug dependent individuals. They assessed 85 women and 116 men who were inpatients in a drug and alcohol program. A total of 60.8% of the patients were diagnosed with ASP. Those patients with ASPD were predominantly drug dependent (61.7% of drug dependent men and 80% of drug dependent women had ASPD). They recommended that treatment programs address aspects of ASPD which could lead to poorer functioning or to high risk sexual behaviors.

Miller, Abrams, Dulit & Fyer (1993) studied the comorbidity issue from the other way around: they investigated the prevalence and impact of substance abuse on a population of patients diagnosed with BPD at discharge from the hospital. They found that of the 92 charts reviewed, 52 of these BPD patients also had a substance use disorder, while 40 of them did not. They compared these two groups on a number of dimensions. Comorbid affective disorders were common in both groups. The groups were different in terms of the social and economic functioning where the impact of substance abuse was "profound" on these patients. For example, 52% of non-substance abusing BPD patients were employed as compared with only 10% of those with a substance abuse problem. Twenty-seven percent of the substance abusing patients described themselves as "promiscuous" while none of the non-substance abusing patients did so. In making general comparisons between these two groups the authors remarked that those patients who had a substance abuse problem entered the hospital with "markedly depleted resources and options". As compared with the non-substance abusing BPD patients, they were either unemployed or under employed, poorly educated, and many had turned to prostitution; this applied equally to men and women.

Carroll, Ball, & Rounsaville (1993) investigated not only the prevalence of ASPD among a large sample of cocaine abusers (n=399), but also addressed the problem of differing diagnostic criteria among systems by using three different sets of criteria for making their diagnoses. They compared the DSM-III-R criteria with those of the Research Diagnostic Criteria (RDC). The RDC has two sets of criteria for diagnosing ASPD: a standard set and a restrictive one which excludes any behaviors that occur during the period of time when the individual is using psychoactive substances. Their subject population included cocaine abusers in either in- or out-patient treatment as well as a community sample of non-treatment seekers. The three systems yielded quite different results. Fifty-three percent were diagnosed with ASP according to the DSM-III-R criteria; 29% were diagnosed with RDC criteria; and, 7% were diagnosed with ASP according to the RDC

restrictive criteria. In order to asses the short and long term consistency of these diagnoses they attempted to re-interview subjects one month and then again one year after the initial interview. They found poor reliability for the RDC criteria and moderate consistency for the DSM-III-R criteria. Despite these differences across diagnostic systems, they did find some consistencies including: cocaine abusers with ASP when compared to those without ASP, regardless of the system used to diagnose it, began their drug use at a younger age, had more involvement with the legal system, higher severity ratings in other psychosocial problem areas and higher rates of comorbidity, particularly affective disorders and alcoholism. They also found that contrary to previous reports which have suggested that substance abusers with ASP tend to leave treatment early or avoid it altogether, their sample reported significantly more treatment involvement and fewer months of abstinence.

Kranzler, Satel, & Apter (1994) assessed 50 cocaine dependent in-patients for Axis II diagnoses and associated features such as additional Axis I disorders. They found that 70% of this population met criteria for at least one Axis II personality disorder. Many of these patients were diagnosed with more than one personality disorder and 13.2% were given diagnoses from all three Axis II clusters (A, B, & C). They found a significant correlation between the number of Axis II diagnoses and the number of depressive disorders. In their discussion of these findings they noted that much of the research on comorbidity in cocaine abusers has focused on depressive disorders and depressive symptoms. They pointed out that Axis II pathology may predispose individuals who abuse cocaine to develop depressive-type syndromes. They encouraged clinicians to diagnose and treat the underlying personality pathology of cocaine dependent patients although they add that the relevance of Axis II pathology to differential treatment outcome remains an unanswered question.

Halikas, Crosby, Pearson, Nugent, & Carlson (1994) assessed 207 treatment seeking cocaine abusers for both Axis I and Axis II comorbid psychopathology. Sixty-two percent of this sample met criteria for at least one current comorbid disorder, and 73% met

lifetime criteria for at least one additional disorder. They found that ASPD, affective and anxiety disorders accounted for most of the psychopathology. They note that the psychiatric diagnosis preceded the substance abuse diagnosis in the majority of cases.

Rouser, Brooner, Regier, & Bigelow (1994) investigated psychiatric distress in antisocial drug abusers with a focus on additional personality disorders as a mediating factor. 167 opioid abusers in out-patient treatment were assessed for both Axis I and Axis II diagnoses. Psychiatric distress was measured with the Symptom Checklist-90 (SCL-90). Thirty-nine per cent met criteria for an Axis II diagnosis. Of those, 38% were diagnosed with ASPD only: 24% mixed ASPD and another Axis II disorder: and 38% with an Axis II diagnosis other than ASPD. They found significant differences in the level of psychiatric distress among the four groups, with the general finding that the subgroup without an Axis II diagnosis and the subgroup with only ASPD had lower levels of psychiatric distress than the other two subgroups. They pointed out that this study provides clear evidence for the clinical heterogeneity of substance abusers diagnosed with ASPD. They identified a subgroup of substance abusers with ASPD who experience high symptom distress and personality traits which resulted in "vulnerability to chronic and pervasive neuroticism and emotional instability".

Links, Heslegrave, Mitton, Van Reekum & Patrick (1995) researched the consequences of comorbidity of BPD and substance abuse. As in the Miller et al. (1993) study, these researchers examined the impact of substance abuse on patients previously diagnosed with BPD. They examined the prognostic significance of BPD plus a comorbid substance abuse disorder in a group of 88 patients diagnosed with BPD at hospital admission and then contacted for follow up seven years later. They found that 26.4% met criteria for BPD and substance abuse, 41.1% met criteria for BPD only, 9.3% met criteria for substance abuse only and 23.3% met criteria for traits of BPD. On a standard measure of borderline pathology they also found that the subgroup of patients with BPD and substance abuse scored significantly higher than the other subgroups on impulse-action,

affects and psychosis measures. These patients also tended to self-mutilate, and make suicidal threats or gestures more than the other groups. These findings suggest several clinical implications including that the comorbidity of these two disorders should guide clinicians in their treatment of such patients.

Cottler, Price, Compton & Mager (1995) examined subtypes of antisocial behavior among drug abusers. They interviewed 545 substance abusers who were either in treatment or who resided in a women's shelter. They found that 44% of the men and 27% of the women met DSM-III-R criteria for ASPD; 33% of the men and 42% of the women met criteria for adult ASPD without a childhood history of conduct disorder; 5% of the men and 2% of the women met criteria for childhood conduct disorder which did not progress into adult ASPD; and 18% of the men and 29% of the women did not qualify for either ASPD or childhood conduct disorder. The two subgroups of those who met full criteria for ASPD (with a history of childhood conduct disorder) and those who met criteria for ASPD without a history of childhood conduct disorder were almost identical on measures of social, emotional, and physical consequences of drug use. Based on their results these investigators recommended that the criteria for ASPD be broadened to included those who do not make a strict diagnostic history of conduct disorder.

Barber et al. (1996) reported on the prevalence and correlates of personality disorders among 289 cocaine dependent individuals enrolled in out-patient treatment. They found that 48% had at least one personality disorder diagnosis and 18% had two or more. Of those diagnosed with a personality disorder, 65% had a cluster B diagnosis with ASPD and BPD being most common. They also found that those patients who had an Axis II diagnosis were also significantly more likely to have additional Axis I disorders and more severe psychiatric symptoms. For example, patients with BPD had the highest level of depression. Patients with personality disorders also had significantly higher scores on the Addiction Severity Index (ASI) than those without personality disorders. On the other hand, there was no evidence that patients with personality disorders had more severe

cocaine abuse problems. They indicated that these findings lend support to clinicians' reports that Axis II psychopathology is at the root of the difficulties encountered during treatment rather than specific addiction problems.

MCMI Studies

The Millon Clinical Multiaxial Inventory (MCMI) is a 175 true/false item self-report, diagnostic instrument of 24 clinical scales which is designed to measure both enduring personality features as well as acute clinical symptoms and syndromes. It has been used in numerous studies and clinical settings, including specifically with substance abusing populations. The MCMI has been used with substance abusers with one of three aims: to identify patients with a substance abuse problem; to diagnose personality disorders and Axis I disorders; and, to identify and predict important dimensions related to treatment outcome (Craig & Weinberg 1992). The results of those studies which investigated the prevalence of personality disorders contribute further evidence that there is a high rate of personality disorder comorbidity among substance abusers as had been demonstrated by studies discussed above which used other diagnostic methods such structured interviews. I will present some background on Millon's ideas about personality since this instrument was not originally designed to measure precisely personality disorders as they are described in the DSM system (although revised versions of the MCMI do bring it into closer concordance with DSM diagnostic criteria).

The scales of the MCMI were initially derived from Millon's comprehensive theory of personality and psychopathology. The organizing principals of his "biopsychosocial" theory (Craig & Weinberg 1992) include basic styles of personality functioning which refer to both healthy as well as character disordered individuals. Personality psychopathology results from "deficient, imbalanced or conflicted modes of ecological adaptation and reproductive energy". That is to say that due to a range of "biological, psychological, environmental, and social reasons some people will develop rigid and maladaptive"

characters (Strack and Lorr 1997). Three evolutionary polarities-- self/other; pleasure/pain; and, passive/active--describe the dimensions along which one must respond to internal and external factors. The manner can be one that is either "deficient", imbalanced" or "conflicted" where a personality disorder is present (Craig & Weinberg 1992; Millon 1977). For example, personalities which are "deficient" "lack the capacity to experience or to enact certain aspects of the three polarities", such as someone considered to be schizoid who tends to experience neither pleasure nor pain (Millon & Davis 1997). Millon understands personality to be an "intrinsically multioperational construct" that is to say that the domains of behavior, cognition, affect and unconscious process all contribute to the "matrix" of the person, and must be taken into account in determining a diagnosis.

The psychometric properties of the MCMI inventories have been investigated and debated since the first version of the MCMI was published in 1977. Several distinct areas regarding the construct and predictive validity of the MCMI have been examined. Some researchers in the field of personality assessment have argued that Millon's personality disorder scales, while interesting and perhaps even more compelling than some of the DSM definitions, do not accurately measure DSM Axis II personality disorders. Millon posits that his instrument, which is now in its third version, has been modified to correspond more closely with the current DSM (DSM-IV) than the two previous versions. He notes that he was a member of the committee which formulated the Axis II disorders for the DSM-IV and that his participation assures greater conceptual correspondence. He asserts that while his instrument adequately reports on DSM-IV personality disorders, it goes beyond that in capturing the subtleties of character pathology in ways that the atheoretical DSM system cannot (Flynn et al., 1995; Millon & Davis 1997; Millon 1985; Millon 1986; Widiger et al. 1985; Widiger et al. 1986). Millon made changes in versions II and III including the addition of two personality disorder scales in version II and another in version III. He also added a clinical syndrome to version III. In order to bring the MCMI-III into closer correspondence to DSM-IV, 95 items in version II were replaced in version

III. The scoring system was also changed in order to strengthen the validity of the base rate scores.

Studies have found conflicting evidence for the accuracy of the MCMI in diagnosing certain problems. For example, Bryer, Martines & Dignan (1990) found that the MCMI-I was not sufficiently effective in diagnosing alcohol and drug abuse in a population of substance abuse patients which raised questions about the validity and clinical utility of those particular scales. It is important to note, however, that Millon has made revisions to his instrument in versions II and III which have reportedly made the instrument more reliable. In addition, the discrepancy such as the one found in the above mentioned study, has not been widely demonstrated with the scales that measure pervasive personality styles/disorders. Rather, the studies that have examined the test-retest stability of the personality disorder scales have found acceptable levels of consistency of the personality disorder scales (Craig & Weinberg 1992; McMahon, Flynn & Davidson 1985).

Although some questions have remained as to the correspondence of MCMI scales with the DSM, and about the reliability of certain scales for diagnosing particular disorders (especially the Axis I or clinical syndromes), the MCMI-III has gained wide acceptance as a tool for measuring personality pathology in both clinical and research settings (Wetzler & Dubro 1990). As mentioned above, the MCMI has been used frequently to investigate the presence of personality disorders in substance abusers, and a review of the most relevant studies follows. One note about these previous studies: these investigators used either the MCMI-I or MCMI-II, whereas in the present study the MCMI-III, which is purported to give more accurate accounts and have improved on criterion and convergent validity, was utilized.

Empirical Studies Using MCMI

In a study of 100 opiate addicts, Craig (1984) compared the MCMI profiles of program dropouts and completers. He found no significant differences between the two

groups on any scale. He concluded that predictions about treatment dropout should be based on clinical judgment.

Craig, Verinis, and Wexler (1985) conducted a comparative study of 100 opiate addicts and 106 alcoholics. A cluster analysis of the MCMI profiles yielded major differences in personality styles between the opiate addicts and alcoholics. They found two salient clusters for the opiate addicts. One group scored highest in the narcissistic and anti-social personality styles whereas a second group of opiate addicts was shown to have higher scores in the passive/aggressive and avoidant personality styles. For the alcoholics one group also scored high in the passive/aggressive scale but they also had high scores on the borderline and paranoid severe personality disorders. This group also scored high on the anxiety scale. A second group of alcoholics had high scores in the dependent, avoidant, passive/aggressive and schizoid personality styles. This group also scored as highly anxious and depressed. The differences they found between these two groups suggests that there may be merit to the idea that substance abusers seek out particular substances which help "medicate" certain kinds of underlying psychological difficulties.

The MCMI was used in a study of 45 opiate addicts and 31 polysubstance abusers in order to determine Axis II diagnosis. Four subtypes were found after the test results were analyzed with a cluster analysis (Calsyn & Saxon 1988). They identified a narcissistic/antisocial type, a dependent type, a negativistic type and a subgroup that had no disorder. The opiate addicts were more likely to be the narcissistic/antisocial type whereas the polysubstance abusers tended to score highest on schizoid, avoidant and passive-aggressive scales.

Craig (1988) studied the prevalence rates of personality disorders among 121 opiate addicts using the MCMI, and compared his results to those of previously published studies which had used structured psychiatric interviews in forming diagnoses. He found that the rates were comparable across the two methods for diagnosing personality disorders,

although the MCMI tended to over diagnose paranoia and under diagnose antisocial disorders.

Stark and Campbell (1988) used the MCMI with 100 polysubstance abusers in outpatient treatment in order to find out if patients who leave treatment prematurely have any significant personality disorder features. There were no differences in the two groups of completers and dropouts in terms of demographic variables or drug of choice. They found that treatment completers had higher scores on several scales including avoidant, dependent, paranoid, thought disorder, major depression, and delusional disorder. This suggests that those who completed treatment suffered from more severe psychopathology.

A study published in 1989 by Dougherty and Lesswing found that the MCMI diagnosed high rates of personality disorders in a sample of 100 inpatient cocaine addicts. Most of the diagnoses were narcissistic/antisocial, withdrawn/passive-aggressive, and dependent personality disorders.

Craig and Olson (1990) compared the MCMI profiles of 107 cocaine addicts and 86 opiate addicts in order to see if there were any differences in personality style between them. In conducting a univariate analysis they found only one significant difference between the two groups, namely that cocaine users were significantly more likely than heroin users to be diagnosed as antisocial (51% vs. 21%). In performing multivariate analyses, however, they found that four clusters emerged and that there were significant differences between groups based on personality style rather than on drug of choice. These results suggest that substance abusers do not choose their specific drug based on a need to self-medicate particular affect states as is proposed in the pharmacodynamic theory (Khantzian 1985).

Calsyn and Saxon (1990) used the MCMI to identify personality disorder subtypes among 73 opioid addicts and 37 cocaine addicts entering out patient treatment. They also compared the two groups in terms of these subtypes. They found that the MCMI diagnosed Axis II disorders in 90% of opiate addicts and 97% of cocaine addicts. There

were no significant differences in the two groups in terms of personality disorder subtypes: 36% of the opioid addicts and 28% of the cocaine addicts were found to be narcissistic/antisocial: 20% of the opioid and 42% of the cocaine addicts were found to be withdrawn/negativistic.

In a study comparing psychopathology and personality in four different forms of substance abuse, Campbell and Stark (1990) used the MCMI and the SCL-90R with 16 opiate, 16 amphetamine, 34 cocaine, and 29 marijuana abusers. The MCMI scores were compared with those of a non-drug abusing psychiatric sample. Results from this comparison showed that the substance abusers had significantly higher levels of psychopathology than the psychiatric sample on 18 of the 20 MCMI scales. There was only one significant difference among the four groups of substance abusers with respect to personality disorders. In this finding the amphetamine abusers scored significantly higher on the schizoid scale than the other three groups. The authors stated that the absence of broader significant differences between these groups on personality disorder scales do not support the pharmacodynamic theory of substance abuse.

Donat, Walters and Hume (1992) looked at the MCMI differences between alcoholics (n=163), cocaine abusers (n=64), or mixed use (n=103) who were in in-patient treatment. Unlike previous studies, which they critiqued for overlooking important demographic variables, they factored the effects of age, sex and race into the analyses. They found differences not only between the drug vs. alcohol vs. combined groups, but also those based on demographic factors. Moreover, when demographic factors of race, sex and age were accounted for, the observed differences between the substance abuse groups became quite small.

In a study that compared MCMI profiles of a sample of severe substance abusers (n=144) and a sample of non-substance abusers seeking outpatient psychotherapy (n=1000), Yeager, DiGiuseppe, Resweber & Leaf (1992) found a large number of significant differences between these two groups. They found statistically significant

differences on six of eleven personality disorder scales. Substance abusers scored significantly higher on the schizoid, narcissistic, antisocial, and paranoid scales. The general clinic population scored significantly higher on the compulsive and, surprisingly, borderline scales. They pointed out that the differences in this case were due to the relatively depressed scores of the substance abusers on these two scales rather than the elevation of the clinic group's scores. These findings led the authors to recommend that the personality disorder diagnoses in substance abusing patients be considered in treatment planning, particularly with patients who have severe substance abuse problems, so that appropriate treatment strategies can be employed.

Lesswing and Dougherty (1993) used a battery of psychological tests including the MCMI-II to assess and compare a group of alcoholics (n=94) and cocaine dependent individuals (n=99) who were in in-patient treatment for their substance abuse problems. They found a very high prevalence of personality disorders for both groups, although some differences between groups emerged from their analyses. The cocaine abusers had a pattern of more severe personality disorders (paranoid, schizotypal, and borderline) than the alcoholics. They note, however, that DSM-III-R Axis II disorders appeared more prevalent than Axis I symptomotology in both groups. Based on their findings, they recommended "sophistication" in treating the substance abusing patient including a matching of psychotherapeutic technique with personality dysfunction and drug of abuse.

Marlowe, Husband, Bonieskie, Kirby, & Platt (1997) compared the prevalence rates of personality disorders in a cohort of 144 treatment seeking cocaine dependent men using the SCID-II, and the MCMI-II in making diagnoses. They were interested in finding out if a self-report measure would yield comparable diagnoses to those made during a SCID-II interview because this interview requires substantial time and training on the part of clinicians. The MCMI-II was chosen as the self-report measure because it is seen as being closest to DSM-III-R of all the available self-reports designed to diagnose personality disorders. They stressed, however, that this study was not done to establish accuracy of

either the MCMI-II or SCID-II, but rather to find out if comparable information about character pathology could be obtained from these two diagnostic methods. Results showed low to moderate congruence between MCMI-II and SCID-II. The MCMI-II generally produced considerable diagnostic overlap, with subjects averaging 3.47 Axis II diagnoses as compared with 1.24 Axis II diagnoses when using the SCID-II. In the conclusion they noted that the MCMI-II confirmed a preponderance of Cluster B diagnoses (antisocial, borderline, histrionic, and narcissistic) as has been found in other studies, but tended to lack sensitivity to Cluster A diagnoses, particularly paranoid personality disorder. Despite the discrepancies between these two methods, these results confirmed those of previous studies which have found high rates of Axis II disorders among cocaine dependent individuals. They advocated careful diagnosis of these disorders because of the negative impact that Axis II pathology seems to have on treatment effectiveness and outcome.

Taken as a whole, these investigations, which used the MCMI to assess personality disorders among a range of substance abusing groups, concur with the general findings and recommendations of the studies where the methodology consisted primarily of structured clinical interviews: personality disorders are highly prevalent in substance abusers, and treatment strategies should somehow address these personality dysfunctions so as to enhance the chances of positive treatment outcome and decrease chances of relapse.

III. TREATMENT

The heterogeneity of cocaine abusers with respect to the presence of a comorbid psychiatric disorder has led to the development of treatment protocols where both the substance abuse problem and additional psychopathology are addressed. The approach to treatment in the situation of "dual diagnosis" generally involves a dual strategy where medication and often some form of psychotherapy or counseling are combined. Interest in using medication (pharmacotherapy) to treat cocaine dependence developed independently

from the aim of treating comorbid Axis I psychopathology in cocaine abusers, so a few words on the background of this field of investigation may be helpful.

As cocaine use in this country mushroomed through the mid- and late-1980's, treatment providers were challenged to come up with methods for helping abusers to regain abstinence. Psychotherapeutic approaches were seen as inadequate for helping to curb the intense cravings that keep so many cocaine users stuck in the revolving door of periods of abstinence and relapse to drug use. Pharmacological agents were sought which might decrease or eliminate cocaine craving and thereby assist in maintaining abstinence. As of yet, there is no methadone-like equivalent for cocaine, but pharmacological agents have been investigated based on the hypothesis that cravings could be curtailed at a neurobiological level. Laboratory studies during the late 1980's and into the 1990's have revealed a great deal of information about the neurophysiological mechanisms of cocaine on the brain, and have shown that long-term and high intensity cocaine use may lead to functional changes in certain neurotransmitter systems. Investigators have sought medications, therefore, which could rectify these changes and help reduce cravings on a biological level (Kleber 1995; Kosten 1989). Researchers have investigated several classes of medication for reducing cocaine cravings including antidepressants, dopamine agonists, antipsychotics, and stimulants.

In a 1989 article, Kosten discussed the issues involved in using medication to treat cocaine abuse. The points to consider are 1. whom to treat; 2. when to treat; 3. what treatments to use; 4. where to treat; and, 5. how to match patient to medication. He emphasized the importance of using medication to treat patients with "psychiatric vulnerability", that is patients with comorbid disorders and refers to the "self-medication" hypothesis as a motivating factor for individuals with depression, ADHD, and cyclothymic/bipolar disorders in using cocaine. He added that it would be a mistake to think of medication as a "magic bullet" which would do away with cocaine addiction. Rather, he encouraged the use of medication as an adjunct to psycho-social treatments

which are aimed at resolving the patient's psychological problems. Kleber (1995) referred to medications as providing "a window of opportunity" when a patient's cravings are reduced adequately to permit a period of abstinence allowing psychological treatments to ensue. The importance of psycho-social treatments is underscored by the mixed results that have been found in studies, particularly in patients without identified Axis I comorbidity, to various pharmacotherapies (Kosten 1992).

There are reports in the literature of both case studies and larger single- and double-blind treatment studies where medication has been used, sometimes in conjunction with some form of psychotherapy or counseling, to investigate the efficacy of particular medications in ameliorating cocaine dependence and, in a some instances, comorbid Axis I psychopathology. I will review the literature of phamacotherapies in treatment of cocaine dependence (focusing on single- or double-blind treatment studies) in conjunction with depression and then with ADHD. Following those studies will be a brief review of studies that examined the success of various psycho-social treatments for cocaine dependence. I will conclude this section with a discussion of studies that evaluated the relative efficacy of medication and psycho-social treatments when used together and systematically evaluated.

Pharmacological Treatment of Depression

The rationale for pharmacological treatment of cocaine dependence is based on the effect that cocaine has on the action of neurotransmitters. Tricyclic antidepressant medication, particularly desipramine, has been used in clinical trials to treat both the neurochemical aspect of cocaine craving as well as a concurrent diagnosed depressive disorder. Studies of the efficacy of desipramine have been carried out with cocaine abusers with pre-existing depression (primary depression), those who become depressed after developing a cocaine problem (secondary depression) as well as those cocaine users without depression on the hypothesis that the medication will reduce the cravings and withdrawal symptoms which follow after cessation of cocaine use (Daigle et al 1988). This

research is based on the model of neurochemical alterations taking place in the brain subsequent to prolonged and intense cocaine abuse. Neurochemical alterations have been observed in animals as a result of chronic cocaine use, namely that they develop a dopamine receptor supersensitivity and it is believed that this occurs in humans as well. Agents such as desipramine, which reduces receptor sensitivity, have, therefore, been tested to see if it helps diminish cocaine craving and use (Kosten 1992). More recently, however, researchers using positron emission topography (PET scans) have presented evidence which challenges this hypothesis (Volkow, Wang, Fowler, et al. 1997; Volkow, Wang, Fischman, et al. 1997). This research has found that the release of dopamine appears to vary in different parts of the brain which suggests that the dopamine release in cocaine abusers is more complex than initially was thought.

Many of the studies investigating the treatment of cocaine dependence with pharmacotherapies have been conducted with cocaine abusers who are in methadone maintenance programs. This population has certain advantages for recruitment into treatment studies, most prominent among these is that they are already engaged in a drug treatment program which requires almost daily attendance, so recruitment of subjects becomes a relatively small obstacle in carrying out the research protocol. However, this population is not considered to be representative of cocaine abusers overall and some have found them generally less responsive to treatment (Levin, pers. comm.).

These studies tend to examine separately the outcomes of reduction in depressive symptoms and in cocaine use and/or craving. The relationship between depressive symptoms and cocaine use, thus, is one about which speculation continues. For example, one double-blind study found that a group of methadone-maintained depressed cocaine abusers on active medication (desipramine) reported feeling better psychologically as compared with those on placebo, but their cocaine use did not improve. In this case, the placebo grouped demonstrated progressively less drug use than the desipramine group. The investigators conjectured that for those patients who are feeling

less depressed, the negative consequences of continued cocaine use may be less acute and therefore they may have lost an incentive for decreasing their drug use (Arndt, Dorozynsky, Woody, McLellan, & O'Brien 1992).

In contrast to the above mentioned study, other studies have found that depressed cocaine dependent patients tend to improve not only in terms of their depressive symptoms, but also in a reduction of their cocaine use, or at least, in an increase in the number of consecutive days of abstinence. Ziedonis and Kosten (1991) reported that in a double-blind trial comparing depressed versus non-depressed methadone-maintained cocaine dependent patients who were either receiving medication (desipramine or amantadine) or placebo, the depressed patients on active medication used significantly less cocaine than those on placebo. They also found that the non-depressed patients on placebo did significantly better in treatment than the depressed patients on placebo. There were no differences in cocaine craving or use at the end of the twelve week study between the groups of non-depressed patients regardless of treatment condition (Kosten, Morgan, Falcione, & Schottenfeld 1992).

Pharmacological Treatment of Attention Deficit Hyperactivity Disorder

The most widely used medication to treat ADHD in both children and adults is methylphenidate. Methylphenidate (Ritalin) is a stimulant, and when used to treat ADHD, has the paradoxical effect of diminishing hyperactivity while also reducing inattention and distractibility. The stimulant properties of cocaine are described by patients as providing relief from the symptoms of ADHD in ways similar to methylphenidate, at least earlier on in the course of cocaine use, when the amount and frequency tends to be more controlled. Khantzian published a case report in 1983 where he treated successfully with methylphenidate a patient who was diagnosed who had both ADHD and severe cocaine dependence (Khantzian 1983). Positive results were also found using methylphenidate to

treat several cocaine abusing patients with ADHD in another case report (Khantzian, Gawin, Riordan & Kleber 1984).

There have not been any double-blind placebo-controlled studies of pharmacological treatment of cocaine dependence in individuals with ADHD. Levin and colleagues are currently investigating the efficacy of both methylphenidate and buproprion (an antidepressant that has been used to treat ADHD in adults and children) in an open trial to treat adults with both ADHD as well as cocaine dependence. The preliminary data from the methylphenidate arm of this study indicates that this medication reduces patients' ADHD symptoms and significantly reduce their cocaine use. In addition, there is no evidence that the patients in this study abused their study medication which has been a concern voiced by some practitioners who have cautioned against using a stimulant with substance abusing patients (Levin et al., submitted; Ziedonis, 1992).

Psychological Treatments of Cocaine Dependence

Psychological approaches are the most widely used methods for treating cocaine abuse (Carroll, 1992). Many of the treatment approaches currently in use with cocaine abusers were initially developed for use with other populations or problems, such as alcoholism or depression and were adapted to meet the needs of the cocaine abusers. Treatment programs traditionally embraced a twelve-step philosophy (most commonly associated with Alcoholics Anonymous) with an emphasis on group work, but this has changed as researchers and clinicians have begun to understand more about substance abuse in general and cocaine abuse specifically (Wallace 1992). Individual psychotherapy was, until relatively recently, however, thought to be inappropriate for substance abusers. Indeed, among some psychoanalytically oriented clinicians, treatment is often deferred until the patient addresses his/her substance abuse problem elsewhere (Najavits & Weiss 1994).

With the growing awareness of individual psychotherapy's importance in treating substance abuse, a number of manualized treatments have been developed, (or adapted to

address substance abuse) and empirically tested. Psychological treatments of cocaine abuse fall roughly into two categories: those that are predominantly psychodynamic (Supportive-Expressive Therapy; Interpersonal Therapy; and, Motivational Interviewing)and those that are predominantly cognitive, behavioral or cognitive-behavioral (Relapse Prevention: Cognitive-Behavioral Therapy; Contingency Contracting; Behavioral Treatment; Cue Exposure; Network Therapy; and, Aversion Therapy: See Najavits & Weiss (1994) for a good review). Regardless of orientation, there is general agreement that there are several phases of recovery in substance abuse and that the treatment approach should vary accordingly (Kaufman, 1989; Najavits & Weiss, 1994; Wallace 1992).

The studies evaluating these psychotherapies targeted the patients' drug use behavior and none were designed to address directly any Axis I or Axis II comorbidity that may have been present. However, some have used the "psychiatric severity" score of the Addiction Severity Index (ASI) as either an outcome measure, or as a means for categorizing patients into low, medium and high levels of psychiatric distress (Carroll et al., 1991; McLellen 1986). For example, in a study comparing psychotherapy plus drug counseling to drug counseling alone, Woody, McLellan, Luborsky & O'Brien (1990) found that those patients with severe psychiatric symptoms had better outcomes with the combined treatments than with counseling alone. In addition to the studies which expressly evaluate individual psychological treatments, in many of the pharmacological studies, the patients also received some form of psychotherapeutic intervention, but in almost all cases the impact of the psychotherapy on treatment outcome was not evaluated. Attention to the thoughts feelings and behaviors that are considered characteristic of Axis II personality disorders as such has not been measured or discussed directly in these investigations.

Relapse Prevention

One of the cognitive-behavioral therapies, Relapse Prevention (RP), has been tested empirically with several different treatment conditions. It is also the psychological

treatment used in this study and, therefore, will be discussed. RP is based primarily on a coping skills model, where relapse is more likely to occur if the person does not have adequate coping skills to handle cocaine cravings bought on during "high-risk situations". The underpinnings of this treatment model are Bandura's notions of social learning and concept of self-efficacy. The concept of self-efficacy applied to a cocaine user posits that a person who does not believe that s/he has the capacity or capability to resist cravings and urges is unlikely to do so (Bandura 1977, Bandura 1986, Marlatt 1985; Marlatt and George 1984). There are numerous articles and book chapters about the use of RP in treating a range of addictive disorders which was first developed by Marlatt and Gordon (1985) to treat alcohol abuse . This cognitive-behavioral treatment has since been adapted and empirically tested in treating cocaine dependence, polysubstance abuse, and marijuana dependence (Carroll 1996); DeJong 1994; Marlatt & Barret 1995; Rawson, Obert, McCann & Marinelli-Casey 1993; Roffman, Stephens & Simpson 1989; Wallace 1989) as well as other addictive behaviors.

RP was adapted for use with cocaine abusers by Kathleen Carroll and colleagues, which they describe as "a collection of interdependent techniques incorporated into a psychotherapeutic approach which is intended to enhance self-control" in individuals who abuse cocaine (Carroll, Rounsaville, & Gawin 1991). The techniques typically employed in this approach include addressing the patient's ambivalence about giving up cocaine, identifying high risk situations which could lead to relapse, instruction and practice of both cognitive and behavioral strategies for coping with high risk situations, self-monitoring and behavioral analysis of cocaine use, strategies for identifying and coping with cravings and thoughts related to cocaine use, planning for emergency situations and coping (instead of catastrophizing) a lapse in abstinence, instruction in problem solving skills and making lifestyle changes which support and enhance abstinence (Carroll, 1996).

There have been four controlled empirical studies of RP for use with cocaine abusers. Carroll and colleagues have conducted two of those studies. In the first study

they compared RP to Interpersonal Psychotherapy (IPT; Rounsaville, Gawin, & Kleber 1985; Carroll et al. 1991). In this investigation patients were randomly assigned to either RP or IPT for 12 weekly individual sessions. Differences between the two groups in terms of treatment completion, number of continuous weeks of abstinence or being considered recovered at termination were not statistically significant. However, when the data was stratified in terms of severity of use, those patients with high severity who received RP did significantly better in all areas as compared with those who received IPT. Those patients with lower severity of cocaine use did equally well in both treatments. They conclude that based on these results and those of the pharmacological studies, that purely psychotherapeutic treatments may be appropriate for some cocaine abusers.

A study conducted by Wells, Peterson, Gainey, Hawkins, & Catalano(1994) compared RP to supportive psychotherapy based on a Twelve-Step approach, both delivered in group format. 110 cocaine abusers in out-patient treatment received either one of these two types of psychosocial therapy during a twenty-four week period. They found that patients in both groups decreased their drug use over time and that the more treatment received, the better the patient outcome. However, they did not find differences between the two groups in terms of decrease in substance use or program retention.

Schmitz et al. (1997) compared individual to group formats in treating cocaine abusers with RP. Thirty-two patients were randomly assigned to either individual or group format RP therapy for 12 outpatient sessions during a two month period. There was an overall statistically significant improvement on most measures, such as addiction severity, coping and craving for cocaine, for all patients, regardless of treatment format. However, those in the group format reported using cocaine on significantly fewer days and significantly fewer cocaine related problems than those in the individual format. In the 12 and 24 month follow-up assessments, the differences between the two groups disappeared.

In a unique investigation, Carroll and colleagues compared RP to supportive Clinical Management (CM) and pharmacotherapy with either desipramine or placebo in a

2X2 factorial design (Carroll et al. 1994). All groups showed significant improvements after twelve weeks of treatment, but significant main effects for psychotherapy or medication were not found for important outcome measures, such as treatment retention or reduction in cocaine use, at the end of the treatment protocol. When patients were stratified by severity of cocaine use, however, it was found that higher severity patients who were treated with RP did significantly better than those receiving CM. They also found that those diagnosed with comorbid depression had a greater reduction in cocaine use than the nondepressed patients and that the depressed patients who received RP did better than those in CM. Desipramine was associated with a greater reduction in symptoms of depression than was placebo; however, it was not associated with any greater reduction in cocaine use (Carroll, Nich & Rounsaville 1995).

IV. The Effect of Personality Disorders on Treatment Outcome

There is general agreement that the presence of a personality disorder has a negative effect on treatment for a wide range of Axis I disorders. A review of studies which assessed treatment outcomes, or various aspects of functioning, of patients with personality pathology who were being treated for a variety of Axis I disorders (including mood disorders, panic disorder, obsessive-compulsive disorder and substance abuse/dependence disorders) found that the presence of comorbid personality disorders or pathological personality traits adversely effected patient functioning and treatment outcomes (Reich & Vasile 1993). In addition to examining the relationship of Axis II diagnoses to various features of treatment (e.g. retention and outcome), work has also been done which considers particular personality traits such as neuroticism, alexithymia and sensation-seeking as influencing treatment response (Ball, Carroll & Rounsaville 1994; Brooner, Herbst, Schimdt, Bigelow & Costa 1993; Keller, Carroll, Nich & Rounsaville 1995).

Few studies have considered the range of personality disorders as they may impact treatment outcome of substance abusers. Most studies have examined only the role that a

diagnosis of ASPD plays in treatment response and outcome. An often cited study of sociopathy and psychotherapy outcome with opiate addicts found that patients who had the two diagnoses of opiate dependence and ASPD did not benefit from "professional" psychotherapy. However, those patients who were also depressed as well as opiate addicted and had ASPD had an overall positive response to psychotherapy. These patients benefited almost as much as those patients without any sociopathy. The authors concluded that the poor response to psychotherapy of opiate addicts with ASPD was due to their great difficulty in forming meaningful relationships. They added that in order to benefit from psychotherapy, a meaningful patient-therapist relationship needs to be established and, indeed, was the strongest predictor of positive outcome (Woody, McLellan, Luborsky, & O'Brien 1985).

Many of the studies that examined the relationship between personality disorders and features of treatment outcome and/or related variables (such as life satisfaction or psychological functioning) tend to have serious methodological flaws in a variety of areas including method of diagnosis (for example, clinical impression without a method for assuring reliability) (Clopton, Weddige, Contreras, Fliszar, & Arredondo 1993), and failure to control for amount or type of treatment conditions received by study participants (Clopton et al. 1993; Nace and Davis 1993; Stark and Campbell 1988). Results from these studies must, therefore, be interpreted cautiously. The findings are mixed. On the one hand, patients diagnosed with a personality disorder along with a substance abuse disorder do not have statistically significant poorer treatment outcomes. On the other hand, because the amount and type of psychological and supportive treatments were not standardized, more disturbed patients received more intensive treatment and auxiliary services. One conclusion that can be inferred from these studies, therefore, is that for patients with comorbid substance abuse and personality disorders, successful treatment outcomes are more likely when efforts to address the underlying personality disorders are incorporated into the treatment program.

Conclusion

Substance abuse treatments in general and cocaine abuse treatments specifically have come a long way in the past decade or so in developing and rigorously evaluating novel approaches for assisting people who are stuck in chronic disorders where relapse is common. The recognition of the diagnostic heterogeneity, in terms of comorbid psychopathology, of treatment-seeking cocaine abusers has led to the development of more precisely targeted treatments. Clinical trials designed to address both cocaine abuse as well as comorbid Axis I disorders have shown some promise in helping individuals more fully than was previously possible. The problems associated with Axis II disorders, that is to say difficulties stemming from underlying character pathology, have not, however, received the same attention in terms of treatment research focus and design. The wealth of data demonstrating the high prevalence of Axis II disorders among cocaine abusers invites further study of personality pathology within this population. This investigation, therefore, sought to discover what role, if any, character pathology, as measured by the MCMI-III, played in treatment response and completion.

Statement of the Problem

Do cocaine abusers with personality disorders, as measured by the MCMI-III respond differently to treatment than those without regardless of the presence of any comorbid Axis I diagnosis?

Hypotheses:

1. There will be a relatively random distribution of personality disorder diagnoses, as measured by the MCMI-III in each of the three Axis I subgroups: ADHD, depressed, and no comorbidity. If this is so, then it will be important to consider the impact of an Axis II diagnosis in the treatment paradigm of cocaine abusers in general.

2. There will be a significant positive association between worse treatment response and outcome, and the presence of an Axis II personality disorder (or greatest number of concurrent personality disorders), as measured by the MCMI-III. Treatment response and outcome will be measured by a number of factors including: self-report of cocaine use and cocaine cravings; percentage of cocaine free urine samples collected during treatment; number of days that are cocaine free during treatment; number of days subject remains in treatment; and, scores of drug use severity and psychiatric severity as measured by the Addiction Severity Index interview.

3. Previous studies of substance abusers have found a high percentage of them to have comorbid personality disorders. Given that Axis II diagnoses are present in most of this study's population and that the presence of a comorbid personality disorder will have a meaningful impact on treatment response and outcome, it was hypothesized that the three subgroups will be impacted differently from each other in the following ways:

3a. It is hypothesized that for the ADHD group there will not be any relationship between the presence of an Axis II diagnosis and treatment response and outcome for several reasons. This subgroup attended a more structured program than those in the other subgroups. Individuals with ADHD, in particular, will benefit from the organization and structure they receive in their thrice weekly visits (Weinstein 1994). In addition, it is believed that the motivation for treatment of individuals in the ADHD treatment protocol is enhanced simply by being diagnosed with ADHD. For most of these subjects, this is the first time that they have a way of understanding lifelong behavioral and psychological difficulties. They will benefit from this information and from feeling understood by the treating professionals. It is hypothesized, therefore, that the impact of having Axis II pathology will be mitigated somewhat for this subgroup (Kane et al 1990).

3b. It is hypothesized that for subjects in the depressed subgroup, the presence of an Axis II diagnosis will be negatively associated with treatment response and outcome.

Studies of the effect of personality disorders on the treatment outcome of depressive disorders have found poorer treatment outcome in depressed patients with a personality disorder as compared with those without on a number of different measures (Reich 1990; Reich & Vasile 1993; Shea et al. 1990).

3c. It is hypothesized that for the subjects in the non-comorbidity subgroup, the presence of an Axis II diagnosis will be negatively associated with treatment response and outcome . Unlike the patients in the other subgroups, who are motivated to varying degrees to ameliorate their comorbid Axis I disorders in addition to overcoming their cocaine problems, the non-comorbid patients do not seek relief for additionally identified or acknowledged psychiatric problems. They may feel, therefore, that they can accommodate the negative consequences of continued cocaine use. Absence of Axis I comorbidity for these patients (the presence of which can be a motivating factor) might mean that Axis II pathology was most salient for this subgroup. The lack of consideration of disturbed personality features in treatment design, therefore, might have the greatest impact on measures of treatment success for these patients.

4. Patients with personality disorders in the antisocial personality spectrum (MCMI-III diagnoses: antisocial and aggressive/sadistic) who do not have any additional Axis I or Axis II diagnoses will have poorer treatment response and outcome than those who do have comorbid Axis I or Axis II diagnoses. Previous studies have suggested that substance abusing patients who are diagnosed with ASP without additional Axis I or Axis II diagnoses may do less well in treatment (Arndt, et al. 1994; Brooner et al. 1993; Leal et al. 1994; Rouser et al. 1994)

Methodology

Introduction:

In this study of treatment-seeking, cocaine-dependent patients, the relationship of comorbid Axis II personality disorders, to various measures of treatment outcome was investigated. Personality disorders were diagnosed with a widely used self-report measure, the Millon Clinical Multiaxial Inventory-III (MCMI-III; Millon 1994). Treatment outcome was measured by considering length of stay in treatment, percentage of cocaine free urine samples, number of consecutive days abstinent from cocaine, changes in self-reported cocaine cravings, and changes in psychiatric and drug use severity scores on a standardized interview widely used in substance abuse research, the Addiction Severity Index (ASI; McLellan et al., 1980). Analyses were conducted to determine if the presence of a comorbid personality disorder has any effect on these measures of treatment response and outcome.

This study utilized data that was culled from ongoing, or recently completed treatment studies of cocaine dependent patients at the New York State Psychiatric Institute (NYSPI) in New York City, and whose principal investigators are Frances R. Levin, MD and Edward Nunes, MD. These studies are focused on the investigation of the efficacy of several pharmacological agents for the treatment of cocaine dependence and, in most cases, the comorbid Axis I disorders of depression or ADHD. These studies were initiated in 1995 and are funded by the National Institute on Drug Abuse (NIDA). The data for this study came from four separate studies which differ somewhat in design. For example, one of the studies was single-blind (non-comorbid treated with pergolide), one was an open trial (comorbid ADHD treated with either methylphenidate or buproprion), and two of the studies are double-blind placebo controlled (non-comorbidity treated with respiridone/placebo and depressed treated with desipramine/placebo). In addition, in some

cases individuals who began treatment in one treatment study were withdrawn for reasons of clinical worsening and treated openly with medication and continuing RP psychotherapy. Examples of patients who began treatment enrolled in one study, but who were later discontinued from their initial placement include a few patients who were without evidence of depression were entered into a non-comorbidity study, but then subsequently became depressed, and those patients who were entered into the comorbid depression study, but whose depressive symptoms worsened during treatment and were then removed from the double-blind desipramine study and treated openly with the antidepressant Effexor (TM) for the duration of the study protocol. Cocaine craving and use data was collected on these subjects who receive treatment outside the strict confines of one of the study protocols, and therefor this data was included in the analyses for the present study. Additional differences among subject groups will be described in more detail below. (See Table One at the end of this chapter for greater detail of the studies' structure.)

Treatments

1. ADHD: Patients in the ADHD treatment protocol were medicated with either methylphenidate (a stimulant frequently used to treat ADHD, and whose trade name is Ritalin) or buproprion (an atypical antidepressant which has been shown recently to be effective in treating ADHD, and whose trade name is Wellbutrin). Patients in the ADHD subgroup were scheduled to attend three visits per week. During each of those visits patients had direct contact with a research assistant (RA) and nurse in order to conduct data collection and monitor patients' physical well being. Interactions during visits consisted of obtaining vital signs and a urine sample, and administration of self-report measures (cocaine cravings, cocaine use and psychiatric symptoms). Patients met with the psychiatrist for structured assessments once weekly, and once weekly with the therapist for indivual Relapse Prevention psychotherapy. Patients received study medication at each visit. Patients were compensated with $5 to defray transportation costs at each visit.

2. Depressed: Patients attended appointments twice weekly during the first two weeks of the treatment study and once weekly thereafter. Desipramine was administered in a double-blind placebo crossover design. Desipramine is a tricyclic antidepressant which has shown some success in treating depressed cocaine abusers, particularly in ameliorating depressive symptoms. After an initial one-week placebo wash-out period, non-responders to placebo were then randomized to either medication or placebo. After twelve weeks in either treatment condition the blind was broken and patients were treated with either venlafaxine, desipramine or no medication. Patients met with RA, nurse, psychologist and psychiatrist during each visit in order to complete study measures and to participate in RP as in the ADHD study. If a patient's conditioned worsened during the course of the study, the medication blind was broken and the patient was placed on active anti-depressant medication, usually venlafaxine (Effexor). Patients received $25 for every six weeks of participation in treatment study.

3. No Axis I Comorbidity: The following two groups were combined to form one subgroup (non-Axis I comorbidity) for the purposes of this present study, but because they were initially developed as independent protocols and structured with some differences, they are described separately. It should also be noted that the data from these two non-comorbidity protocols were recently combined for analyses which examined the efficacy of these two medications in treating cocaine dependence. The paper presenting these analyses has yet to be submitted for publication.

3a. No Axis I Comorbidity-Risperidone: Risperidone is most frequently used as an antipsychotic medication. Medication was administered according to a double blind placebo crossover design. After an initial two-week placebo wash-out period, non-responders to placebo were then randomized to either respiridone or placebo. Patients received either active medication or placebo for a six-week period and were then crossed over to the other treatment condition after the initial period had elapsed. Patients were crossed over again at the end of the second six-week period. Patients attended

appointments twice weekly for the first two weeks and once weekly thereafter. They met with RA, nurse, psychologist and psychiatrist during each visit in order to complete study measures and to participate in RP as in the ADHD study. Patients received $25 every six weeks.

3b. No Axis I Comorbidity-Pergolide: Pergolide has been used to treat Parkinson's disease. Medication was dispensed according to a single blind placebo design. After an initial two-week placebo wash-out period, subjects were placed on active medication but were not informed of the treatment condition. After twelve weeks in the study, all patients received a placebo. Patients attended twice weekly appointments at which time they would meet with a RA and a nurse for the taking of vital signs and a urine sample, and either a psychiatrist for structured assessments, or a therapist for a RP session. Patients received $5 at each visit.

These studies clearly differed with regard to a number of variables in study design including visits per week that a study participant is expected to make. For example, patients in the ADHD study attended appointments three times per week whereas in the other studies patients were expected to attend appointments once or twice weekly. At the very least, this means that patients were focusing on their cocaine use and treatment to differing degrees depending on which study they were in, and this could impact treatment outcome. In most important aspects, however, the design and procedures of these four separate pharmacological treatment trials are similar, if not identical.

Description of Sample:

All of the subjects were residents of the New York metropolitan region. They were respondents to newspaper advertisements or public service radio announcements offering free treatment for cocaine abuse at the NYSPI. Most of the newspaper ads were placed in The Village Voice or the New York Free Press; both publications are distributed free in Manhattan. Some of the advertisements also specified the problems of either depression or

ADHD accompanying the cocaine abuse. (See appendix for sample recruitment ads.) Subjects were initially screened by telephone to establish cocaine as the principal drug of abuse and an appointment was made to begin an extensive psychiatric and medical evaluation. After completing the evaluation, subjects who met study criteria and who did not meet any of the exclusion criteria signed informed consent and entered a treatment protocol.

Table 2 presents demographic and baseline drug use characteristics of the study sample. As can be seen in the table, the sample was composed almost equally of the three Axis I subgroups. The sample was mainly male (86%), Caucasian (60%), not currently married or living with a significant other (74%), under 40 years old (72%), had a high school diploma or better (86%), worked at least part-time (62%), and about half have had some form of previous treatment (52%).

The average number of days cocaine use in the month prior to enrolling in treatment was 12.5 with a standard deviation of roughly 8 days. The mean amount spent per each cocaine use was $50 (SD = $37). Subjects reported experiencing cravings an average of 18 days during the prior month (SD = 10 days), and cravings of moderate intensity (M = 2.4, SD = .9). (See Table Two at the end of this chapter.)

Description of Measures

Measures:

Subjects were assessed during the evaluation period, regularly during treatment, and at termination. The independent measure, MCMI-III personality disorder diagnosis was administered upon entry into a treatment protocol. The dependent measures were administered at various points during the protocol: Primary outcome measures were length of time in treatment, reduction in frequency of cocaine use as verified through urine toxicology screens obtained at every visit, psychological and drug severity composite scores of the Addiction Severity Index, and changes in the frequency and intensity of cocaine craving.

Independent Measure

Millon Clinical Multiaxial Inventory, third edition (MCMI-III):

The MCMI-III is a 175-item true-false inventory that provides diagnoses which closely correspond to both Axis I and Axis II. The scales, while reflective of a DSM-IV diagnostic terminology and taxonomy, are also derived from Millon's own theoretical notions about personality disorders. He has written widely on this theoretical system on which he bases classifications of syndromes and which have provided a framework for the development of the MCMI scales (see: Millon 1969/1983; Millon 1981; Millon & Klerman 1986; Millon 1990; Millon & Davis 1995). The essential features of Millon's system conceive of basic styles of personality functioning that consist of a matrix composed of two basic dimensions:

> The first dimension pertains to the primary source from which patients enhance their lives and gain comfort and satisfaction (positive reinforcements) or attempt to avoid emotional pain and distress (negative reinforcements)... The second dimension of the theoretical matrix reflects the basic pattern of adaptive or coping behavior that the patient characteristically employs to maximize rewards and minimize pain. (Millon 1994, pp. 10-11)

Within the first dimension he postulates five possible types: detached, discordant, dependent, independent and ambivalent. The second dimension consists of two basic behavioral approaches: active and passive.

The terminology of the MCMI-III is aimed at an eighth grade reading level. It measures 24 clinical scales including eleven moderately severe personality disorder scales

(schizoid, avoidant, depressive, dependent, histrionic, narcissistic, antisocial, aggressive/sadistic, compulsive, passive-aggressive, self-defeating), three more severe personality pathology scales (schizotypal, borderline, paranoid), and eleven clinical syndrome scales which correspond to DSM-IV Axis I disorders including eight moderate (anxiety, somatoform, bipolar, dysthymic, alcohol dependence, drug dependence, post-traumatic stress) and three severe (thought disorder, major depression, delusional disorder) clinical syndromes. There are also three modifier scales: disclosure, desirability and debasement. These scales are intended to identify distortions which may appear in patients' responses and are factored in when determining the diagnoses. The personality disorder scales and the modifier scales were used in the analyses of this study.

The test was normed on a clinical population and it is not meant to be used with a normal population. Raw scores are converted to Base Rate (BR) scores, transformed scores that ensure that the proportion of patients who score above each scale's cutoff point matches the actual prevalence among a representative national population of patients who possess each scale's corresponding disorder and completed the test. A BR score of 75 on a personality disorder scale indicates the "trait" prevalence rate, whereas a BR score of 85 on a personality disorder scale indicates the prevalence rate of a "disorder" (Millon 1994, p. 27).

The MCMI-I and MCMI-II have been used with substance abusers for several purposes including: 1. to identify patients with substance abuse problems (Bryer et al. 1990; Calsyn et al 1991); 2. to assess the personality of identified substance abusers (Brown 1992; Calsyn & Saxon 1991; Campbell & Stark 1991; Craig & Olson 1990; Lesswing & Dougherty 1993;Yaeger et al. 1992); 3. to predict dimensions related to treatment outcome, such as response to treatment or program attrition (Stark & Campbell 1988); 4. to assess clinical disorders other than personality disorders among substance abusers (Flynn & McMahon 1983). In a review of studies which used the MCMI (I & II) to assess various aspects of substance abusers, Craig and Weinberg (1992) note that there

is some evidence indicating that this tool has tended to over diagnosis paranoia with this population. They also note that little work has been done using the MCMI and predictive validity regarding treatment outcome with substance abusers.

Millon discusses changes to this newest version of the instrument. that improve its concordance with advances in his own theoretical understanding of personality disorders as well as bringing his scales more closely in line with the DSM-IV personality diagnoses. In terms of this latter concern, an additional personality disorder scale was added to the MCMI-III. Also, cross-validation and cross-generalization studies have contributed to the improvement of subsequent versions of the MCMI in several respects including the test items, scales. scoring procedures. algorithms and interpretive text (see Choca, et al.. 1992; Craig 1993; Hsu & Maruish 1992; Maruish 1994).

Reliability

Internal consistency: Using a cross validation sample (n=398), alpha coefficients measuring internal consistency were determined. For the clinical personality patterns the alpha coefficients range from a low of .66 on the compulsive scale to a high of .89 on the avoidant and depressive scales.

Test-retest reliability was determined over an interval of 5-14 days with a sample of 87 subjects. Test-retest reliability ranges from a low of .88 on the aggressive (sadistic) scale to a high of . 93 on the depressive and antisocial scales.

Validity

The validity of MCMI-III scale scores was assessed by calculating correlation's between the BR scores for each scale and (a) clinician ratings and (b) collateral test scores including: the Beck Depression Inventory; the General Behavior Inventory; the Michigan Alcohol Screening Test; the Impact of Events Scale; The State-Trait Anxiety Inventory; the

Symptom Checklist-90-Revised; and, the MMPI-2. The diagnostic efficiency of the MCMI-III BR scores were also examined.

Scoring

Raw scores for the scales are calculated through a several step process. In the first step, a response is assigned a value of one if it is indicated and a zero if it is not indicated. Those values are then multiplied by either one or two, and these weighted scores are then summed to determine the raw scale scores. Exceptions to this procedure involve items on the "desirability" and "debasement" scales where all items have a weight of one. In addition the "disclosure" score is calculated differently from all other scales. The raw score for this scales the sum of the raw scores on Scales 1 through 8B.

Raw scores are then converted to Base Rate (BR) scores using a value included in a transformation table derived by Millon. Subsequent to this calculation, several other adjustments may be made to the score. These adjustments include: a "disclosure" adjustment which is based on the score on the "disclosure" scale; an "anxiety/depression" adjustment based on elevations in the Anxiety and/or Dysthymia Scales; Inpatient adjustments are made in order to compensate for the tendency of some recently hospitalized patients to deny the severity of their current emotional state; a "denial/complaint" adjustment is made to certain profiles depending on the BR scores of the personality scales.

The profiles derived from the MCMI may be considered invalid if any one of the following conditions occurs: a) the subject's/patient's gender is not indicated; b) age is less than 18 or unknown; c) there are 12 or more missing (or double marked) responses; d) two or more Validity scale items (#s 65, 110, 157) are endorsed. These items have an extremely low endorsement rate and if they have been selected it may indicate that the subject did not pay sufficient attention to item content or may not have been able to read and understand the items; e) the raw score on the Disclosure scale is less than 34 or greater than 178 which would indicate that the subject either significantly under- or overreported

symptoms to such a degree that the results cannot be reliably interpreted; and, f) none of the BR scores on the clinical Personality Scales are above 59.

Once a patient/subject has completed the MCMI-III inventory, the results are entered into a computer program which scores the protocol. A report consisting of the raw and BR scores on all 24 clinical scales as well as the three modifying indices is presented numerically and graphically. A base rate score of 75 indicates presence of traits of a disorder and a base rate score of at least 85 indicate the presence of a disorder. A narrative report accompanies the calculated scores as well as DSM-IV diagnoses for both Axis I and Axis II. The computer scoring system is published by National Computer Systems.

It should be noted, however, that there were particular limitations in using a self-report measure in order to determine an Axis II diagnosis with substance abusers. Although care was taken to insure that subjects were not in acute distress while filling out the MCMI-III, their responses were likely skewed towards either greater pathology in general or greater sociopathy specifically because they tended to endorse items which reflected thoughts, feelings and behaviors that were characteristic of a "drug-using self". For example, it is common for someone who is craving cocaine to lie about some aspect of behavior, whereas during periods of abstinence lying may not be something that person would do. Carroll, Ball and Rounsaville (1993) found that when behaviors occurring only during periods of drug use are not included in diagnostic assessment for ASPD, for example, then the rate of this diagnosis among cocaine users fell to only 7%.

Dependent Measures

1. Cocaine Craving Scale (Gawin and Kleber 1984):

This is a 20-point analog scale used to measure patients' subjective experience of cocaine craving. This paper and pencil task required that the patient mark a line indicating his or her craving since the previous visit. It was developed by Gawin and Kleber in order to assess cocaine craving in a group of cocaine abusing patients who were participating in a

pharmacological treatment study. The scale is similar to ones that have been used in previous drug abuse and pharmacological research. The face validity of this scale is demonstrated by a high correlation between craving, as indicated by this instrument, and cocaine use on the one hand, and absence of craving and abstinence on the other. It is useful to have a measure of craving in cocaine treatment research since it is this intrapsychic, subjective experience which leads the patient to initiate cocaine use (Halikas, Kuhn, Crosby, Carlson, & Crea, 1991).

2. Urine toxicology drug screens and self-report of use:

Urine samples were collected at each visit to the treatment program and were tested for benzoylecgonine, the major urinary metabolite of cocaine, which remains in the urine for a much longer period of time than does cocaine, using an enzyme immunoassay test.

Patients were interviewed by either a nurse or research assistant at each visit about their drug and alcohol use, including amount consumed, since their previous attendance at the treatment program.

3. The Addiction Severity Index (ASI):

The ASI was administered monthly during treatment to assess multidimensional aspects of outcome and general functioning. The ASI is a structured interview that assesses past and current (past 30 days) functioning in seven problem areas: medical, employment, alcohol use, drug use, legal, psychiatric, and family/social relationships. In each of the areas, objective questions are asked measuring the number, extent, and duration of problem symptoms in the patient's lifetime and in the past 30 days. Two sets of summary scores can be obtained from the interview for each of the problem areas: composite scores (CSs) and interviewer severity rating scores (ISRs). CSs are based solely on patients' self-report, and are computed for each area by weighing and summing scores for items that reflect more current functioning within a specific problem area, and are

suitable for evaluating change over time and other research purposes. CSs have been recommended for use in treatment outcome studies where the focus in on change (McDermott, et al., 1996; McLellan, Luborsky, Cacciola, Griffith, McGahan & O'Brien, 1985). Patients are asked to rate the severity of their problems and the extent to which they feel that treatment for those problems is important to them based on a five point scale: from 0 (not at all) to 4 (extremely).

ISRs are composed of the interviewer's subjective evaluation of the need for additional treatment in a given area. Correspondence of ISRs and CSs are generally high in samples of substance abusers (Carey, Cocco, & Correia, 1997). The instrument has been shown to be reliable and valid (McLellan et al., 1985). Test-retest reliability coefficients of .83 or higher have been reported for all scales (McLellan, et al., 1992). In this study, only the drug use and psychiatric severity CSs were used in the data analyses because drug use is the primary focus of this treatment protocol, and psychiatric distress is thought to be directly impacted by the presence of a personality disorder.

4. Length of time in treatment

Patient attendance at the treatment program was monitored by clinical staff members. When a patient failed to attend an appointment persistent efforts were made to contact the patient and reschedule for the next convenient time. Generally, a patient was phoned several times if s/he failed to show up for a scheduled or rescheduled appointment.

Procedures

All subjects initially signed a "screening consent" which allowed the staff to begin an evaluation. Subjects were evaluated by either a MA or PhD level psychologist and/or a psychiatrist in order to determine DSM-IV Axis I diagnoses and to rule out major psychiatric disorders with a structured clinical interview (Structured Clinical Interview for either DSM-III-R or DSM-IV: SCID-SAC; Nunes, Goehl, & Seracini, 1990; SCID-IV;

First, Spitzer, Gibbon, & Williams, 1995). An adaptation of the ADHD module of the SCID originally designed for interviewing children was used to determine an ADHD diagnosis. Blood laboratory work-ups, electrocardiograms and urinalyses were conducted for medical clearance. Several additional substance use interviews and comorbidity interviews, where applicable, were also conducted. Subjects were also evaluated medically through a physical examination, providing a detailed medical history, electrocardiogram, and laboratory tests (CBC with differential, electrolytes, BUN, creatinine, liver function tests, and thyroid function tests). Pregnancy in women was determined by a blood pregnancy test. Once eligibility for one of the treatment protocols was determined, subjects met with a study psychiatrist to discuss the risks and benefits associated with the treatment protocol and alternative forms of treatment. Study consent was signed at that time if the subject elected to do so. The evaluation process lasted between one and three weeks depending on patient's ability to schedule and attend appointments and the complexity of the subject's drug and psychiatric history.

After subjects were admitted to one of the four treatment groups (comorbid ADHD; comorbid depression; or no Axis I comorbidity and treated pharmacologically with either Pergolide or Respiridone) they were interviewed with the ASI by a research assistant trained in administration of this instrument. Subjects completed the MCMI-III to determine personality disorder diagnoses. Subjects competed the MCMI-III only if it was determined that they were not either currently under the influence of cocaine or suffering from acute withdrawal. In addition to the pharmacological intervention described above, subjects received "doses" of a standardized psycho-social treatment which is described below.

Relapse Prevention

This cognitive-behavioral treatment which emphasizes coping skills training was originally developed by Marlatt and Gordon and adapted for cocaine abusers by Kathleen Carroll at Division on Substance Abuse, Department of Psychiatry at Yale University

School of Medicine. Further adaptations were made to the RP treatment manual by this author in order to address ADHD-related symptoms. The goal of treatment is abstinence from cocaine through identification of high-risk situations for relapse and the implementation of more effective coping strategies.

Therapists

Three experienced therapists (two doctoral level and one master's level) saw all subjects in weekly Relapse Prevention therapy. All therapists received training in RP conducted by a clinical psychologist with extensive experience with the treatment approach. The training included a didactic seminar covering the treatment manual, theoretical background, and videotaped case examples. Therapists were supervised in weekly sessions by a licensed clinical psychologist where session videotapes were reviewed and case material was discussed.

Statistical Treatment of the Data:

The demographic characteristics of the sample is be described with frequencies and percentages. Correlations between all the dependent measures and demographic data have been performed.

All analyses addressing the study hypotheses were performed with the covariate variable of initial severity of cocaine use which has been found to be an important factor in previous outcome studies of cocaine dependent treatment-seekers (Carroll et al., 1994).

Hypothesis 1: A Chi Square was used to determine if Axis II personality disorders (MCMI-III score>84), Axis II personality disorder traits (MCMI-III score 75-84), and no Axis II personality disorders were evenly distributed among the three subgroups: comorbid ADHD, comorbid depression, no Axis I comorbidity.

Hypotheses 2, 3a, 3b, and 3c: The interaction effects of Axis I and Axis II diagnoses were determined using a 2 X 2 X 3 repeated measures MANCOVA [Axis II group (yes/no) X Time (pre/post) X Axis I group], with the covariate of initial severity of

cocaine use, for each of the dependent variables (Cocaine Craving, cocaine use as measured by urine toxicology screens and self-report, drug use severity and psychiatric severity as measured by the ASI composite scores, and length of time in treatment). Post hoc analyses were performed for any significant results found for hypotheses 3a, 3b and 3c.

Hypothesis 4: A 2 X 2 repeated measures ANCOVA was used to determine if there was a significant interaction of a comorbid Axis I disorder or an additional Axis II disorder and antisocial personality disorder (MCMI-III scales 6a-antisocial, and 6b-aggressive/sadistic) for each of the dependent variables.

TABLE 1.

DESCRIPTION OF THREE STUDY SUBGROUPS

Study Name	Characterization of Subjects	Design	Duration	Outcome Measures	Instruments/ measures
Cocaine Dependence and ADHD	n=17 Caucasian (14) African-Am. (1) Hispanic (2) Male (15); Female (2) Mean age = 36	1. Open trial: either methylphenidate or buproprion; no placebo 2. Outpatient 3. Single site 4. Three visits/week 5. RP therapy 1X/week	12 weeks	1. Cocaine craving and use 2. Drug use 3. Improvement in functioning 4. Treatment completion	1. Cocaine Craving Scale 2. Urine drug screens 3. Self-report of use 4. Drop-Outs 5. ASI 6. MCMI-III
Cocaine Dependence and Depression	n=19 Caucasian (8) African-Am. (3) Hispanic (7) Male (16) Female (3) Mean age = 34	1. Double-blind: Desipramine or placebo in 12 week cross over phases 2. Outpatient 3. Single site 4. one or two visits/week 5. RP therapy 2X/week for 3 weeks; 1X/week thereafter.	12 weeks	1. Cocaine craving and use 2. Drug use 3. Improvement in functioning 4. Treatment completion	1. Cocaine Craving Scale 2. Urine drug screens 3. Self-report of use 4. Drop-Outs 5. ASI 6. MCMI-III
No Axis I Comorbidity-Medicated with Pergolide or Risperidone	n=15 Caucasian (8) African-Am. (5) Hispanic (2) 8. Male (13); Female (2) 9. Mean age = 39	1a. Pergolide: Single-blind with placebo comparison group 1b. Risperidone: Double-blind 2. Outpatient 3. Single site 4a. Pergolide: Visits 2/wk 4b. Risperidone: Visits 1/wk 5a. Pergolide: RP therapy 1/week 5b. Risperidone: RP therapy 2X/week for 3 weeks; 1X/week thereafter.	12 weeks	1. Cocaine craving and use 2. Drug use 3. Improvement in functioning 4. Treatment completion	1. Cocaine Craving Scale 2. Urine drug screens 3. Self-report of use 4. Drop-Outs 5. ASI 6. MCMI-III

TABLE 2.

DEMOGRAPHICS AND CHARACTERISTICS OF STUDY SAMPLE AT BASELINE

CHARACTERISTIC	FREQUENCY	PERCENT	MEAN (SD)
Axis I diagnosis			
ADHD	17	34.0	
depression	18	36.0	
no comorbidity	15	30.0	
gender			
female	7	14.0	
male	43	86.0	
race			
African-American	8	16.0	
Caucasian	30	60.0	
Latino	12	24.0	
marital status			
single	27	54.0	
married/cohab	13	26.0	
sep/div/widowed	10	20.0	
age, years			35.4 (7.0)
24-31	15	30.0	
32-39	21	42.0	
40-47	12	24.0	
48-55	1	2.0	
56+	1	2.0	
education			13.9 (2.7)
less than high school	7	14.0	
graduated high school	9	18.0	
some college	19	38.0	
graduated college	7	14.0	
post college grad	8	16.0	

Characteristics of Study Sample at Baseline, continued:

CHARACTERISTIC	FREQUENCY	PERCENT	MEAN (SD)
employment status			
unemployed	19	38.0	
employed part-time	14	28.0	
employed full-time	17	34.0	
treatment history			
no previous treatment	23	48.0	
yes previous treatment 26	52.0		
cocaine measures/past 30 days			
number of days use			12.5 (8.1)
1-10	29	58.0	
11-20	13	26.0	
21-30	8	16.0	
amount spent ($) /use			50 (36.7)
1-20	11	22.0	
21-40	16	32.0	
41-60	14	28.0	
61-80	2	4.0	
81-100 5	10.0		
101-120	--	--	
121-140	--	--	
141-160	--	--	
161-180	1	2.0	
181-200	1	2.0	
number of days crave*			18.4 (9.6)
1-10	10	20.0	
11-20	21	42.0	
21-30	18	36.0	
craving intensity (0-4)**			2.4 (.9)
0	3	6	
1	3	6	
2	16	32	
3	25	50	
4	1	2	

Note: *=data not available from one subject; **=data not available from two subjects

RESULTS

This study investigated the effects of Axis II personality disorders on treatment response and outcome of cocaine-dependent patients enrolled in clinical trials at the Division on Substance Abuse at the New York State Psychiatric Institute. Patients were evaluated on a variety of measures related to cocaine use and psychological symptoms at baseline and then regularly throughout the twelve weeks of treatment. These patients were grouped according to comorbid Axis I diagnosis: one subgroup was comprised of patients with comorbid attention deficit hyperactivity disorder (ADHD), another subgroup was composed of patients who were diagnosed with a comorbid unipolar depressive disorder (referred to hereafter as "Dep.", and a third subgroup included patients who did not have any comorbid Axis I disorder (referred to hereafter as "N/C" for no Axis I comorbidity).

Treatment response and outcome was evaluated by the following measures: length of stay in treatment, change in two composite scores of the Addiction Severity Index (drug use and psychological), percent and absolute number of cocaine-free urine samples given during treatment, and percent change in cocaine craving as reported by patients during treatment. The Independent variable, patients' personality disorder diagnoses, was determined using a self-report measure, the Millon Clinical Multiaxial Inventory, third edition (MCMI-III).

The patients' self-reported weekly cocaine use was also intended to be included as one of the dependent variables. This item was dropped, however, when poor correlations between urine and self-report data were found which may have indicated that patients were sometimes lying about their cocaine-use. A case could be made for including self-reported use data because urine samples typically will show positive for cocaine use only if the urine sample is collected within three days of the most recent use, and it is conceivable that a self-report of use and a urine sample would not coincide. Insofar as several other sources of data were available, and judged to be more reliable, the decision to proceed conservatively

was made, and, therefore, the weekly self-reported use variable was eliminated from the analyses.

CHECKING GROUPS AND STUDY ASSUMPTIONS AT BASELINE: DIFFERENCES BETWEEN THREE AXIS I SUBGROUPS

Preliminary analyses were conducted to determine differences between the three Axis I subgroups in order to check assumptions on both dependent and independent variables at baseline . Categorical variables included: race, marital status, history of previous treatment, employment and route of cocaine use. Continuous variables included several cocaine-related variables including: raw value of amount of cocaine present in initial urine sample, numbers of days in the previous 30 on which patient craved cocaine, the intensity of cocaine craving, the number of days in the previous 30 on which the patient used cocaine, and amount of money spent on cocaine during each use. Additional continuous variables included: baseline ASI drug and psychological severity scores; scores on the MCMI-III personality disorder subscales and modifying indices.

In order to check differences on continuous variables at baseline, a series of one-way analyses of variance (ANOVAs) with Axis I diagnosis as the independent variable were performed. Bonferroni post hoc tests were conducted when significant ANOVAs were found in order to determine which of the three subgroups differed from the others. Tables 3, 4, and 5 present the results of the ANOVAs with significant differences found on several variables. Dep. subjects were found to have a significantly greater number of days on which they craved cocaine (M = 24.61, SD = 7.13) than both the ADHD, (M= 16.25, SD = 9.90) and N/C, (M= 13.20, SD =8.06) subjects: F (2,46) = 8.32, p =.0008. (See Table 3 at the end of this chapter.)

Both the ADHD and Dep. subjects had significantly higher scores on the ASI psychological severity composite scores [ADHD: (M=.41, SD = .19); Dep: (M = .47, SD

= .15)] than the N/C subjects. (M=.22. SD = .20): F (2, 43) = 7.39, p =.0017. (See Table 4 at the end of this chapter.)

There were eight significant differences between the Axis I subgroups on subscales of the MCMI-III which can be seen in Table 5. The Dep. subjects had significantly higher scores than the N/C subjects on several scales including the debasement modifying index: a measure of the individual's tendency to represent him/herself in an extremely negative light, and which may be a distortion of the individual's psychological problems. Differences were found on the passive-aggressive subscale, the self-defeating subscale and, the borderline subscale. Both the ADHD and Dep subgroups had significantly higher scores than the N/C subgroup on two MCMI-III subscales: depressive, and, dependent. The N/C group had significantly higher scores than the ADHD subgroup on the narcissistic and compulsive MCMI-III subscales.

In addition to these results, which were significant at the .050 level or better, there were two additional differences at the statistical trend level. Both of these findings are for modifying indices. A statistical trend was found for the disclosure scale which is a measure of a patient's willingness to be frank and self-revealing or reticent and secretive (F (2, 47) = 3.14, p = .053) with a lower score for the N/C group than either the ADHD or Dep. groups. A statistical trend was also found for the desirability scale which is an indicator of the degree to which the test's results may have been affected by a patient's tendency to appear socially attractive, morally virtuous or emotionally well-balanced (F (2, 47) = 2.92, p = .063). On this measure, the N/C subgroup had higher scores than the other two subgroups.

Chi square analyses were conducted in order to check for differences on categorical variables among the three Axis I subgroups. A trend was found for race, $\chi^2(4) = .916$, p = .06. No significant differences were found on the other categorical variables of gender, marital status , previous treatment, route of cocaine use, or employment.

DIFFERENCES BETWEEN SUBJECTS WITH ANY MCMI-III PERSONALITY DISORDER (PDs) AND THOSE WITHOUT (N/PDs)

Two sets of analyses were conducted to check for differences at baseline between PDs and N/PDs. T-tests for independent samples were conducted for the continuous variables and chi squares were conducted for categorical data. No differences were found on categorical variables. A difference was found on the baseline ASI psychological severity composite score, $t(44) = -3.20$, $p=.003$, with the N/PDs having lower composite scores ($M = .24$, $SD = .20$) than the PDs ($M = .43$, $SD = .18$).

DIFFERENCES BETWEEN SUBJECTS WITH ANTISOCIAL PERSONALITY DISORDER (MCMI-III 6A &6B) (ASPD) AND THOSE WITHOUT (N/ASPD)

Four sets of analyses were conducted to determine differences on continuous and categorical variables for subjects either with traits of ASPD (MCMI-III score of at least 75: ASPD-t), and those with an ASPD diagnosis (MCMI-III score of at least 85: ASPD), and those without any ASPD diagnosis: N/ASPD. No differences were found on the categorical variables at baseline for these groups using a chi square test. No differences were found for continuous variables between ASPD-t and N/ASPD. A significant difference for craving intensity was found for ASPD ($M = 2.71$, $SD = .47$), vs. N/ASPD ($M = 2.19$, $SD = 1.01$) with ASPD having greater cravings than the N/ASPDs: $t(45.12) = -2.39$, $p = .02$.

HYPOTHESIS 1

It was hypothesized that there would be a relatively random distribution of MCMI-III personality disorders across the three Axis I subgroups. This hypothesis was not supported by a chi square analysis which found an unequal distribution of personality disorder diagnoses, $\chi^2(2) = 6.69$, $p = .034$. Fifteen of the 17 ADHD subjects (88.2%), thirteen of the 18 depressed subjects (72.2%), and 7 of the 15 N/C subjects (46.7%) had

a personality disorder. When the presence of personality disorder traits rather than full diagnoses was analyzed, however, no significant differences were found among the three Axis I subgroups, $\chi^2(2) = 2.52$, $p = .28$, ns The analysis was also completed for presence of personality disorder traits. All of the ADHD subjects (100%) had personality disorder traits, whereas 94.4% of the depressed subjects and 86.7% of the N/C were shown to have personality disorder traits. The frequencies of MCMI-III personality disorder diagnoses and traits are given in Table 6.

HYPOTHESIS 2

Hypothesis 2 stated that there would be a significant positive association between worse treatment response and outcome (as measured by the dependent variables) and presence of Axis II personality disorders or the greatest number of concurrent personality disorders. Partial correlations were conducted to analyze the main effects of presence of personality disorder on the total subject population for whom all dependent variable data was available (N=32). Analyses were conducted for the presence of personality disorder diagnosis and personality disorder traits as well as the presence of the greatest number of personality disorders and greatest number of personality disorder traits.

Two of the partial correlations were found to be statistically significant. The relationship between a change in cocaine craving and personality disorder diagnosis was negative and statistically significant ($r(31) = -.35$, $p = .045$). This suggests that subjects with a personality disorder had a lower change in craving than those without a personality disorder. A positive, and statistically significant relationship was found for final ASI psychological, severity composite scores and subjects with the greatest number of personality disorder traits ($r(31) = .34$, $p = .05$). This result suggests that subjects with the greatest number of personality disorder traits had greater ASI psychological, severity scores at the end of treatment than subjects with fewer personality disorder traits. No other statistically significant relationships were found. It should be noted that there were not

enough subjects without any personality disorder traits to compute the correlations for that variable. (See Table 7.)

Main effects for personality disorder were also tested with a series of ANCOVAs (which also yielded results for hypothesis 3, see below) and, again, a statistically significant result was found only on the change in craving variable (F (1,42) = .37, p = .04) indicating that PD subjects differed from N/PD subjects. (see Table 8). This result must be interpreted in light of the interaction effects of Axis I subgroup and Axis II, however, and will be presented in a discussion of hypothesis 3.

HYPOTHESIS 3, a, b, & c

Hypothesis 3 addresses the interaction effects of personality disorders and each Axis I subgroup specifically. It was hypothesized that the ADHD-PD subgroup and the ADHD-N/PD would not differ on treatment response and outcome variables, whereas the other Axis I subgroups (Dep and N/C) would differ on these variables, namely that PD subjects would do worse than N/PD subjects. A series of ANCOVAs were conducted, one for each of the dependent variables, and subsequent post hoc ANCOVAs were performed when a significant result was found in order to determine the direction of the differences indicated. As in the prior analyses, a covariate of number of days use in the 30 prior to beginning treatment was used in order to control for initial severity. Tables 8, and 9 present the preliminary analyses, and Tables 10, 11, 12, and 13 present the post hoc findings of these ANCOVAs. (Post Hoc Tables can be found in the appendices.)

Changes in craving demonstrated main effects for Axis I, Axis II, and for the interaction of Axis I and Axis II (F (2, 42) = 4.03, p = .025) which supports the main hypothesis that personality disorder would have an impact on treatment response and outcome variables. The post hoc analysis for interaction effects on changes in craving found significant results only for the ADHD subgroup (F (1, 14) = 4.68, p = .048). The combined adjusted means indicate, however, that PD subjects had significantly less change

in craving than N/PD which does not support hypothesis 3a (Combined adjusted means: PD = .30; N/PD = .85). No significant differences were found for the Dep and N/C subgroups which suggests that subjects with a personality disorder do not differ from those who do not have a personality disorder on cocaine cravings during treatment.

On the variable of number of "clean" urine samples, a significant difference was found only for the Axis I subgroup (F (2, 42) = 4.37, p = .019). Post hoc analyses, shown in Table 11, indicate that the ADHD subgroup had a significantly greater number of clean urine samples than both the Dep and N/C subgroups. No significant differences were found for the percent of clean urine samples. Axis I diagnoses main effects were statistically significant for length of time in treatment (F (2,43) = 3.60, p = .036). No significant differences were found for Axis II or for an interaction of Axis I and Axis II. Post hoc analyses for length of time in treatment are shown in Table 12. Both the ADHD and Dep subgroups remained in treatment a significantly longer period of time than the N/C subgroup. These results do not support any of the study hypotheses.

ASI drug and psychological severity composite scores were analyzed using 3-way MANCOVAs. As shown in Table 9, a main effect was found for the ASI drug scores within subject groups for repeated measures for the variable "Time" (F (1,28) = 5.96, p = .021) indicating that baseline ASI drug scores were significantly greater than final scores for all subjects. This indicates that all subjects improved during treatment, regardless of their Axis I or Axis II diagnoses, on their ASI drug scores. No significant differences were found for the variables of Axis I subgroup, Axis II diagnosis, or interaction of either of these variables with each other or with "time". Table 9 also presents a significant interaction effect between Axis I subgroup and Time for ASI psychological severity scores (F (2,28) = 4.85, p = .019) suggesting that there was a different rate of change in the ASI psychological scores for the three Axis I subgroups.

Post hoc analyses, in Table 13, show that the three Axis I subgroups differed significantly from each other on psychological severity scores at baseline (F (2, 48) = 8.74,

$p = .001$), with both the ADHD and Dep subgroups having significantly higher scores than the N/C subgroup. The combined adjusted means for the three groups are as follows: ADHD = .436; Dep = .47; N/C = .21. The three groups do not differ significantly at termination on the ASI psychological severity scores. The variable of Axis II personality disorder did not show any significant effect on either of the ASI scales at either baseline or termination. These results, therefore, do not support the study hypotheses.

HYPOTHESIS 4

Hypothesis 4 stated that subjects who were diagnosed with ASPD (MCMI-III subscales 6a and/or 6b) and who did not have any concurrent Axis I or Axis II diagnoses would do worse in treatment than ASPD subjects who had a comorbid diagnosis on either Axis I or Axis II. This hypothesis could not be tested, however because only one of the subjects fit this criteria, and clearly this is an inadequate sample size for conducting statistical analyses. Among the N/C subgroup, aside from the one subject who fit this hypothesis' criteria (and even this subject had traits of additional personality disorders), there was one additional subject diagnosed with ASPD, but this subject had an additional Axis II diagnosis. In order to look more in depth at ASPD subjects, therefore, analyses were conducted on all subjects who had an ASPD diagnosis as well as additional personality disorder diagnoses or personality disorder traits. No significant differences were found on the dependent variables between groups of ASPD subjects.

The ASPD subject pool expands when those individuals with ASPD **traits** as well as ASPD diagnoses are included for analyses. A series of ANCOVAs for the dependent variable (except for ASI composite scores which were analyzed using repeated measures ANCOVAs) were used to determine differences between these, albeit impure, ASPD groups. Table 14 shows that significant differences were found between the three Axis I-ASPD (diagnosis and traits) subgroups on number of clean urine samples (F (2, 33) = 7.03, $p = .003$), percentage of clean urine samples (F (2, 33) = 3.97, $p = .029$), and length

of time in treatment (F (2, 33) = 5.29, p = .01) A significant trend was found between groups for change in craving (F (2,32) = 2.55, p = .094).

Post hoc analyses demonstrated that the ADHD-ASPD group had significantly more clean urine samples and a greater overall percentage of clean urine than either of the other two groups (see Tables 16 and 17 in appendices). As is shown in the post hoc analyses in Table 15 (see appendices), the ADHD-ASPD and the Dep-ASPD groups were equal and both had greater changes in craving than the N/C-ASPD groups. Table 18 (see appendices) shows that the ADHD-ASPD and Dep-ASPD groups did not differ in terms of how long they remained in treatment, however they both remained longer than the N/C-ASPD group.

There were no significant differences between the three groups on either of the ASI composite scores (see Table 19). The ASI drug severity composite scores decreased for all three ASPD groups, whereas significant differences were found within the three groups over time on the ASI psychological severity composite score.

As can be seen in Table 20 (see appendices), the Dep-ASPD group's scores on the ASI psychological severity scores decreased significantly over time, while the ADHD-ASPD and N/C-ASPD scores did not.

These results suggest that, when defined broadly to include not only ASPD diagnoses but also ASPD traits and to discount additional comorbid Axis II diagnoses, there were several outcome measures including length of time in treatment and change in cocaine craving where the N/C did statistically worse than the two Axis I-ASPD comorbid subgroups.

Table 3

Means, Standard Deviations, and One-Way Analysis of Variance of Axis I Subgroups on Baseline Measures and Subscales of MCMI-III[a]

	Axis I Subgroups			
	ADHD (n=17) M (SD)	Depressed (n=18) M (SD)	No Comorbidity (n=15) M (SD)	F Ratio[b]
Cocaine Measures				
first urine sample[c]	3207 (2661)	3268 (2302)	3134 (2377)	.011
number of days crave[d]	16 (10)	24 (7)	13 (8)	8.3 ***
craving intensity[e]	2.3 (1.0)	2.7 (.6)	2.1 (1.0)	1.96
number of days use[d]	10 (8)	15 (7)	12 (9)	0.97
amount $ spent/use	57 (41)	35 (13)	60 (46)	2.55

Notes: [a]Values are reported as mean (SD). [b]df= (2,46) [c]Raw value for urine level.
[d]Range is 0-30 days. [e]Range is 0 to 4, higher scores indicate greater craving intensity.
***p = .001

Table 4

Means, Standard Deviations, and One-Way Analysis of Variance of Axis I Subgroups on Baseline ASI Drug and Psychological Composite Scores[a]

	Axis I Subgroups			
	ADHD (n=17) M (SD)	Depressed (n=18) M (SD)	No Comorbidity (n=15) M (SD)	F Ratio[b]
ASI composite scores[c]				
psychological	0.41 (0.20)	0.47 (0.15)	0.22 (0.20)	7.39***
drug	0.31 (0.20)	0.25 (0.08)	0.22 (0.06)	1.77

Notes: [a]Values are reported as mean (SD).
[b]df= (2,44) [c]Range is 0 to 1, higher scores indicate higher problem severity. ***p< .001

Table 5

Means, Standard Deviations, and One-Way Analysis of Variance of Axis I Subgroups on Subscales of MCMI-III[a]

	Axis I Subgroups			
	ADHD (n=17) M (SD)	Depressed (n=18) M (SD)	No Comorbidity (n=15) M (SD)	F Ratio[b]
MCMI-III personality disorders[c] subscale and modifying indices[d] scores				
X (disclosure)[d]	75 (14)	77 (12)	66 (16)	2.92†
Y (desirability)[d]	49 (21)	49 (18)	63 (17)	3.14††
Z (debasement)[d]	67 (15)	75 (9)	57 (13)	8.34***
1- schizoid	50 (28)	68 (21)	59 (22)	2.31
2A-avoidant	58 (27)	67 (18)	51 (28)	1.83
2B-depressive	82 (16)	83 (14)	55 (30)	9.25***
3-dependent	69 (23)	68 (18)	47 (29)	4.35*
4-histrionic	43 (22)	36 (21)	48 (12)	1.45
5-narcissistic	51 (19)	53 (16)	66 (14)	3.79*
6A-antisocial	82 (7)	75 (17)	74 (14)	1.89
6B-aggressive/sadistic	70 (10)	63 (13)	64 (12)	2.00
7-compulsive	28 (15)	32 (16)	44 (16)	4.53*
8A-passive-aggressive	65 (22)	74 (11)	55 (25)	3.88*
8B-self-defeating	70 (16)	73 (16)	56 (27)	3.44*
S-schizotypal	58 (20)	65 (18)	49 (25)	2.18
C-borderline	71 (15)	74 (15)	56 (24)	4.16*
P-paranoid	49 (19)	52 (20)	51 (26)	0.08

Notes: [a]Values are reported as mean (SD). [b]df= (2,47) [c]A score of 75 indicates presence of traits of personality disorder, and a score of 85 indicates presence of the disorder. [d]Modifying indices are used in the calculation of raw scores into base rate scores.
*Significant at the p<.05 level; ***significant at the p<.001 level.
†trend at the .063 level; ††trend at the .053 level

Table 6.

FREQUENCIES OF MCMI-III DIAGNOSES: TRAITS[a] AND DISORDERS[b]

	ADHD (n=17) disorder (trait)	Depressed (n=18) disorder (trait)	No Axis I Comorbidity (n=15) disorder (trait)
MCMI-III Scale			
Schizoid (1)	0 (4)	4 (10)	1 (3)
Avoidant (2a)	0 (5)	4 (5)	1 (5)
Depressive (2b)	9 (11)	9 (14)	2 (6)
Dependent (3)	3 (10)	2 (7)	1 (4)
Histrionic (4)	0 (1)	0 (0)	0 (0)
Narcissistic (5)	2 (2)	1 (1)	3 (2)
Antisocial (6a)	8 (14)	3 (12)	2 (11)
Sadistic/aggressive(6b)	3 (4)	1 (1)	0 (4)
Compulsive (7)	0 (0)	0 (0)	0 (0)
Passive-Aggressive (8a)	4 (8)	1 (10)	0 (3)
Self-Defeating (8b)	3 (6)	4 (11)	0 (4)
Schizotypal (S)	0 (1)	2 (4)	0 (1)
Borderline(C)	3 (5)	5 (10)	1 (2)
Paranoid(P)	0 (0)	0 (3)	0 (2)
ASPD combined (6a & b) (DIAGNOSIS ONLY)	9	7	2

NOTE: [a]75 cut-off for traits;
[b]85 cut-off for disorders

Table 7.

Partial Correlation Results for Hypothesis Two

Controlling for number of days use during the 30 days prior to commencing treatment.

	Axis II Groups N = 31			
Treatment Response and Outcome Variables	Personality Disorder Diagnosis	Personality Disorder Traits[a]	Greatest # of Personality Disorder Diagnoses	Greatest # of Personality Disorder Traits
% clean urine	.08	----------	.16	.15
# clean urine	.12	----------	.13	.11
Change in Craving	-.35*	----------	-.14	-.28
Length in Treatment	.12	----------	-.08	.05
Final ASI Psych Severity Composite Score	.10	----------	.25	.34*
Final ASI Drug Severity Composite Score	.02	----------	-.04	.04

Note. [a] = Not enough subjects without Axis II traits on this variable to compute.
*p = <.05

Table 8.

ANCOVA Results for Hypothesis 3.

Dependent Variables Source	df	SS	MS	F	p
Change in craving					
Axis I (A)	2	1.03	.51	7.49	.002
Axis II (B)	1	.30	.30	.37	.04
A x B	2	.55	.28	4.03	.025
Covariate	1	.05	.05	.71	ns
Error	42	2.88	.07		
Total	48	4.81	1.21		
Number of clean urine samples					
Axis I (A)	2	86.84	43.42	4.37	.019
Axis II (B)	1	.17	.17	.02	ns
A x B	2	1.19	.60	.06	ns
Covariate	1	30.75	30.75	3.0	ns
Error	43	427.22	9.94		
Total	49	546.17	84.88		
Percentage of clean urine samples					
Axis I (A)	2	3790.41	1895.20	2.06	ns
Axis II (B)	1	244.12	244.12	.27	ns
A x B	2	618.93	309.47	.34	ns
Covariate	1	6454.89	6454.89	7.03	.01
Error	43	39499.97	918.60		
Total	49	50608.32	9822.28		
Length of time in treatment					
Axis I (A)	2	68.13	34.06	3.60	.036
Axis II (B)	1	5.12	5.12	.54	ns
A x B	2	5.28	2.64	.28	ns
Covariate	1	8.31	8.31	.88	ns
Error	43	406.79	9.46		
Total	49	493.63	59.59		

Table 9.
Repeated Measures ANCOVA Results for Hypothesis 3: ASI Psych and Drug Composite Severity Scores

Dependent Variables Source	df	SS	MS	F	p
ASI Psych Composite Scores					
Between Subjects					
Axis I (A)	2	.04	.02	.35	ns
Axis II (B)	1	.03	.03	.63	ns
A x B	2	.18	.09	1.77	ns
Covariate	1	.11	.11	2.08	
Error	27	1.38	.05		
Total	33	1.74	.30		
Within Subjects					
Time (A)	1	.02	.02	.62	ns
Axis I (B) x Time	2	.25	.12	4.85	.019
Axis II (C) x Time	1	.04	.04	1.57	ns
A x B x C	2	.03	.01	.51	ns
Error	28	.72	.03		
Total	34	1.06	.22		
ASI Drug Composite Scores					
Between Subjects					
Axis I (A)	2	.00	.00	.10	ns
Axis II (B)	1	.00	.00	.27	ns
A x B	2	.01	.00	.26	ns
Covariate	1	.08	.08	6.17	.019
Error	27	.33	.01		
Total	33	.42	.09		
Within Subjects					
Time (A)	1	.09	.09	5.96	.021
Axis I (B) x Time	2	.02	.01	.61	ns
Axis II (C) x Time	1	.00	.00	.01	ns
A x B x C	2	.02	.01	.58	ns
Error	28	.43	.02		
Total	34	.56	.13		

Table 14.

ANCOVA Results for Hypothesis 4: ASPD Diagnosis and Trait Subjects.

Dependent Variables Source	df	SS	MS	F	p	
Change in craving						
Axis I	2	.37	.19	2.55	.094	
Covariate	1	.52	.52	7.14		ns
Error	32	2.35	.07			
Total	35	4.81	1.21			
Number of clean urine samples						
Axis I	2	155.16	77.58	7.03	.003	
Covariate	1	13.96	13.96	1.26		ns
Error	33	364.29	11.04			
Total	36	544.92				
Percentage of clean urine samples						
Axis I	2	7335.7	3667.87	3.97	.029	
Covariate	1	1709.45	1709.45	1.85		.183
Error	33	30523.5	925.95			
Total	36	40308.19	1119.67			
Length of time in treatment						
Axis I	2	95.14	47.57	5.29	.010	
Covariate	1	2.19	2.19	.24		ns
Error	33	296.98	9.00			
Total	36	394.27	10.95			

Table 19.

Repeated Measures ANCOVA Results for Hypothesis 4: ASI Psych and Drug Composite Severity Scores of ASPD Diagnosis and Trait Subjects

Dependent Variables Source	df	SS	MS	F	p	
ASI Psych Scores						
	Between Subjects					
Axis I (A)	2	.25	.12	2.14	ns	
Covariate	1	.24	.24	4.19		
Error	23	1.34	.06			
	Within Subjects					
Time (A)	1	.06	.06	4.31	.49	
Axis I (B) x Time	2	.18	.09	6.02	.008	
Error	24	.36	.01			
ASI Drug Scores						
	Between Subjects					
Axis I (A)	2	.00	.00	.16	ns	
Covariate	1	.09	.09	7.09		
Error	22	.27	.01			
	Within Subjects					
Time (A)	1	.09	.09	4.97	.036	
Axis I (B) x Time	2	.06	.03	1.76	ns	
Error	23	.42	.02			

DISCUSSION

Substance abuse is one of the most pervasive problems facing our society. Individuals, families, and whole communities have been devastated by the various facets associated with substance abuse. An enormous financial drain is incurred through money spent on the criminal justice system, as well as funds lost due to reduced worker productivity, and allocations for a variety of drug-related services such as treatment. Cocaine continues to be the most problematic illegal drug used in the United States as demonstrated by current epidemiological data. Cocaine related-deaths reportedly increased between 1995 and 1996 in seven of nine American cities surveyed (NIDA 1997). The need to address the problem of cocaine abuse from multiple perspectives cannot be underestimated.

More specialized treatments have been developed which reflect an increased sophistication in the mental health community as to its understanding of the complexity of the diverse population of cocaine abusers. Studies of comorbid psychopathology among cocaine abusers, for example, have demonstrated high rates of both Axis I and Axis II disorders. The approach of combining pharmacological and psychological treatments has shown some promise in helping people both to stop using cocaine and to prevent future relapses. Controlled clinical trials have found that these combined treatments have been particularly helpful for individuals who not only have a cocaine abuse problem, but also have another Axis I psychiatric disorder such as depression or ADHD. The difficulties involved with treating the underlying character pathology so commonly found among cocaine abusers, however, has not received as much systematic scrutiny as has the comorbid Axis I disorders. This study was intended as a step in contributing to our understanding of the effect of Axis II personality disorders on treatment response and outcome of cocaine-dependent patients.

The major finding of this study was that personality disorders, as measured by the MCMI-III, have little impact on treatment response and outcome among these patients. Before presenting the findings associated with the main hypothesis in greater detail, I will discuss some of the results of the analyses of the basic assumptions of the study.

Differences at Baseline:

The presence of any comorbid psychopathology, whether it be Axis I or Axis II, resulted in significantly higher psychological severity scores on the Addiction Severity Index (ASI) at baseline. This finding certainly makes sense intuitively, since patients with more diagnosed psychopathology would be expected to experience greater psychological distress. Another finding, that depressed patients were found to have significantly greater cocaine cravings than either the ADHD or N/C patients at baseline, suggests that there may be a more powerful experience of internal depletion and wish to escape from dysphoric gloom on the part of the depressed patients.

Differences Between Subgroups on MCMI-III:

The preliminary analyses of MCMI-III overall score differences as well as the analysis of hypothesis 1 (which predicted random distribution of Axis II diagnoses across the three subgroups) can be viewed as related, and so will be discussed together. There were ten significant (or nearly so) differences on the MCMI-III personality disorder and modifying indices scales which were not necessarily indicative of actual diagnoses (that is, below a score of 85). In terms of actual MCMI-III diagnoses, a significant difference was found in that the N/C subgroup had fewer actual diagnoses. This particular finding resembles that of a study conducted by Barber, et al. (1996) where cocaine-dependent patients with personality disorders were more likely to receive another Axis I diagnosis. Closer examination of the differences on the modifying indices, however, raises some questions about the potential for misrepresentation on the MCMI-III.

The N/C subgroup had nearly statsitically significantly greater scores on the desirability modifying index and significantly lower scores on the disclosure and debasement modifying indices in comparison to both the ADHD and depressed subgroups and the depressed subgroup respectively. Millon (1994) states that this sort of profile found in the N/C subgroup can indicate an attempt to portray oneself in the most positive way possible and thereby create a false impression. This suggests, therefore, that the significantly lower number of MCMI-III diagnoses for the N/Cs may be due in part to a positively-toned response style which under-represented the actual degree of psychopathology present. The clinical experience of this author and of colleagues with those patients certainly is consonant with this possibility.

On the other hand, the number of personality disorder diagnoses of the ADHD and depressed subgroups may have been elevated due to currently elevated "state" distress caused by the Axis I comorbidity. Millon (1994) acknowledges, that although he has made an effort at reducing the distorting effect of acute "state" distress on longer standing "trait" character factors, some inaccuracy will likely result do to this limitation of any self-report measure. This may help to account for the result that 88% of the ADHD subgroup was identified as having a personality disorder since ADHD endures from early childhood. This contrasts with major depression which is more episodic in nature. In the case of ADHD, therefore, the distinction between "state" and "trait" can become blurred.

Personality disorder traits (scores of at least 75) were distributed evenly among the three subgroups suggesting that at a lower level of psychopathological severity these cocaine-dependent patients were more similar to each other than not.

Treatment Response and Outcome of Patients with Personality Disorders versus Patients without Personality Disorders (Hypotheses 2 and 3):

Patients with personality disorders did not have overall poorer treatment outcome or response as compared to patients without personality disorders. Change in cocaine

craving was the only measure which showed a poorer outcome for PD patients versus N/PD patients, and this was only among the ADHD subgroup. On all other measures (length of time in treatment, percentage and number of clean urine samples, change in ASI drug and psychological severity composite scores) the PD patients and N/PD patients were similar. A study by Stark and Campbell (1988) where they used the MCMI-I with 100 polysubstance abusers also found that severity of psychopathology was not useful in predicting attrition from treatment which is accord with the current findings. The change in craving finding, which was poorer only for the ADHD/PD subgroup stands out for a couple of reasons, The entire ADHD subgroup had the best treatment response and outcome overall (discussed below), so this measure of an intrapsychic "need" for cocaine did not translate into increased drug use. Perhaps the greater frequency of clinic visits (three-time per week visits of the ADHD patients as opposed to the once or twice weekly visits of the other two subgroups) spurred increased attentiveness to cocaine related thoughts and feelings. Those ADHD patients with personality disorders may have experienced those needs more acutely than the less disturbed ADHD non-personality disordered patients, and, therefore, reported greater cravings.

The results from this study indicate that patients with personality disorders did just as well in treatment as patients with less severe psychopathology. This finding contrasts with the literature which suggests that not only are patients with personality disorders more incapacitated at the outset of treatment, but also that they are likely to fare poorly in treatment until the underlying pathological personality dimensions are addressed. Several possibilities could help to account for this study's results.

As was noted in the introduction chapter of this dissertation, there has been little in the way of systematic study of the effect of Axis II disorders on treatment outcome in a sample of substance abusers. One reason for this may well be the particular difficulty in making accurate Axis II diagnoses with a substance abusing population. Weiss, Mirin and Griffen (1992) published a review of studies that investigated psychiatric comorbidity

among substance abusers with the aim of alerting researchers to the difficult, yet important, methodological issues to bear in mind when attempting to make such diagnoses. This review only looked at studies of comorbid Axis I disorders because of "the difficulty in distinguishing between addiction-related symptoms and enduring personality traits." One can infer from this, therefore, that even greater clinical sensitivity and judgment would be required to diagnose personality disorders among substance abusers, and perhaps a self-report measure, no matter how sophisticated, may be inadequate to make the finely grained distinction between "addiction-related symptoms and enduring personality traits." (Additional concerns regarding diagnostic procedures are raised in this article and will be discussed under the topic of limitations in study methodology.)

In addition to a possible lack of diagnostic precision, which may have contributed to the findings' lack of support of the study's hypotheses, one must also consider elements of the treatment approach which appear to have mitigated the negative effects of having a personality disorder. Most of these patients improved to some degree whether they were on active medication (as in the ADHD subgroup) or on placebo (potentially for depressed and N/C subgroups). The psychological treatment provided to all study patients was a cognitive-behavioral treatment (Relapse Prevention) which helps patients develop greater self-control. For example, behavioral strategies for avoiding potential drug use situations are suggested and sometimes rehearsed in the sessions which help the patient to think ahead and anticipate high-risk situations. These situations are as often internally generated (e.g., feeling lonely on the week-end) as externally (e.g., getting paid). In addition to the very concrete behavioral suggestions which are an integral part of this treatment approach, identification and explorations of emotions and cognitions associated with drug use comprise much of the therapy sessions. Patients are encouraged to explore their ambivalence about giving up cocaine, and to self-monitor their thoughts and feelings related to drug use. They are encouraged to plan ahead for emergencies and are instructed in using

a "problem-solving" approach when they feel overwhelmed by life stressors. They are helped at making lifestyle changes which assist in maintaining abstinence (Carroll 1996).

In many respects RP incorporates aspects of treatment which address some of the central features of certain personality disorders. In an article discussing the treatment of substance abusers with personality disorders, O'Malley, Kosten, and Renner (1990) remark that maintaining abstinence is difficult and "requires the development of a greater degree of frustration tolerance, impulse control and adaptive coping resources." These psychological tasks are implicit within the RP approach.

A study done by Vollrath, Alnaes, and Togerson (1994) which investigated the relationship between coping and MCMI-II personality disorder scales in 240 out-patients found that patients with personality disorders tended to make little use of active coping skills and social supports. These patients, rather, were found to "disengage from goals and to discharge negative emotions." The structure of RP and its explicit focus on setting goals, learning and practicing active coping skills directly some of the deficits found among the dually-diagnosed patients in this study.

In a descriptive, clinical article Southwick and Satel (1990) discuss the benefits to treatment with borderline patients to be garnered by exploring the meanings of their substance use problems. These authors clearly come from a psychodynamic perspective and describe the substance abuser as suffering "from a serious emotional disorder and manifests the disorder, in large part, through a craving for and dependence on the drug. The drug serves as a temporary replacement for defects in psychic structure and as such can regulate drives, control affects and bolster defenses." Yet they insist that a focus on substance abuse early in treatment provides a vehicle for discussing thoughts and feelings which many of their borderline patients are unable to do within a more open-ended exploration:

> Clinicians' interest in the psychological meanings of substance abuse can enhance the therapeutic alliance, and in turn, lead to increased verbal productivity. Each of the above patients anticipated condemnation for drug

> use and seemed relieved by our inquiring rather than punitive stance. They seemed to speak more articulately about their internal states during interviews specifically devoted to substance abuse. By contrast, affective material was rarely disclosed when more general questions about emotional experiences were asked. Finally, we believe that patients can learn about themselves as they and the clinicians begin to uncover the meanings of their drug abuse. Stimulating the patient's curiosity about the role of drugs in psychological life seemed to facilitate the awareness of internal states. Developing such a skill is central to psychotherapeutic work with individuals whose affective insight and vocabulary are limited.

Although The psychotherapeutic approach used in the treatment studies which provided the subjects for this study was cognitive-behavioral and not psychodynamic, several of the central features of RP provide a safe, structured, and ego-enhancing framework which appears to benefit the patients whether or not they are diagnosed with a personality disorder.

Treatment Response and Outcome of Patients According to Axis I Subgroup-findings associated with study hypotheses 3a, b, & c:

The ADHD group as a whole, regardless of presence or absence of personality disorder, had the best overall treatment outcome insofar as they had a significantly greater number of clean urine samples, which is the most accurate measure of how much cocaine was used during treatment, than the other two subgroups. In terms of the other dependent variables, both the ADHD and depressed subgroups remained in treatment significantly longer than the N/C subgroup; on the ASI drug and psychological severity composite scores, all subgroups improved significantly over time.

Several factors may have contributed to the overall improvements of the ADHD subgroup. Firstly, all patients in this subgroup were on active medication for the entire duration of the study. Kosten (1989) and Kleber (1995) both have pointed out that medication can provide a "window of opportunity" when the patient's cravings are under greater control and psychotherapy can help the patient to work on maintaining abstinence and resolving psychological problems. In addition, the more highly structured ADHD

treatment study made the patients focus on their substance abuse problem much more consistently than the patients in the other two subgroups were asked to do.

The poorer outcome of the N/C group, particularly in terms of early drop-outs, replicates findings of other studies where patients without comorbid Axis I disorders have not done as well in treatment as patients with another Axis I disorder. Arndt, et al. (1992) comment that " for those patients who are feeling less depressed, the negative consequences of continued cocaine use may be less acute and therefore they may have lost an incentive for decreasing their drug use."

Treatment Response and Outcome of Patients with Antisocial Personality Disorder (Hypothesis 4):

As was stated in the Results chapter, an analysis of pure ASPD patients could not be conducted because there were an insufficient number fitting this specific category. As an alternative analyses between ASPD-trait patients with no comorbid Axis I but with comorbid Axis II were compared to ASPD-trait patients with comorbid Axis I and II. These are rather loose categories, so the results form these analyses should be interpreted with caution. Those ASPD patients who also had an Axis I diagnosis did better in terms of remaining in treatment and change in cocaine cravings. The ADHD-ASPD patients had the highest number and percentage of clean urine samples, and the depressed-ASPD patients improved significantly on the ASI psychological severity scores while the other two groups did not. All of the ASPD patients improved on the ASI drug severity composite scores.

These results raise questions more to do with diagnostic criteria and methods for identifying ASPD than for what we can learn about these particular groups. Carroll et al. (1993) conducted an ASPD prevalence study of 399 cocaine abusers using three different sets of diagnostic criteria: DSM-III-R, Research Diagnostic Criteria, and Research Criteria, restricted. In this latter system any behaviors that takes place during a period of active drug use is excluded. They found that diagnoses of ASPD ranged widely depending on the

system used. Rouser et al. (1994) looked at heterogeneity of ASPD substance users and levels of "psychiatric distress". They found that the presence of additional Axis II diagnoses were a mediating factor. Those ASPD substance abusers who have additional Axis II diagnoses experience high symptom distress and personality traits which result in "vulnerability to chronic and pervasive neuroticism and emotional instability".

Limitations of the Study

This study found few effects of personality disorders on treatment response and outcome of cocaine abusers. In addition to some of the points made above regarding the findings several additional issues should be considered regarding particular limitations. In the Weiss et al. (1992) cited above several key concerns are raised regarding diagnosing comorbid psychopathology in substance abusers. Firstly, there is issue of when a patient should be evaluated for the presence of additional psychopathology. Some invetigators evaluated patients only after a day or two of abstinence while others waited until two weeks into a drug and alcohol-free hospitalization before attempting to evaluate a patient for comorbid disorders. The patient's presentation may very likely be effected by the length of time since his/her most recent drug use which could, in turn, influence the diagnostic assessment. In this study, no uniform procedure is in place for deciding when enough time has elapsed to diagnose additional psychopathology or when to administer the MCMI-III. It is not uncommon, in fact, for a patient to attend a diagnostic interview session having used cocaine the previous night.

Another relevant point raised in the Weiss et al. (1992) paper deals with the determination of abstinence criteria. When trying to determine if, for example, a patient is depressed due to substance use or substance withdrawal or if there is a pre-existing depression, clear guidelines must be established as to how much "clean" time is required in order to make a diagnosis. As was indicated above, this distinction is doubly difficult with

regard to making Axis II diagnoses and this was not uniformly explained to patients before they completed the MCMI-III.

Marlowe et al. (1997) completed a study comparing structured interviews (SCID II for DSM-III-R) versus a self-report measure (MCMI-II) in making Axis II diagnoses among cocaine abusers and found poor concordance between the two methods. They were careful not to privilege one set of measures over the other, but did recommend that the MCMI be used as an initial screening instrument and that positive diagnoses be followed up with an assessment interview. In this study SCID-II interviews were conducted with the ADHD patients, this data was not included, however, because no such interviews were conducted with the depressed and N/C patients.

Recommendations for Future Research and Clinical Practice:

Despite the lack of statistically significant findings which support the study hypotheses, several issues emerge from this study which warrant further investigation. The difficulty of making accurate diagnoses of character pathology among substance abusers has been demonstrated in this study. There are several possibilities for trying to improve reliability of personality disorder diagnoses. More careful procedures for administering self-report measures should be followed so that the patient can report, to the best of his/her ability, on abstinence symptomotology/personality styles. Other ways of diagnosing personality disorders or character pathology among substance abusers may elicit better data than can be obtained with a self-report measure. Perry (1992) recommends using a clinical interview as opposed to the structured SCID-II or self-report measures because "personality patterns are best revealed by the recurring patterns one finds when taking a systematic history". Projective tests, such as the Rorschach and Thematic Apperception Test, may be better suited to an investigation of personality dynamics and patterns which in many ways are outside of conscious awareness. This approach may

ultimately be the most meaningful in terms of helping us learn important information about our patients, even if these methods do not yield DSM Axis II diagnoses.

The contributions made by various psychotherapeutic approaches and particular therapist characteristics to the amelioration of the patients' personality disorder-related deficits are other areas for future study suggested by this study. Najavits and Weiss (1994) in a review of therapist effectiveness in the treatment of substance abusing patients note that "unique qualities of therapists may influence treatment outcome" in these patients more than other factors. In addition, Woody et al. (1985) emphasized that a meaningful patient/therapist relationship was the strongest predictor of positive outcome in their treatment studies of substance abusers.

APPENDICES

Table 10.

ANCOVA Results of Post Hoc Test for Change in Craving.

Comparison	Source	df	SS	MS	F	p	
ADHD							
	Axis II	1	.46	.46	4.68	0.048	
	Covariate		1	.16	.16	1.59	n. s.
	Error		14	1.38	.10		
	Total		16	2.00	.72		
Depressed							
	Axis II	1	.02	.02	.63	n. s.	
Covariate		1	.00	.00	.13	n. s.	
	Error		15	.38	.03		
	Total		17	.40	.05		
No Axis I Comorbidity							
	Axis II	1	.00	.00	.04	n. s.	
Covariate		1	.00	.00	.01	n. s.	
	Error		11	1.01	.09		
Total		13	1.01	.09			

Table 11.

ANCOVA Results of Post Hoc Test for Number of Clean Urine Samples.

Comparison	Source	df	SS	MS	F	p
ADHD vs. Depressed						
	Axis I	1	106.06	106.06	10.11	.003
	Covariate	1	26.62	26.62	121	n. s.
	Error	32	335	10.49		
	Total	34	467.68	143.17		
Depressed vs. No Axis I						
	Axis I	1	2.98	2.98	.64	n. s.
	Covariate	1	10.68	10.68	2.27	n. s.
	Error	30	140.83	4.69		
	Total	32	154.49	18.35		
No Axis I vs. ADHD						
	Axis I	1	147.17	147.17	11.27	.002
	Covariate	1	28.80	28.80	2.21	n. s.
	Error	29	378.66	13.06		
	Total	31	554.63	189.03		

Table 12.

ANCOVA Results of Post Hoc Test for Length of Time in Treatment.

Comparison	Source	df	SS	MS	F	p	
ADHD vs. Depressed							
	Axis I	1	.28	.28	.03	n. s.	
	Covariate	1	.04	.04	.00	n. s.	
	Error	40	331.07	8.28			
	Total	42	331.39	8.60			
Depressed vs. No Axis I							
	Axis I	1	39.00	39.00	3.17	.09	
	Covariate	1	16.20	16.20	1.32		
	Error	31	381.35	12.30			
	Total	33	436.55	67.50			
No Axis I vs. ADHD							
	Axis I	1	64.81	64.81	5.50	.024	
	Covariate	1	2.80	2.80	.24	n. s.	
	Error	38	447.64	11.78			
	Total	40	515.25	79.39			

Table 13.

ANCOVA Results of Post Hoc Test for ASI Psych Severity Composite Scores.

Comparison	Source	df	SS	MS	F	p	
Baseline	Axis I		2	.55	.28	8.74	.001
	Covariate		1	.12	.12	3.82	.06
	Error		48	1.52	.03		
	Total		51	2.19	.43		
Final	Axis I	2	.16	.08	1.55	ns	
	Covariate		1	.00	.00	.05	ns
	Error		32	1.65	.05		
	Total		35	1.81	.13		

Additional Post Hoc Analyses on ASI Psych Severity at Baseline:

Comparison	Source	df	SS	MS	F	p	
ADHD vs. Depressed	Axis I		1	.02	.02	.54	ns
	Covariate	1	.05	.05	1.77	ns	
	Error		36	1.09	.03		
	Total		38	1.16	.1		
Depressed vs. No Axis I	Axis I	1	.48	.48	16.48	.000	
	Covariate		1	.07	.07	2.48	ns
	Error		36	1.09	.03		
	Total		38	1.16	.10		
No Axis I vs. ADHD	Axis I		1	.38	.38	10.76	.002
	Covariate		1	.12	.12	3.37	.08
	Error		33	1.17	.04		
	Total		35	1.67	.54		

Table 15.

ANCOVA Results of Post Hoc Test for Change in Craving for ASPD Diagnosis and Trait Subjects.

Comparison	Source	df	SS	MS	F	p
ADHD X Depressed						
	Axis I	1	.06	.06	.67	ns
	Covariate	1	.41	.14	4.79	
	Error	23	1.98	.09		
	Total	16	2.00	.72		
Depressed X N/C						
	Axis I	1	.11	.11	4.04	.059
	Covariate	1	.11	.11	4.05	
	Error	19	.54	.03		
	Total	21	.40	.05		
N/C X ADHD						
	Axis I	1	.36	.36	3.56	.073
	Covariate	1	.57	.57	5.64	
	Error	21	2.13	.10		
	Total	23	3.13	.14		

Table 16.

ANCOVA Results of Post Hoc Test for Number of Clean UrineSamples for ASPD Diagnosis and Trait Subjects.

Comparison	Source	df	SS	MS	F	p
ADHD vs. Depressed						
	Axis I	1	82.52	82.52	6.63	.017
	Covariate	1	17.11	17.11	1.37	
	Error	23	286.41	12.45		
	Total	25	404.46		16.18	
Depressed vs. N/C						
	Axis I	1	3.88	3.88	.70	ns
	Covariate	1	.48	.48	.09	
	Error	20	110.91	5.55		
	Total	22	114.96	18.35		
N/C vs. ADHD						
	Axis I	1	133.26	133.26	9.00	.007
	Covariate	1	15.83	15.83	1.07	
	Error	22	325.75	14.81		
	Total	24	480.00	20		

Table 17.

ANCOVA Results of Post Hoc Test for Percentage of Clean Urine Samples for ASPD Diagnosis and Trait Subjects.

Comparison	Source	df	SS	MS	F	p
ADHD vs. Depressed						
	Axis I	1	3177.42	3177.4	3.46	.076
	Covariate	1	1995.88	1995.88	2.18	
	Error	23	21092.3	917.06		
	Total	25	27444.24	1097.77		
Depressed vs. N/C						
	Axis I	1	470.18	470.18	.74	ns
	Covariate	1	358.01	358.01	.56	
	Error	20	12719.7	635.99		
	Total	22	13440.87	610.95		
N/C vs. ADHD						
	Axis I	1	6760.62	6760.62	5.50	.028
	Covariate	1	1279.6	1279.60	1.04	
	Error	22	27020.36	1288.20		
	Total	24	35386.96	1474.46		

Table 18.

ANCOVA Results of Post Hoc Test for Length of Time in Treatment for ASPD Diagnosis and Trait Subjects.

Comparison	Source	df	SS	MS	F	p
ADHD vs. Depressed						
	Axis I	1	5.24	5.24	1.02	ns
	Covariate	1	6.38	6.38	1.24	
	Error	23	118.25	5.14		
	Total	25	128.04	5.12		
Depressed vs. N/C						
	Axis I	1	46.94	46.94	3.77	.066
	Covariate	1	6.37	6.37	.51	
	Error	20	249.09	12.45		
	Total	33	436.55	67.50		
N/C vs. ADHD						
	Axis I	1	86.63	86.63	8.79	.007
	Covariate	1	1.32	1.32	.13	
	Error	22	216.94	9.86		
	Total	24	306.24	12.76		

Table 20.

ANCOVA Results of Post Hoc Test for ASI Psych Severity Composite Scores for ASPD Diagnosis and Trait Subjects.

Comparison	Source	df	SS	MS	F	p	
ADHD	Time		1	.00	.00	.18	ns
	Error	13	.21	.02			
Depressed	Time		1	.25	.25	13.94	.007
	Error		7	.13	.02		
N/C	Time		1	.00	.00	.80	ns
	Error	4	.02	.01			

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Millon Clinical Multiaxial Inventory

TEST DIRECTIONS:

The following pages contain a list of statements that people use to describe themselves. They are printed here to help you in describing your feelings and attitudes. Try to be as honest and serious as you can in marking the statements.

Do not be concerned if a few statements seem unusual: they are included to describe people with many types of problems. If you agree with a statement or decide that it describes you, fill in the "T" to mark it True. If you disagree with a statement or decided that it dose not describe you, fill in the "F" to mark it False. Try to mark every statement, even if you are not sure of your choice. If you have tried your best and still cannot decide, mark "F" for False>

There is no time limit for completing the inventory, but it is best to work as rapidly as is comfortable for you. This form will be scored by computer and the results will be kept confidential.

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1. T F Lately, my strength seems to be draining out of me, even in the morning.

2. T F I think highly of rules because they are a good guide to follow.

3. T F I enjoy doing so many different things that I can't make up my mind what to do first.

4. T F I feel weak and tired much of the time.

5. T F I know I'm a superior person, so I don't care what people think.

6. T F People have never given me enough recognition for the things I've done.

7. T F If my family puts pressure on me, I'm likely to feel angry and resist doing what they want.

8. T F People make fun of me behind my back, talking about the way I act or look.

9. T F I often criticize people strongly if they annoy me.

10. T F What few feelings I seem to have I rarely show to the outside world.

11. T F I have a hard time keeping my balance when walking.

12. T F I show my feelings easily and quickly.

13. T F My drug habits have often gotten me into a good deal of trouble in the past.

14. T F Sometimes I can be pretty rough and mean in my relations with my family.

15. T F Things that are going well today won't last very long.

16. T F I am a very agreeable and submissive person.

17. T F As a teenager, I got into lots of trouble because of bad school behavior.

18. T F I'm afraid to get really close to another person because it may end up with my being ridiculed or shamed.

19. T F I seem to choose friends who end up mistreating me.

20. T F I've had sad thoughts much of my life since I was a child.

21. T F I like to flirt with members of the opposite sex.

22. T F I'm a very erratic person, changing my mind and feelings all the time.

23. T F Drinking alcohol has never caused me any real problems in my work.

24. T F I began to feel like a failure some years ago.

25. T F I feel guilty much of the time for no reason that I know.

26. T F Other people envy my abilities.

27. T F When I have a choice, I prefer to do things alone.

28. T F I think it's necessary to place strict controls on the behavior of members of my family.

29. T F People usually think of me as a reserved and serious-minded person.

30. T F Lately, I have begun to feel like smashing things.

31. T F I think I'm a special person who deserves special attention from others.

32. T F I am always looking to make new friends and meet new people.

33. T F If someone criticized me for making a mistake, I would quickly point out some of that person's mistakes.

34. T F Lately, I have gone all to pieces.

35. T F I often give up doing things because I'm afraid I won't do them well.

36. T F I often let my angry feelings out and feel terribly guilty about it.

37. T F I very often lose my ability to feel any sensations in parts of my body.

38. T F I do what I want without worrying about its effects on others.

39. T F Taking so-called illegal drugs may be unwise, but in the past I found I needed them.

40. T F I guess I'm a fearful and inhibited person.

41. T F I've done a number of stupid things on impulse that ended up causing me great trouble.

42. T F I never forgive an insult or forget an embarrassment that someone caused me.

43. T F I often feel sad or tense right after something good has happened to me.

44. T F I feel terribly depressed and sad much of the time now.

45. T F I always try hard to please others, even when I dislike them.

46. T F I've always had less interest in sex than most people do.

47. T F I tend to always blame myself when things go wrong.

48. T F A long time ago, I decided it's best to have little to do with people.

49. T F Since I was a child, I have always had to watch out for people won were trying to cheat me.

50. T F I strongly resent "big shots" who always think they can do things better than I can.

51. T F When things get boring, I like to stir up some excitement.

52. T F I have an alcohol problem that has made things difficult for me and my family.

53. T F Punishment never stopped me from doing what I wanted.

54. T F There are many times, when for no reason, I feel cheerful and full of excitement.

55. T F In recent weeks, I feel worn out for no special reason.

56. T F For some time now I've been feeling guilty because I can't do things right anymore.

57. T F I think I am a very sociable and outgoing person.

58. T F I've become very jumpy in the last few weeks.

59. T F I keep very close track of my money so I am prepared if a need comes up.

60. T F I just haven't had the luck in life that others have had.

61. T F Ideas keep turning over and over in my mind and they won't go away.

62. T F I've become quite discouraged and sad about life in the past year or two.

63. T F Many people have been spying into my private life for years.

64. T F I don't know why, but I sometimes say cruel things just to make others unhappy.

65. T F I flew across the Atlantic 30 times last year.

66. T F My habit of abusing drugs has caused me to miss work in the past.

67. T F I have many ideas that are ahead of the times.

68. T F Lately, I have to think things over and over again for no good reason.

69. T F I avoid most social situations because I expect people to criticize or reject me.

70. T F I often think that I don't deserve the good things that happen to me.

71. T F When I'm alone, I often feel the strong presence of someone nearby who can't be seen.

72. T F I feel pretty aimless and don't know where I'm going in life.

73. T F I often allow others to make important decisions for me.

74. T F I can't seem to sleep, and wake up just as tired as when I went to bed.

75. T F Lately, I've been sweating a great deal and feel very tense.

76. T F I keep having strange thoughts that I wish I could get rid of.

77. T F I have a great deal of trouble trying to control an impulse to drink to excess.

78. T F Even when I'm awake, I don't seem to notice people who are near me.

79. T F I am often cross and grouchy.

80. T F It is very easy for me to make many friends.

81. T F I'm ashamed of some of the abuses I suffered when I was young.

82. T F I always make sure that my work is well planned and organized.

83. T F My moods seem to change a great deal from one day to the next.

84. T F I'm too unsure of myself to risk trying something new.

85. T F I don't blame anyone who takes advantage of someone who allows it.

86. T F For some time now I've been feeling sad and blue and can't seem to snap out of it.

87. T F I often get angry with people who do things slowly.

88. T F I never sit on the sidelines when I'm at a party.

89. T F I watch my family so closely I'll know who can and who can't be trusted.

90. T F I sometimes get confused and feel upset when people are kind to me.

91. T F My use of so-called illegal drugs has led to family arguments.

92. T F I'm alone most of the time and I prefer it that way.

93. T F There are members of my family who say I'm selfish and think only of myself.

94. T F People can easily change my ideas, even if I thought my mind was made up.

95. T F I often make people angry by bossing them.

96. T F People have said in the past that I became too interested an too excited about too many things.

97. T F I believe in the saying "early to bed and early to rise"...

98. T F My feelings toward important people in my life often swing from loving them to hating them.

99. T F In social groups I am almost always very self-conscious and tense.

100. T F I guess I'm no different from my parents in becoming somewhat of an alcoholic.

101. T F I guess I don't take many of my family responsibilities as seriously as I should.

102. T F Ever since I was a child, I have been losing touch with the real world.

103. T F Sneaky people often try to get the credit for things I have done or thought of.

104. T F I can't experience much pleasure because I don't feel I deserve it.

105. T F I have little desire for close friendships.

106. T F I've had many periods in my life when I was so cheerful and used up so much energy that I fell into a low mood.

107. T F I have completely lost my appetite and have trouble sleeping most nights.

108. T F I worry a great deal about being left alone to take care of myself.

109. T F The memory of a very upsetting experience in my past keeps coming back to haunt my thoughts.

110. T F I was on the front cover of several magazines last year.

111. T F I seem to have lost interest in most things that I used to find pleasurable, such as sex.

112. T F I have been downhearted and sad much of my life since I was quite young.

113. T F I've gotten into trouble with the law a couple of times.

114. T F A good way to avoid mistakes is to have a routine for doing things.

115. T F Other people often blame me for things I didn't do.

116. T F I have had to really rough with some people to keep them in line.

117. T F People think I sometimes talk about strange or different things than they do.

118. T F There have been times when I couldn't get through the day without some street drugs.

119. T F People are trying to make me believe that I'm crazy.

120. T F I'll do something desperate to prevent a person I love from abandoning me.

121. T F I go on eating binges a couple of times a week.

122. T F I seem to make a mess of good opportunities that come my way.

123. T F I've always had a hard time stopping myself from feeling blue and unhappy.

124. T F When I'm alone and away from home, I often begin to feel tense and panicky.

125. T F People sometimes get annoyed with me because they say I talk too much or too fast.

126. T F Most successful people today have been either lucky or dishonest.

127. T F I won't get involved with people unless I'm sure they'll like me.

128. T F I feel deeply depressed for no reason I can figure out.

129. T F Years later I still have nightmares about an event that was a real threat to my life.

130. T F I don't have the energy to concentrate on my everyday responsibilities anymore.

131. T F Drinking alcohol helps when I'm feeling down.

132. T F I hate to think about some of the ways I was abused as a child.

133. T F Even in good times, I've always been afraid that things would soon go bad.

134. T F I sometimes feel crazy-like or unreal when things start to go badly in my life.

135. T F Being alone, without the help of someone close to depend on, really frightens me.

136. T F I know I've spent more many than I should buying illegal drugs.

137. T F I always see to it that my work is finished before taking time out for leisure activities.

138. T F I can tell that people are talking about me when I pass by them.

139. T F I'm very good at making up excuses when I get into trouble.

140. T F I believe I'm being plotted against.

141. T F I feel that most people think poorly of me.

142. T F I frequently feel there's nothing inside me, like I'm empty and hollow.

143. T F I sometimes force myself to vomit after eating.

144. T F I guess I go out of my way to encourage people to admire the things I say or do.

145. T F I spend my life worrying over one thing or another.

146. T F I always wonder what the real reason is when someone is acting especially nice to me.

147. T F There are certain thoughts that keep coming back again and again in my mind.

148. T F Few things in life give me pleasure.

149. T F I feel shaky and have difficulty falling asleep because painful memories of a past event keep running through my mind.

150. T F Looking ahead as each day begins makes me feel terribly depressed.

151. T F I've never been able to shake the feeling that I'm worthless to others.

152. T F I have drinking problem that I've tried unsuccessfully to end.

153. T F Someone has been trying to control my mind.

154. T F I have tried to commit suicide.

155. T F I'm willing to starve myself to be even thinner than I am.

156. T F I don't understand why some people smile at me.

157. T F I have not seen a car in the last ten years.

158. T F I get very tense with people I don't know well because they may want to harm me.

159. T F Someone would have to be pretty exceptional to understand my special abilities.

160. T F My current life is still upset by flashbacks of something terrible that happened to me.

161. T F I seem to create situations with others in which I get hurt or feel rejected.

162. T F I often get lost in my thoughts and forget what's going on around me.

163. T F People say I'm a thin person, but I feel that my thighs and backside are much too big.

164. T F There are terrible events from my past that come back repeatedly to haunt my thoughts and dreams.

165. T F Other than my family, I have no close friends.

166. T F I act quickly much of the time and don't think things through as I should.

167. T F I take great care to keep my life a private matter so no one can take advantage of me.

168. T F I very often hear things so well that it bothers me.

169. T F I'm always willing to give in to others in a disagreement because I fear their anger or rejection.

170. T F I repeat certain behaviors again and again, sometimes to reduce my anxiety and sometimes to stop something bad from happening.

171. T F I have given serious thought recently to doing away with myself.

172. T F People tell me that I'm a very proper and moral person.

173. T F I still feel terrified when I think of a traumatic experience I had years ago.

174. T F Although I'm afraid to make friendships, I wish I had more than I do.

175. T F There are people who are supposed to be my friends who would like to do me harm.

Addiction Severity Index

Drug/Alcohol Use

Route of Administration Types:
1. Oral 2. Nasal 3. Smoking 4. Non-IV injection 5. IV
Note the usual or most recent route. For more than one route, choose the most severe. The routes are listed from least severe to most severe.

	Past 30 days	Lifetime Route
01. Alcohol (any use at all)		
02. Alcohol (to intoxication)		
03. Heroin		
04. Methadone		
05. Other opiates/analgesics		
06. Barbiturates		
07. Sedatives/Hypnotics/Tranquilizers		
08. Cocaine		
09. Amphetamines		
10. Cannabis		
11. Hallucinogens		
12. Inhalants		
13. More than 1 substance per day		

14. According to the interviewer, which substance is the major problem?

14b. <optional> According to patients, which substance is the major problem?

15. How long was your last period of voluntary abstinence from this major problem?

16. How many months ago did this abstinence end?

17. How many times have you had:
    Alcohol DT's?
    Overdosed on Drugs?

18. How many times in your life have you been treated for:
    Alcohol Abuse?
    Drug Abuse?

19. How many of these were detox only?

20. How much money would you say you spent during the past 30 days on:
    Alcohol?
    Drugs

21. How many days have you been treated as an outpatient for alcohol or drugs in the past 30 days?

21b. <optional> How many days have you been treated as an in-patient for alcohol or drugs in the past 30 days?

22. How many days in the past 30 have you experienced:
    Alcohol problems?
    Drug problems?

For questions 23 & 24 ask the patient to use the Patient Rating scale. The Patient is rating the need for additional substance abuse treatment.

23. How troubled or bothered have you been in the past 30 days by these:
    Alcohol problems?
    Drug problems?

24 How important to you now is treatment for these?
    Alcohol problems?
    Drug problems?

INTERVIEWER RATING

25. How would you rate the patient's need for treatment:
    Alcohol problems?
    Drug problems?

CONFIDENCE RATINGS

Is the above information significantly distorted by:

26. Patient's misrepresentation? 0 - No 1 - Yes

27. Patient's inability to understand? 0 - No 1 - Yes

Addiction Severity Index

PSYCHOLOGICAL STATUS

1. How many times have you been treated for any psychological or emotional problems:

In a hospital or inpatient setting?

Outpatient/private patient?

>Do not include substance abuse, employment or family counseling.
Treatment episode = a series of more or less continuous visits or treatment days, not the number of visits or treatment days.
> Enter diagnosis if known.

2. Do you receive a pension for a psychiatric disability? 0 - No 1 - Yes

Have you had a significant period of time (that was not a direct result of alcohol/drug use) in which you have:

	0 - No 1 - Yes	Past 30 days	lifetime
3. Experienced serious depression, sadness, hopelessness loss of interest, difficulty with daily function?			
4. Experienced serious anxiety/tension-uptight, unreasonably worried, inability to feel relaxed?			
5. Experienced hallucinations- saw things or heard voices that were not there?			
6. Experienced trouble understanding, concentrating, or remembering?			
7. Experienced trouble controlling violent behavior including episodes of rage, or violence?			
8. Experienced serious thoughts of suicide?			
9. Attempted suicide?			
10. Been prescribed medication for any psychological or emotional problems?			

11. How many days in the past 30 have you experienced these psychological or emotional problems?
>This refers to problems noted in questions 3-9.

For questions 12-13 ask the patient to use the patient rating scale.

12. How much have you been troubled or bothered by these psychological or emotional problems in the past 30 days?
>Patient should be rating the problem days from question 11.

13. How important to you now is treatment for these

psychological or emotional problems?

The following items are to be completed by the interviewer:

At the time of the time of the interview, the patient was: 0 - No 1- Yes

14. Obviously depressed/withdrawn

15. Obviously hostile

16. Obviously anxious/nervous

17. Having trouble with reality testing, thought disorders paranoid thinking

18. Having trouble comprehending, concentrating, remembering

19. Having suicidal thoughts

INTERVIEWER SEVERITY RATING

20. How would you rate the patient's need for psychiatric/psychological treatment?

CONFIDENCE RATING

21. Patient's misrepresentation? 0 - No 1 - Yes

22. Patient's inability to understand? 0 - No 1 - Yes

COCAINE CRAVING REPORT

STUDY_____PATIENT ID#_____DATE_____

1. Check the box which best indicates, on average, HOW FREQUENTLY (how many times a day) you have experienced craving for cocaine SINCE YOUR LAST VISIT.

FREQUENCY - HOW MANY TIMES PER DAY:

☐ 0 (0) ☐ 1 (1) ☐ 2 (2) ☐ 3-5 (3)

☐ 6-10 (4) ☐ 11-20 (5) ☐ More than 20 (6)

2. Check the box below which best indicates, on the average, HOW LONG the craving for cocaine has lasted SINCE YOUR LAST VISIT.

DURATION - HOW LONG DOES AN AVERAGE URGE LAST (in minutes):

☐ 0-5 min. (0) ☐ 6-10 min. (1) ☐ 11-20 min. (2) ☐ 21-30 min. (3)

☐ 31-45 min. (4) ☐ 46-60 min. (5) ☐ 1-2 hour (6) ☐ 2 hr.+ (7)

3. Overall, how has your "craving" for cocaine changed FROM YOUR LAST VISIT?

☐ Increased (1) ☐ No Change (0) ☐ Decreased (-1)

4. How do you think your medication has affected your craving for cocaine SINCE YOUR LAST VISIT?

Greatly Reduced	Somewhat Reduced	No Change	Somewhat Increased	Greatly Increased
☐ (-2)	☐ (-1)	☐ (0)	☐ (1)	☐ (2)

5. Have you experienced any side effects SINCE YOUR LAST VISIT? (Describe below.)

_____

_____

_____

_____

COCAINE CRAVING REPORT (CONT.)

STUDY_____PATIENT ID#_____DATE_____

6. During THE PAST 24 HOURS how much or how little have you felt you WANTED cocaine? (Score with a vertical mark through the line at that point between very little and very much that best describes your feelings.)

very little ——— very much

7. During THE PAST 24 HOURS how much or how little have you felt you NEEDED cocaine? (Score with a vertical mark through the line at that point between very little and very much that best describes your feelings.)

very little ——— very much

8. SINCE YOUR LAST VISIT how much or how little have you felt you WANTED cocaine? (Score with a vertical mark through the line at that point between very little and very much that best describes your feelings.)

very little ——— very much

9. SINCE YOUR LAST VISIT how much or how little have you felt you NEEDED cocaine? (Score with a vertical mark through the line at that point between very little and very much that best describes your feelings.)

very little ——— very much

NEW YORK STATE PSYCHIATRIC INSTITUTE
COLUMBIA UNIVERSITY DEPARTMENT OF PSYCHIATRY

CLINICAL INVESTIGATION CONSENT FORM

Purpose of Study

The purpose of this research study is to examine the effects of three different potential treatment medications, methylphenidate, desipramine, and bupropion, which may reduce cocaine use, or may decrease the pleasurable effects of cocaine, as well as reduce ADHD-like syndrome symptoms.

Study Procedures

This study involves 12 weeks of outpatient treatment. If you agree to participate, you will come to the DES Cocaine Clinic of the Psychiatric Institute for a screening process, which involves a series of evaluations and psychiatric interviews. These interviews will ask you questions about your mental health, physical health, and drug use history. As part of the interview, we may ask you questions about criminal activities that you might have participated in. Although we would prefer that you answer all of the questions, you may refuse to answer any that make you too uncomfortable. In addition, we would like your permission and help in contacting a family member, preferably one of your parents, to fill out a questionnaire rating your behavior during childhood. Relatives will simply be told that we are conducting a survey, and would like them to fill out a questionnaire rating your behavior during childhood (see Family Information Sheet). You will also undergo a routine physical and neurological examination, and we will need to draw your blood (approximately 4-6 teaspoons) for routine medical testing. If you are a woman, you will also have blood drawn for a pregnancy test (approximately 2 teaspoons). You may be required to have extra evaluations and interviews. If you are eligible, you will be accepted into the study.

Once you are accepted into the study, you will need to come to the DES Cocaine Clinic at the Psychiatric Institute 3 times each week for a period of 12 weeks for all of the evaluations, psychotherapy sessions, medication, monitoring of vital signs, urine collection (for drug screening), and blood drawing. Each visit should take approximately 2 hours. At the end of the 12 weeks of treatment, you will have a final physical examination. Even if you do not stay for the entire 12 weeks, we would like you to show up for a final physical to make sure you are healthy. You will also be asked to come to the research center 3 months after you complete the study for follow-up evaluations and questionnaires.

The treatment medication will be given to you either in capsule or tablet form. Assignment to medication is random, by chance. You will be told how to take the medication, and will receive enough medication until your next appointment. Your medication will be given to you in a pill organizer. You are required to bring the pill organizer to each appointment. Should this become a problem, we will hold the $5.00 subject payment until you return the organizer.

During the course of the study, you will be asked to fill out several questionnaires and to provide a urine specimen each time you come (3 times per week). Your vital signs will be monitored during each visit. In addition, you will be asked to provide 2-4 teaspoons of blood per week to test for medication levels in your body. For a woman, pregnancy blood testing will be done once a month during the study (approximately 2

teaspoons of blood each time) when blood is drawn for other tests. Furthermore, you will receive weekly evaluations by your treating psychiatrist. At the beginning and end of the study, an electrocardiogram (EKG) will be performed to evaluate the functioning of your heart. An electrocardiogram is a noninvasive test in which metal leads are placed on the chest using an adhesive bandage, similar to a band-aid.

In addition, you will be required to show up for weekly psychotherapy sessions with a therapist at the DES Cocaine Clinic. As part of your therapy, the therapist may wish to contact a close family member or friend. Your permission will be asked for this contact (see Addendum 2). Refusal of this contact will not jeopardize your participation in the study. Your permission will also be asked to have your psychotherapy sessions audio/videotaped (see Addendum 3). Refusal of the audio/videotape consent will not jeopardize your participation in the study.

You may be discharged from the study for the following reasons: 1) you are hospitalized; 2) you become pregnant; 3) you are not compliant in taking study medication (i.e., you miss 3 consecutive medication days, or fail to provide urine and blood samples); or 4) you miss more than 3 consecutive therapy sessions. If you are withdrawn from the study, you will continue to receive treatment from the clinic you initially received treatment, or you will be referred to another treatment clinic.

Risks

The major risk of participation is related to the side-effects of taking the medications. Immediate and long term risks of these medications are well known. Methylphenidate is a stimulant used in the treatment of hyperactivity, while desipramine and bupropion are both anti-depressants. The side effects of the medications may include drowsiness, dry mouth, constipation, headaches, dizziness, nausea, agitation, weight loss, or mild increases in heart rate and blood pressure. Other more serious possibly lethal risks usually associated with higher doses or overdose include: irregular heart beats, coma, or cessation of heart functioning or breathing. Additionally, there have been rare reports of psychotic episodes associated with higher doses. When taking bupropion there is an increased risk of having a seizure, therefore it is very important that you inform the psychiatrist if you have ever had a seizure. In order to minimize the risk of having side effects, the doses of the medications will be gradually increased, and you will not be given doses higher than those provided in clinical treatment settings. Your psychiatrist may raise or lower the dose of your medication as needed. You will not be given more than a visit-to-visit supply of medication at one time. There is the risk of misuse and abuse of these medications, therefore, it is important that you take these medications only as prescribed. Furthermore, this medication should be safe-guarded from all family members and friends who might have access to it.

Side effects and risks should be reduced, since we will watch you closely; it is important that you tell us if you experience any unusual feelings. Since one of these medications may make you sleepy, we suggest that you limit your activities such as driving a car and operating machinery. In addition, we don't want you to use other drugs, including alcohol, since the effects of these drugs may be greater or unpredictable when used with the treatment medication. Use of cold medications such as Seldane or other over-the-counter medications should be discussed with your physician before taking them.

Medication blood levels will be obtained weekly in order to monitor the amount of medication in your blood, in order to prevent toxicity, and to make sure that you are taking your medication. Although we do not anticipate a serious medical problem when these

medications are combined with illicit drugs, we recommend that you do not use drugs or alcohol while enrolled in this study. Throughout this study, vital signs will be monitored 3 times per week; however, you should not assume that having normal blood pressure or heart rate measurements suggest that combined use of drugs and the treatment medications will be medically safe.

For women: Although methylphenidate, desipramine, and bupropion have not been shown to increase the risk of birth defects, they have not been approved for use in pregnancy. Therefore, you are requested to use a method of contraception with proven efficacy during your participation in the study. If you become pregnant during the study, you will be discontinued from the study, but may continue to receive your standard treatment at your clinic.

Psychotherapy, interviews, assessments, urine collection, and examinations should pose no risks. You may become uncomfortable while being asked personal questions, but the therapy sessions, interviews, and assessments are designed to help you. There are no anticipated risks associated with the questionnaires except the time required to complete them.

Blood drawing is primarily for your safety and the risk involves only brief discomfort when the needle is inserted and the possibility of a minor temporary bruise at the site of the needle puncture. Approximately one-half pint of blood will be taken during the entire study. This is less than the amount drawn for a blood donation.

Benefits

You may or may not benefit personally from participating in this study. If the medication you receive is effective, it may help to reduce your cocaine craving, as well as some of your other problems such as inattention, restlessness or impulsivity. The benefit to society, is that we may find out if any of these medications are useful for treating other people who abuse cocaine and have ADHD-like syndrome symptoms.

Alternative Treatments

Stimulant and antidepressant medication therapies, as well as certain psychotherapy methods, may be helpful in treating the symptoms of ADHD. Alternative treatments for substance abuse include drug free outpatient treatment, inpatient detoxification, or residential treatment.

Compensation

At the completion of the initial screening, you will receive $25 in cash. However, if you do not complete the entire screening process, you will not receive the $25 fee. Full compensation may be given even if questions which make you feel uncomfortable are not answered. During the study you will receive $5 for each visit to the unit, in order to help with transportation costs and encourage attendance. You will be paid $40 for a follow-up visit 3 months after study completion to complete various assessments and questionnaires.

Research Standards and Participants' Rights

Participation in this project is voluntary, and you may refuse to participate or discontinue participation at any time without loss of benefits to which you are otherwise entitled.

We have obtained a Federal Certificate of Confidentiality for this study. This certificate protects the investigators from having to release the names or other identifying characteristics of research subjects. Investigators so authorized may not be compelled in any Federal, State or Local, civil, criminal, administrative, legislative or other proceedings to provide identifying information about research participants, even if subpoenaed. Any family member we contact to fill out the questionnaire regarding your childhood behavior will not be informed about anything you tell us or the nature of the study.

Signed consent forms will be kept in a locked file, and your name will never be used in publications or presentations. Also, all interviews, assessments, etc. will be coded with initials and numbers. Within the research unit, we cannot insure that your medical records and personal histories will not become known, although the research staff are also bound by confidentiality.

New York State Psychiatric Institute does not provide compensation or payment for treatment of research-related injuries. However, you should be aware that participation in this research does not waive any of your legal rights to seek such compensation through the courts.

If a medical emergency occurs on nights or weekends, you should go to the nearest hospital emergency room and have them call (212) 737-4114 and ask for the doctor on call.

By signing this consent form, you are willing to join the research project described to you on this form. The investigators have answered all questions you have asked, and will answer any question you may have in the future if you do not understand something being done, or if you would like information about your responses. You should contact the Principal Investigator, Dr. Herbert Kleber, who can be reached at (212) 960-5570, if you have any questions.

Both the Columbia-Presbyterian Medical Center Institutional Review Board (CPMC-IRB) and the New York State Psychiatric Institute, Columbia University, Department of Psychiatry Institutional Review Board (PIRB) have approved the recruitment of subjects for this study. Should you have any questions about your rights, or any complaints, you may call either the CPMC-IRB at (212) 305-5883 or the PIRB at (212) 960-5758 during office hours.

I have discussed this study with _____, to my satisfaction. I understand that the doctors participating in this research study are also responsible for my clinical care. I understand that my participation is voluntary, and that I can withdraw from the study at any time without prejudice. Signing this form does not waive any of my legal rights. I have read the above and I am presently willing to participate in this research study.

I have been informed that if I believe that I have sustained an injury as a result of participating in this research study, I may contact the Principal Investigator, Dr. Herbert D. Kleber, at (212) 960-5570, or the Office of the Institutional Review Board at (212) 305-5883, so that I can review the matter and identify the medical resources which may be available to me. I understand that:

a. The Presbyterian Hospital will furnish any emergency care determined to be necessary by the medical staff of this hospital;
b. I will be responsible for the cost of such care, either personally or through my medical insurance or other form of medical coverage;
c. No monetary compensation for wages as a result of the injury will be paid to me by Presbyterian Hospital.

Subject's Name_____

Subject's Signature_____

Witness to Consent_____

Investigator's Signature_____

Date_____

ADDENDUM 1

I have discussed the proposed research with this subject and, in my opinion, this subject understands the benefits, risks, and alternatives (including non-participation), and is capable of freely consenting to participate in this research.

DATE_____
SIGNATURE_____
Study Physician

I have examined _____ on _____ for the purpose of determining whether he/she is capable of understanding the purpose, nature, risks, benefits, and alternatives (including non-participation) of the research, making a decision about participation, and understanding that the decision about participation in the research will involve no penalty or loss of benefits to which the subject is otherwise entitled, for Dr. Herbert D. Kleber's research project, Medication Treatment for Dually-Diagnosed Individuals. On the basis of this examination, I have arrived at the conclusion that:

a. The Presbyterian Hospital will furnish any emergency care determined to be necessary by the medical staff of this hospital;
b. I will be responsible for the cost of such care, either personally or through my medical insurance or other form of medical coverage;
c. No monetary compensation for wages as a result of the injury will be paid to me by Presbyterian Hospital.

Subject's Name_____

Subject's Signature_____

Witness to Consent_____

Investigator's Signature_____

Date_____

FAMILY INFORMATION SHEET

We are conducting a study on volunteers at the New York State Psychiatric Institute. Part of this study includes evaluating the impact of childhood behaviors on current life functioning, including gathering information from an individual who knew the "volunteer" when he/she was a child.

If you are willing, we would like to ask you some questions regarding the childhood behaviors of the volunteer, _____. The volunteer has agreed to allow us to contact you. The Principal Investigator for this study is Herbert D. Kleber, M.D. at Colmbia-Presbyterian Hospital. If you have any questions, you can contact Dr. Kleber at (212) 960-5570. This research study has been approved by both the Columbia-Presbyterian Medical Center Institutional Review Board (CPMC-IRB) and the New York State Psychiatric Institute, Columbia University, Department of Psychiatry Institutional Review Board (PIRB). If you have any questions regarding your rights or about the means of this approach, you may contact either the CPMC-IRB at (212) 305-5883 or the PIRB at (212) 960-5758 during office hours.

Please call the following number _____ to indicate whether or not you are willing to answer some simple questions. If we do not receive a telephone call from you by (date) _____, we will attempt to call you. The telephone interview will take approximately 15 minutes.

Family member would like an additional copy of this information sheet. Yes No

I, _____, the subject agree to allow the investigators to contact the following family member(s):

Address and telephone number of family member:

_____

_____

_____
Subject's Signature Date

_____
Investigator's Signature Date

ADDENDUM 1

I have discussed the proposed research with this subject and, in my opinion, this subject understands the benefits, risks, and alternatives (including non-participation), and is capable of freely consenting to participate in this research.

DATE_____
SIGNATURE_____
Study Physician

I have examined _____ on _____ for the purpose of determining whether he/she is capable of understanding the purpose, nature, risks, benefits, and alternatives (including non-participation) of the research, making a decision about participation, and understanding that the decision about participation in the research will involve no penalty or loss of benefits to which the subject is otherwise entitled, for Dr. Herbert D. Kleber's research project, Medication Treatment for Dually-Diagnosed Individuals. On the basis of this examination, I have arrived at the conclusion that:

_____A. This subject has the capacity at this time.
_____B. There is a question about this subject's capacity at this time.
_____C. This subject clearly lacks this capacity.

DATE_____
SIGNATURE_____
Member of Treatment Team
(M.D. or Ph.D.)

ADDENDUM 2

CONSENT FOR SIGNIFICANT OTHER CONTACT

I understand that it may be important for research staff from the Division on Substance Abuse and/or the Depression Evaluation Service Clinic (DES) to discuss my problems periodically with a close family member or someone who knows me well to assess how I am doing, or to aid in case of emergency. I consent to allow the research staff from the Division on Substance Abuse and/or the DES to contact the following person to discuss my case throughout the course of my treatment.

Name: _____

Relationship: _____

Address: _____

_____

_____

Phone: home ( )_____

work ( )_____

Significant other not available: _____

Contact refused: _____

Subject's Signature: _____

Investigator's Signature: _____

Date: _____

ADDENDUM 3

CONSENT FOR VIDEO/AUDIO TAPING DURING PSYCHOTHERAPY SESSIONS

I understand that as part of my participation in the study I will be required to show up for weekly psychotherapy sessions with a therapist at the DES Cocaine Clinic. These sessions will be video/audio taped for the purpose of monitoring my treatment and assuring the quality of the counseling intervention. During the video/audio taping, I understand that the video camera will be aimed at the therapist rather than at myself; my voice, as well as the therapist's voice, will be recorded on the audio track. I understand that the video/audio tapes will be viewed and heard only by the Division on Substance Abuse/DES staff. I understand that these video/audio tapes will be kept in locked file cabinets, and that they will be identified by a number, rather than by my name, in order to protect my confidentiality. These video/audio tapes will be kept for five years, and then destroyed.

I consent to all of my psychotherapy sessions being recorded in this manner during this study.

I understand that I can request that the recording be stopped or that the video/audio tape be erased at any time, either during or after my psychotherapy session.

I understand that my refusal to be video/audio taped will not jeopardize my participation in this treatment study.

The Principal Investigator for this study is Herbert D. Kleber, M.D. at Columbia-Presbyterian Hospital. If I have any questions, I may contact Dr. Kleber at 212-960-5570. This research study has been approved by the Psychiatric Institute-Columbia University Institutional Review Board (NYSPI IRB). If I have any questions regarding my rights or about the means of this approach, I may contact the NYSPI IRB at 212-960-5758.

Subject's Signature: _____

Investigator's Signature: _____

Date: _____

NEW YORK STATE PSYCHIATRIC INSTITUTE
COLUMBIA UNIVERSITY DEPARTMENT OF PSYCHIATRY
CLINICAL INVESTIGATION CONSENT FORM

Pergolide Treatment for Substance Abusers

Purpose of Study

The purpose of this research study is to determine whether pergolide is useful in helping persons who are abusing cocaine. Pergolide has not been tested as a treatment for cocaine abuse. It has been approved for use in the United States as a medication to treat patients with Parkinson's Disease, a neurological disorder which impairs normal body movements.

Study Procedures

Before entering this study, I will have a psychiatric evaluation by one of the psychiatrists within the Division on Substance Abuse, along with a cardiogram, blood tests (approximately 6 tablespoons), and a physical examination. This will also include a urine sample for drug screening and a blood pregnancy test for women. If there are no medical reasons against my being treated with pergolide I will spend up to 3 hours with a psychiatrist or psychologist answering questions about my life and my alcohol and drug use. I will receive psychotherapy treatment at the Depression Evaluation Service (DES) clinic and a psychiatrist at the clinic will prescribe my medication.

I also will be asked to permit the research team to contact a relative or close friend of mine, who will be informed about the study, and whom the research team may contact to monitor my progress in the study.

If I qualify based on these initial interviews and tests I will be enrolled in this study for 26 weeks. I may also have additional clinical evaluations and interviews directly related to this research protocol. Pergolide will be prescribed when the screening process is completed. I will be assigned, at random, to one of two groups. Each group will receive pergolide for 12 consecutive weeks and an inactive placebo for the rest of the time. I will be prescribed medication twice a week. Medication will be dispensed in a pill organizer which I am required to bring to each appointment. Should this become a problem, the $5.00 subject payment will be withheld until the pill organizer is returned. If I experience symptoms such as nausea, dizziness, abnormal body movements, or other bodily changes, the pergolide may be stopped.

I will be required to come to the DES clinic two times a week. Each visit will involve a one hour meeting to discuss side effects of the medication, drug use and craving, an interview to assess psychiatric symptoms, and a brief neurological examination. I will be asked to fill out several questionnaires regarding my psychological symptoms, drug use and craving. The dose of the pergolide might need to be raised or lowered. I will also be required to give a urine sample under observation. In addition, one tablespoon of blood will be drawn on a monthly basis throughout the study to check the functionong of my liver. For women, one tablespoon of blood will be drawn on a monthly basis to test for pregnancy. Furthermore, a cardiogram will be done on a monthly basis to check the functionong of my heart. At the end of the study and three months after the study is completed, I will also meet for an hour with a study psychiatrist or psychologist to answer questions about how I have been doing.

During the study I will receive therapy at the DES clinic once a week. The therapy program

is specifically designed to help treat individuals who abuse drugs.

I may be discharged from the study for the following reasons :
1) I develop distressing psychological symptoms which cannot be stabilized, 2) I miss more than three consecutive therapy sessions, 3) I become hospitalized during the study, or 4) I become pregnant; pregnancy tests will be done each month. If I am withdrawn from this study as a result of lack of participation in group therapy, I will be referred to another clinic for treatment. If I am withdrawn from this study due to psychiatric or medical illness I may continue to receive therapy at the DES clinic for the remainder of the time I was to participate in the study.

Compensation

I may receive $5 for each visit during the study to help with transportation costs. In addition, I will receive $20 for a follow-up visit.

Risks and Benefits

I may benefit directly from the treatment I receive by having a reduction in my drug use and improvement in my problems related to my drug use.

Risks involved in this study are those associated with the use of pergolide, and with possible interactions between pergolide and cocaine or other drugs. The side effects of pergolide include nausea, dizziness, headache, back pain, chest pain, abdominal pain, double vision, constipation, confusion, hallucinations, abnormal body movements, sedation, insomnia, diarrhea, and runny nose. Although this medication has been associated with irregular rhythms of the heart and heart attacks, these serious effects are less likely to occur at the doses that will be used for this study. In addition, during the pacebo phase, I may experience a return of cocaine craviving and/or use. The possible benefits obtained during the treatment phase of the study, Mainly a reduction in drug use and improvement in problems related to drug use, May be lost. However, it is hoped that the non pharmacological treatment that will be continued during the placebo phase will deter these possible negative effects.

Since pergolide may make me sleepy I will restrict activities such as driving a car and operating machinery. In addition, I understand that the use of other drugs, particularly alcohol and other sedatives, is strongly advised against since the effects of these drugs may be greater or unpredictable in combination with the treatment drug. The risks of taking cocaine in combination with pergolide are unknown. I am aware that cocaine may cause heart attacks and other serious heart problems, and it is possible that pergolide might increase the risk of these known complications. There may also be a danger if I use other illicit drugs, such as sedatives and/or alcohol. For example the pergolide might result in my becoming more sleepy or intoxicated than usual. If for any reason I am unable to tolerate pergolide, it will be discontinued and I will be offered additional treatment for the remainder of time I was to participate in the study.

(For women) At this time the safety of pergolide for pregnant women is not known. Therefore, I will not become pregnant or nurse while participating in this protocol, and I agree to use an effective method of birth control for the duration of my participation in the study. This includes sterilization, oral contraceptives, the diaphragm, condoms or abstinence. Pregnancy will be confirmed by blood pregnancy tests before the study and occasionally during the study. I understand that if I suspect that I might be pregnant I must

inform my psychiatrist immediately. If I become pregnant I understand that I will be withdrawn from the study and referred elsewhere for treatment. In addition I will be offered treatment at the clinic for up to 6 months after my participation in this study was discontinued.

A possible risk to blood drawing is the possibility that a small bruise, or rarely, a local infection may develop at the site of the needle puncture.

Psychotherapy, interviews, assessments, urine collection and examinations should pose no risks. However, I may become uncomfortable while being asked personal questions. The disadvantage of questionnaires and other assessments is the time required to complete them.

I understand that pergolide has recently been approved for clinical use in the United States to treat individuals with Parkinson's Disease. Once this study is completed, my treating psychiatrist and I may choose to continue me on pergolide or place me on another medication. Unfortunately, there are currently few, if any, accepted pharmacological treatment for cocaine abuse/dependence. However, couseling and psychotherapy have shown to be helpful for some patients.

Alternative to Study Participation

The alternative to participating in this study would be to receive treatment elsewhere, without the additional interviews and procedures specifically associated with this research protocol.

Research Standards and Participants' Rights

Participation in this project is voluntary, and I may refuse to participate or discontinue participation at any time without loss of benefits to which I am otherwise entitled. I understand that a Federal Certificate of Confidentiality has been obtained for this study. This certificate protects the investigators from having to release the names or other identifying characteristics of research subjects. Investigators so authorized may not be compelled in any Federal, State or Local, civil, criminal, administrative, legislative or other proceedings to provide identifying information about research participants even if subpoenaed. Research records will only be available to research staff, signed consent forms will be kept in a locked file, and my name will never be used in publications or presentations. Also, all interviews, assessments, etc. will be coded with initials and numbers.

I understand that the doctors conducting this research study are also responsible for my clinical care.

Federal regulations require that I be informed about the institution's policy with regard to compensation and payment for treatment of research-related injuries. Short term emergency medical treatment, which has been determined to be necessary by Psychiatric Institute's doctor's, and which is within the capability of the Psychiatric Institute will be provided. In addition, we will provide assistance in arranging follow up care in such instances.

New York State Psychiatric Institute does not provide compensation or payment for treatment of research related injuries. However, I am aware that participation in this

research does not waive any of my legal rights to seek such compensation through the courts.
If a medical emergency occurs on nights or weekends, I should go to the nearest hospital emergency room and have them call (212) 737-4114 and ask for the doctor on call.

By signing this consent form, I am willing to join the research project described to you on this form. The investigators have answered all questions I have asked, and will answer any question I may have in the future if you do not understand something being done or I would like information about your responses. I should contact the Principal Investigator, Dr. Herbert Kleber, who can be reached at 960-5570, if I have any questions.

The New York State Psychiatric Institute Institutional Review Board (NYSPI IRB) have approved the recruitment of subjects for this study. Should I have any question about my rights, or any complaints, I may call the PI IRB at (212) 960-5758 during office hours.

I have discussed this study with _____, to my satisfaction. I understand that my participation is voluntary, and that I can withdraw from the study at any time without prejudice. I have read the above and agree to enter this research study. Signing this form does not waive any of my legal rights.

Subject's Signature _____

Witness to Consent _____

Investigator's Signature_____

Date_____

CONSENT FOR SIGNIFICANT OTHER CONTACT

I understand that it may be important for research staff from the Division on Substance Abuse to discuss my problems with a close family member or someone who knows me well periodically to assess how I am doing, or to aid in case of emergency. I consent to allow the research staff from the Division on Substance Abuse to contact the following person to discuss my case throughout the course of my treatment.

Name:_____

Relationship:_____

Address:_____

_____

Phone: Home _____

Work _____

Significant other not available: _____

Contact refused: _____

Signature:_____

Date:_____

Investigator's Signature:_____

ADDENDUM 1

I have discussed the proposed research with this patient and, in my opinion. this patient understands the benefits, risks, and alternatives (including non-participation) and is capable of freely consenting to participate in this research

_____
Signature

_____
Date

_____
Investigator's Signature

_____
Date

Perg.pilot

ADDENDUM 2

CONSENT FOR VIDEO/AUDIO TAPING DURING PSYCHOTHERAPY SESSIONS

I understand that as part of my participation in the study I will be required to show up for weekly psychotherapy sessions with a therapist at the DES Cocaine Clinic. These sessions will be video/audio taped for the purpose of monitoring my treatment and assuring the quality of the counseling intervention. During the video/audio taping, I understand that the video camera will be aimed at the therapist rather than at myself; my voice, as well as the therapist's voice, will be recorded on the audio track. I understand that the video/audio tapes will be viewed and heard only by the Division on Substance Abuse/DES staff. I understand that these video/audio tapes will be kept in locked file cabinets, and that they will be identified by a number, rather than by my name, in order to protect my confidentiality. These video/audio tapes will be kept for five years, and then destroyed.

I consent to all of my psychotherapy sessions being recorded in this manner during this study.

I understand that I can request that the recording be stopped or that the video/audio tape be erased at any time, either during or after my psychotherapy session.

I understand that my refusal to be video/audio taped will not jeopardize my participation in this treatment study.

The Principal Investigator for this study is Herbert D. Kleber, M.D. at Columbia-Presbyterian Hospital. If I have any questions, I may contact Dr. Kleber at 212-960-5570. This research study has been approved by the Psychiatric Institute-Columbia University Institutional Review Board (NYSPI IRB). If I have any questions regarding my rights or about the means of this approach, I may contact the NYSPI IRB at 212-960-5758.

_____
Signature

_____
Date

_____
Investigator's Signature

_____
Date

Perg.pilot

ADDENDUM 3

CONSENT TO RECEIVE MEDICATION IN NON-CHILDPROOF CONTAINERS

I understand that as part of my participation in this study I will be required to take medication. In order to insure I take my medication correctly, I will be given it in labeled pill boxes. Therefore, I understand that these pill boxes are not childproof and agree to keep these medications out of the reach of children.

_____
signature

_____
date

_____
Investigator's signature

_____
date

IRB # 2649

4/10/96

CONSENT FORM

PRELIMINARY TRIALS OF NOVEL AGENTS FOR COCAINE ABUSE: RISPERIDONE

PURPOSE OF STUDY

The purpose of this research study is to determine whether risperidone (Risperidal), an antipsychotic medication, is useful in helping persons who are abusing cocaine to stop. Risperidone has been recently approved by the FDA for treatment of schizophrenia. It has not been tested as a treatment for cocaine abuse, and it is not known whether it has any effect on cocain use or craving.

STUDY PROCEDURES

Before entering this study I will have a psychiatric evaluation by one of the Depression Evaluation Service (DES) psychiatrists, followed by a cardiogram, blood tests, and a physical exam. If there is no medical contraindication to my being treated with risperidone I will spend 90 minutes with the psychiatrist and up to an additional 90 minutes with a psychologist answering questions about my life. This will include questions about my drug use. I will also be asked to participate in a relapse prevention program at the clinic which will include a weekly meeting with a counselor and weekly group therapy.

I will be asked to permit the research team to contact a significant other (a close friend or relative) in my life, who will be informed about the study, and who the research team may contact to check on my well-being.

At the beginning of the study I will be asked to undergo a research procedure in a laboratory at Psychiatric Institute, which takes about two hours. I will listen to tapes and see videos some of which include people using cocaine, and I will be asked to handle cocaine paraphernalia or "works". My pulse, heart rate, and blood pressure will be monitored and I will be asked some questions about how I am feeling. At the end of the procedure I will go back to the clinic and meet with my counselor.

Over the next 24 weeks I will be asked to come to the clinic twice per week to participate in counseling and see the psychiatrist, for a total of about 4 hours per week. I will be assigned, at random, to one of two groups. Each group will receive risperidone for 12 consecutive weeks and inactive placebo the rest of the time. Neither I nor my psychiatrist or counselor will know exactly when I am on medication and when I am on placebo. I will be asked to take the medication on a daily basis and meet with my psychiatrist every week for the next 24 weeks. Each weekly visit will involve a 15 to 30 minute meeting with my psychiatrist to discuss side effects of the medication, drug use and craving, and any other symptoms. My psychiatrist will raise or lower the dose of my medication as needed. One tablespoon of blood will be drawn at the end of weeks 6, 12 and 18 of my treatment to check risperidone blood levels. I will be asked to give supervised urines twice per week throughout the study. The urine will be tested for drugs, and the purpose of this is to help monitor my progress. At the 6th week, I will be asked to return to the laboratory for the same procedure involving exposure to tapes and "works". At the 6th, 12th, 18th and 24th week I will also be asked to meet for an hour with the psychologist to answer questions about how I have been doing. At the end of the 24 weeks, the

program ends, and I will be referred for further treatment outside the clinic.

I understand that the doctors conducting this research study are also responsible for my clinical care.

COMPENSATION

I will be paid $25 for completion of the baseline assessments, including laboratory procedure, $25 for completion of week 6 assessments, including laboratory procedure, and $25 for completing the assessments at weeks 12, 18 and 24. Therefore I can earn up to a total of $125 during the study.

RISKS AND BENEFITS

I may benefit directly from the treatment I receive with reduction in drug use and improvement in problems related to my drug use.

(For females) I understand that risperidone is of unknown risk to a fetus. I will have a pregnancy test before beginning medication to determine that I am not pregnant. I will use adequate birth control throughout my treatment. I understand that if I suspect that I might be pregnant I must inform my psychiatrist immediately.

Other risks involved in this study are those associated with the use of risperidone, and with possible interactions between risperidone and cocaine or other drugs. The side effects of risperidone may include dry mouth, constipation, dizziness on standing, or sleepiness. These effects can be eliminated with discontinuation of the drug. I will discuss any such effects with my psychiatrist if they occur.

Risperidone may cause muscular side effects including certain types of muscle spasms or muscular rigidity. These effects can be eliminated with discontinuation of risperidone, or may be treated with a small dose of a second medication, Cogentin. Rarely risperidone may cause more serious motor system side effects. Tardive dyskinesia consists of involuntary movements often of the face and tongue. My psychiatrist will examine me regularly for this. These side effects may appear while I am taking the medication or shortly after the medication is stopped and the condition could become permanent. Neuroleptic malignant syndrome includes increased body temperature, severe muscular rigidity, and loss of consciousness or confusion. This is a medical emergency and may lead to death if not promptly treated. I should be taken to an emergency room if these symptoms occur. If I have ever in the past had tardive dyskinesia, or neuroleptic malignant syndrome, or severe muscular side effects from medications I should inform my psychiatrist. It is important to drink plenty of fluids and avoid becoming overheated or dehydrated when excercising or when in hot surroundings.

The interactions between risperidone and cocaine or other drugs are not known at this time. I understand that in individuals with a history of seizures, antipsychotic medications in general can increase the risk of having a seizure. Cocaine also can cause seizures. Therefore taking cocaine while being treated with risperidone may increase the risk of a seizure. If I have ever had a seizure I will inform my psychiatrist. I am aware that cocaine may cause heart attacks and other serious heart problems, and it is possible that risperidone might increase the risk of these. There may also be a danger if I use other illicit drugs, such as

sedatives and/or alcohol. For example the risperidone might result in my becoming more sleepy or intoxicated than usual.

If for any reason I am unable to tolerate risperidone, it will be discontinued and other treatment may be instituted. The only risk to the blood drawing procedures used in this study is the possibility that a small bruise, or rarely, a local infection may develop at the site of the needle puncture. This seldom occurs.

The only risk of the laboratory procedure is that after exposure to the materials (audiotapes, videotapes, and "works") I may experience increased "craving" for cocaine. This might make it harder for me not to use cocaine, or make me more likely to use heavily. However, such cravings are usually short-lived. After the laboratory session I will go to the clinic for a therapy session with my counselor during which cravings and methods for handling them will be addressed.

TREATMENT ALTERNATIVES

I understand that there are a number of different treatment approaches for cocaine abuse which I may consider as alternatives to participating in this program. These include various inpatient or residential treatment programs as well as outpatient programs. However, it is still not clear what the best treatment is for cocaine abuse.

CONFIDENTIALITY

I understand that the records of my participation, including research forms, will be kept in locked cabinets at the clinic and be available only to DES staff. A Certificate of Confidentiality has been received from the Department of Health and Human Services (DHHS). This certificate will protect the investigators from being forced to release any research data in which you are identified, even under a court order or subpoena. This protection, however, is not absolute. It does not, for instance, apply to any state requirement to report certain communicable diseases. This will not affect this study because we don't test for communicable diseases. However we are required by New York State law to report any instances of child abuse to the appropriate authorities. Also, because this research is regulated by the Food and Drug Administration (FDA) and sponsored by the National Institute on Drug Abuse (NIDA), staff from these and other DHHS agencies may review records that identify you. However, it is the policy of these agencies and this investigator(s) that every attempt will be made to resist demands to release information that identifies you. When the results of this study are published, your name will not be used.

RESEARCH STANDARDS AND RIGHTS OF PARTICIPANTS

I understand that I may refuse to participate or discontinue my treatment in this study at any time without loss of benefits to which I might otherwise be entitled. I understand that these benefits include 6 months of relapse prevention counseling at the DES. I understand that the doctors conducting this research study are also responsible for my clinical care.

MEDICAL COMPENSATION FOR RESEARCH RELATED ACTIVITIES

Federal regulations require that I be informed about the institution's policy with regard to compensation and payment for treatment of research related injuries. Short-term emergency medical

IRB # 2649

treatment, which has been determined to be necessary by New York State Psychiatric Institute's doctors, and which is within the capability of New York State Psychiatric Institute will be provided. In addition, we will provide assistance in arranging follow up care in such instances.

The New York State Psychiatric Institute cannot provide compensation or payment for treatment of research related injuries. However, I am aware that participation in this research does not waive any of my legal rights to seek such compensation through the courts.

If a medical emergency occurs on nights or weekends, I should go to the nearest hospital emergency room and have them call (212) 737-4114 and ask for the doctor on call.

I have discussed this research study and consent form with my DES psychiatrist, and he/she has answered all of my questions about the study to the best of his/her ability. I also understand that if I have any questions in the future, I may ask my DES psychiatrist or the principal investigator of this study, Dr. Edward Nunes, who may be reached at (212) 960-5581.

I understand that the New York State Psychiatric Institute/ Columbia University Department of Psychiatry Institutional Review Board has approved the recruitment of subjects for this study and that, if I have any questions about my rights as a research subject or any complaints, I may call the Institutional Review Board at (212) 960-5758 during office hours, Monday through Friday, 9:00 am to 5:00 pm.

I have received a copy of this consent form to keep.

SIGNED:_____

DATE:_____

I have discussed the proposed research with this patient and, in my opinion, the patient understands the benefits and risks of the study and is capable of freely consenting to participate in this research.

SIGNED:_____
(study M.D.)

DATE:

IRB # 2649

CONSENT FOR SIGNIFICANT OTHER CONTACT

I understand that it may be important for the DES staff to discuss my problems with a close family member or someone who knows me well periodically to assess how I am doing, or to aid in case of emergency. I consent to allow the DES staff to contact the following person to discuss my case throughout the course of my treatment.

Name: _____

Relationship: _____

Address: _____

_____

_____

Phone: home( ) _____ work( ) _____

Significant other not available: _____

Contact refused: ____

SIGNED: _____

DATE: _____

PHYSICIAN: _____

IRB # 2647

03/07/96

CONSENT FORM

DESIPRAMINE TREATMENT OF DEPRESSED COCAINE ABUSERS

PURPOSE OF STUDY

The purpose of this research study is to determine whether desipramine (Norpramine), an antidepressant medication, is useful in helping persons who are abusing cocaine and suffering from depression. Antidepressants such as desipramine are clearly useful in the treatment of depression. Their effectiveness in patients abusing cocaine has not been established.

STUDY PROCEDURES

Before entering this study I will have a psychiatric evaluation by one of the Depression Evaluation Service (DES) psychiatrists, followed by a cardiogram, blood tests, and a physical exam. If there is no medical contraindication to my being treated with desipramine I will spend 90 minutes with the psychiatrist and up to an additional 90 minutes with a psychologist answering questions about my life. This will include questions about my drug use. I will also be asked to participate in a relapse prevention program at the clinic which will include a weekly meeting with a counselor and weekly group therapy.

I will be asked to permit the research team to contact a significant other (i.e. close friend or relative) in my life, who will be informed about the study, and who the research team may contact to check on my well-being.

I will be assigned, at random, to take either desipramine or inactive placebo with a 50-50 chance to receive one or the other. Over the next 30 weeks, I will be asked to attend the clinic twice per week for the first 24 weeks and once every two weeks for the remaining 6 weeks to give urine samples and participate in counseling. I will be asked to take the medication on a daily basis and meet with my psychiatrist every week for the first 24 weeks. Each visit with the psychiatrist will involve 15 to 30 minute to discuss side effects of the medication, drug use and craving, and my depression symptoms. My psychiatrist will raise or lower the dose of my medication as needed. One tablespoon of blood will be drawn at the end of weeks 6, 12 and 24 of my treatment to check desipramine blood levels. I will be asked to give supervised urines twice per week throughout the

study. The urines will be tested for drugs. The purpose of this is to help the psychiatrist monitor my progress.

At the end of the first 12 weeks, if my depression has not improved, I will be removed from the study, the blind will be broken, and my psychiatrist and I will find out what I have been taking. I can continue at the clinic for another 6 months, and the psychiatrist will work with me to try to find a medication that will be helpful to me. If I was on placebo I may be offered treatment with desipramine. If I was on desipramine and did not get better, I may be offered treament with other antidepressants. If at the end of 12 weeks my depression is improved, I will continue taking the study medication and seeing my psychiatrist for the next 12 weeks. I will then participate in three counseling sessions, spaced two weeks apart, for the remaining six weeks. At the end of this time (a total of six months of treatment) the program ends, and I may be referred for further treatment outside the clinic.

I understand that the doctors conducting this research study are also responsible for my clinical care.

COMPENSATION

I will be paid $25 for completion of the baseline assessments, $25 for completion of week 6 assessments, and $25 for completing the assessments at weeks 12 and 24. Therefore I can earn up to a total of $100 during the study.

RISKS AND BENEFITS

I may benefit directly from the treatment I receive with relief of my depression and reduction in drug use.

(For females) I understand that desipramine is of unknown risk to a fetus. I will have a pregnancy test before beginning medication to determine that I am not pregnant. I will use adequate birth control throughout my treatment. I understand that if I suspect that I might be pregnant I must inform my psychiatrist immediately.

Other risks involved in this study include those associated with the use of desipramine, and with possible interactions between desipramine and cocaine or other drugs. The side effects of desipramine may include dry mouth, constipation, blurry vision, sleepiness, headache, jitteriness, dizziness (especially on standing up), and reversible decreases in sexual interest or functioning.

These effects can be eliminated with discontinuation of the drug. I will discuss any such effects with my psychiatrist if they occur.

The interactions between desipramine and cocaine or other drugs are not clearly understood at this time. I understand that in individuals with a history of seizures, antidepressant medications in general can increase the risk of having a seizure. Cocaine also can cause seizures. Therefore taking cocaine while being treated with desipramine may increase the risk of a seizure. If I have ever had a seizure I will inform my psychiatrist. I am aware that cocaine may cause heart attacks and other serious heart problems, and it is possible that desipramine might increase the risk of these. There may also be a danger if I use other illicit drugs, such as sedatives and/or alcohol. For example the desipramine might result in my becoming more sleepy or intoxicated than usual.

If for any reason I am unable to tolerate desipramine, it will be discontinued and other treatment may be instituted.

The only risk to the blood drawing procedures used in this study is the possibility that a small bruise, or rarely, a local infection may develop at the site of the needle puncture. This
seldom occurs.

TREATMENT ALTERNATIVES

I understand that there are a number of different treatment approaches for cocaine abuse which I may consider as alternatives to participating in this program. These include various inpatient or residential treatment programs as well as outpatient programs. However, it is still not clear what the best treatment is for cocaine abuse.

CONFIDENTIALITY

I understand that the records of my participation, including research forms, will be kept in locked cabinets at the clinic and be available only to DES staff. A Certificate of Confidentiality has been received from the Department of Health and Human Services (DHHS).This certificate will protect the investigators from being forced to release any research data in which you are identified, even under a court order or subpoena. This protection, however, is not absolute. It does not, for instance, apply to any state requirement to report certain communicable diseases. This

will not affect this study because we don't test for communicable diseases. However we are required by New York State law to report any instances of child abuse to the appropriate authorities. Also, because this research is regulated by the Food and Drug Administration (FDA) and sponsored by the National Institute on Drug Abuse (NIDA), staff from these and other DHHS agencies may review records that identify you. However, it is the policy of these agencies and this investigator(s) that every attempt will be made to resist demands to release information that identifies you. When the results of this study are published, your name will not be used.

RESEARCH STANDARDS AND RIGHTS OF PARTICIPANTS

I understand that I may refuse to participate or discontinue my treatment in this study at any time without loss of benefits to which I might otherwise be entitled. I understand that these benefits include 6 months of free antidepressant medication monitoring with a DES psychiatrist. I understand that the doctors conducting this research study are also responsible for my clinical care.

MEDICAL COMPENSATION FOR RESEARCH RELATED ACTIVITIES

Federal regulations require that I be informed about the institution's policy with regard to compensation and payment for treatment of research related injuries. Short-term emergency medical treatment, which has been determined to be necessary by New York State Psychiatric Institute's doctors, and which is within the capability of New York State Psychiatric Institute will be provided. In addition, we will provide assistance in arranging follow up care in such instances.

The New York State Psychiatric Institute cannot provide compensation or payment for treatment of research related injuries. However, I am aware that participation in this research does not waive any of my legal rights to seek such compensation through the courts.

If a medical emergency occurs on nights or weekends, I should go to the nearest hospital emergency room and have them call (212) 737-4114 and ask for the doctor on call.

I have discussed this research study and consent form with my DES psychiatrist, and he/she has answered all of my questions about the study to the best of his/her ability. I also understand that if I have any questions in the future, I

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may ask my DES psychiatrist or the principal investigator of this study, Dr. Edward Nunes, who may be reached at (212) 960-5581.

I understand that the New York State Psychiatric Institute/
Columbia University Department of Psychiatry Institutional Review Board has approved the recruitment of subjects for this study and
that, if I have any questions about my rights as a research subject or any complaints, I may call the Institutional Review Board at (212) 960-5758 during office hours, Monday through Friday, 9:00 am to 5:00 pm.

I have received a copy of this consent form to keep.

SIGNED:_____

DATE:_____

I have discussed the proposed research with this patient and, in my opinion, the patient understands the benefits and risks of the study and is capable of freely consenting to participate in this research.

SIGNED:_____
DATE:_____
(study M.D.)

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CONSENT FOR SIGNIFICANT OTHER CONTACT

I understand that it may be important for the DES staff to discuss my problems with a close family member or someone who knows me well periodically to assess how I am doing, or to aid in case of emergency. I consent to allow the DES staff to contact the following person to discuss my case throughout the course of my treatment.

Name:_____

Relationship:_____

Address:_____

_____

_____

Phone: home( )_____ work( )_____

Significant other not available:_____

Contact refused:____

SIGNED:_____

DATE:_____

PHYSICIAN:_____

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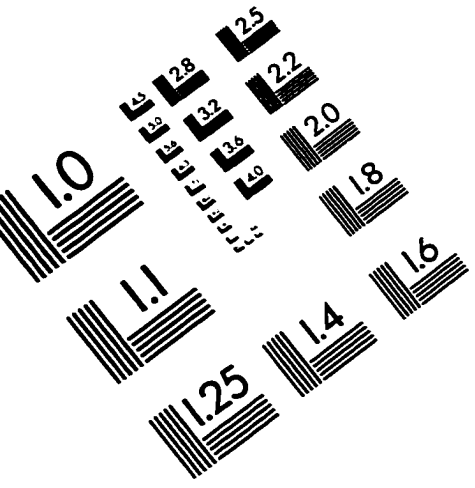
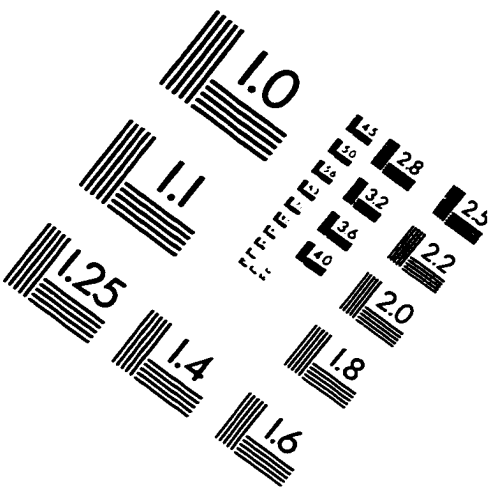
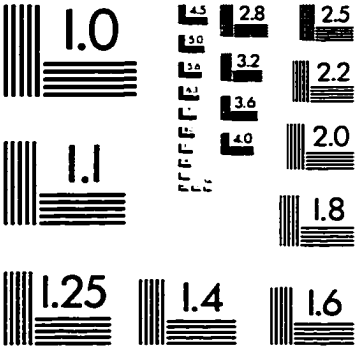
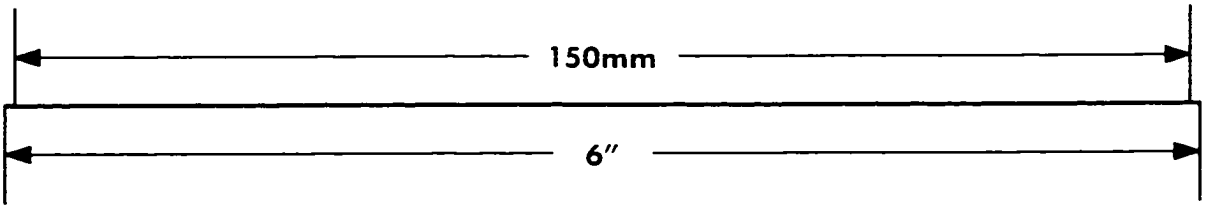
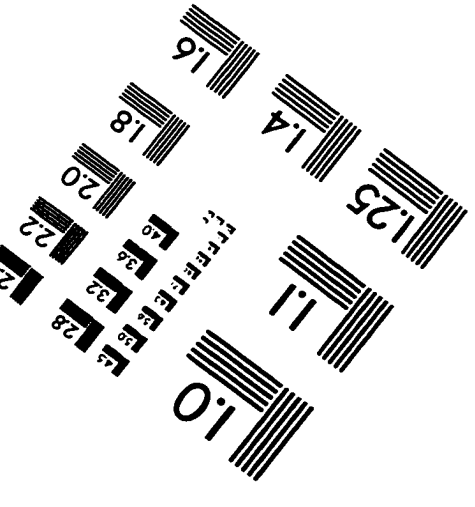
IMAGE EVALUATION TEST TARGET (QA-3)

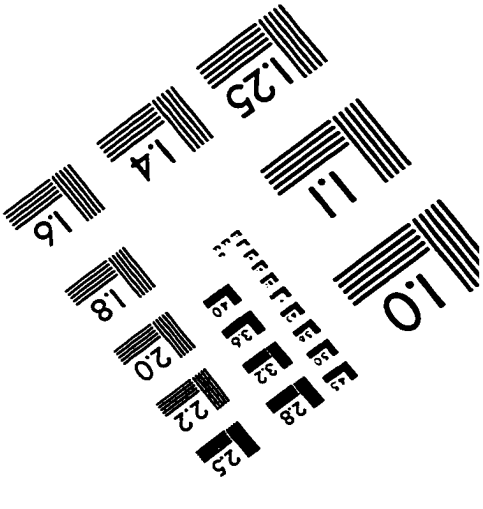












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