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Characteristics of cocaine- and marijuana-dependent subjects presenting for medication treatment trials

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Abstract

Evaluation of the characteristics of individuals presenting for substance abuse treatment can provide important information to help focus treatment services. In this study, demographic and clinical characteristics of individuals presenting for medication trials for the treatment of cocaine or marijuana dependence were compared. Marijuana-dependent subjects were generally younger than cocaine-dependent subjects, more likely to be Caucasian, and completed more years of education. Marijuana-dependent subjects also reported significantly more days using than cocaine-dependent subjects, as well as higher levels of craving. Some differences in psychiatric symptomatology were also noted, with cocaine-dependent subjects more likely to report anxiety symptoms and marijuana-dependent subjects reporting more past depressive episodes. Past and current other drug use was similar between the two groups. These results highlight the significant impairments associated with marijuana and cocaine dependence.

Keywords

marijuana; cocaine; pharmacotherapy

1. INTRODUCTION

The 2004 National Survey on Drug Use and Health indicates that more than 96.7 million (40.2%) of Americans 12 years of age or older have tried marijuana once in their lifetimes and almost 25.4 million (10.6%) have used marijuana in the past year (SAMHSA, 2004). It is estimated that approximately 10% of individuals who ever use marijuana become daily users, and lifetime prevalence rates of marijuana dependence have been approximated at 4% of the population (Johnston et al, 1995; Anthony & Helzer, 1991; Anthony et al, 1994). However, until recently relatively little research has focused on the treatment of marijuana use disorders. One factor that may contribute to the lack of research in this area may be a belief that marijuana abuse rarely occurs as a primary problem, but is instead observed only in the presence of concurrent alcohol and/or other drug abuse (Roffman & Barnhart, 1987). Also, some may believe that marijuana use does not produce a true dependence syndrome, and therefore

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treatment to assist in quitting use is not necessary. However, the limited data available does not support these beliefs. Media advertisements for an anonymous telephone survey of adults who used marijuana and were concerned about their use resulted in a substantial response, and 74% of respondents stated that the only substance they were adversely involved with was marijuana (Roffman & Barnhart, 1987). Other studies have also reported that individuals with marijuana-related problems readily respond to advertisements for treatment, that the majority of respondents do not abuse other substances, and that these respondents report significant psychosocial and psychiatric impairment and multiple signs of marijuana dependence (Stephens et al, 1993; Budney et al, 1998; Copeland et al, 2001). Furthermore, a valid and reliable marijuana withdrawal syndrome has recently been documented in several controlled laboratory and clinical studies (Budney et al., 1999; Budney et al., 2001; Kouri & Pope, 2000; Budney et al., 2004; Haney et al., 2005; Copersino et al., 2006).

Evaluation of the characteristics of individuals presenting for substance abuse treatment can provide important information to help focus treatment services. A previous comparison of marijuana- and cocaine-dependent treatment seekers found that marijuana-dependent subjects reported similar substance use histories and comparable impairments as cocaine-dependent subjects (Budney et al, 1998). However, a limitation of this previous report was differing inclusion criteria for the comparison groups. For example, individuals in the cocaine-dependent group could have concomitant alcohol or marijuana dependence. As a result, 57% of individuals with cocaine dependence also met criteria for alcohol dependence, and 23% of individuals had concurrent marijuana dependence.

In the present study, demographic and clinical characteristics of individuals presenting for medication trials for the treatment of cocaine dependence (CD) or marijuana dependence (MD) were compared. Similar inclusion criteria were employed for both trials, such that other dependencies (with the exception of nicotine or caffeine) were not permitted. As a result, we have the opportunity to compare individuals with only one primary dependency, and may be able to delineate characteristics or problems associated with specific drugs of abuse.

2. METHODS

Participants in both groups were seeking inclusion in outpatient treatment studies for substance dependence at an academic medical center, and were primarily recruited via media advertisements and clinical referrals. Major exclusion criteria for both studies included the presence of other major substance use disorders; past or present significant psychotic, affective, or other Axis I disorders; current use of psychotropic medications such as antidepressants, mood stabilizers, antipsychotic, or antianxiety agents; or having an unstable medical condition. All subjects signed a written informed consent, approved by the University Institutional Review Board, prior to completion of any study-related procedures. Results from the cocaine treatment study have been recently published (Malcolm et al, 2005).

Psychiatric and substance use inclusion criteria were determined by the Structured Clinical Interview (SCID-IV; First et al, 1994). Depression and anxiety was assessed in cocaine-dependent subjects using the Addiction Severity Index (ASI; McLellan et al, 1992) and Zung Anxiety Scale (ZAS; Zung, 1971), respectively, and in marijuana-dependent subjects using the SCID and Beck Anxiety Inventory (BAI; Beck et al, 1988). Both the ASI and SCID collect presence or absence of lifetime and current depression. Classification of low, moderate, and extreme anxiety were based on previously suggested cut-points (Zung, 1971; Beck et al, 1988). The BAI has three cut-points (low, moderate, and extreme). The ZAS has four cut-points; therefore, the two ZAS cut-points of “marked to severe” and “extreme” were combined into one cut-point of extreme anxiety. CD subjects were considered to have low levels of anxiety if the ZAS score was below 45; moderate anxiety if the score was 45–59; and extreme

anxiety if the score was greater than 75. MD subjects were considered to have low anxiety levels if the BAI score was 21 or less; moderate anxiety if the score was 22–35; and extreme anxiety if the score was greater than 36.

Substance use in the thirty days prior to study entry was assessed in both groups using the Time-Line Follow Back (Sobell & Sobell, 1978) and ASI. Craving was assessed in cocaine-dependent subjects using a visual analog scale and in marijuana-dependent subjects using the 12-item Marijuana Craving Questionnaire (Heishman et al, 2001). To allow for comparisons of craving across studies, two methods were implemented. The first method divided each scale range by three to produce three levels of craving that could be compared across studies. The second method standardized the raw values for each study dividing the location and scale of the observed values for both the cocaine (mean(sd)=24.84(28.85)) and marijuana (mean(sd) =45.55(15.09)) study.

Standard parametric and non-parametric methods were used to test the overarching null hypothesis that treatment seeking CD and MD patients present with similar baseline characteristics. Data on 170 participants with cocaine dependence were combined with data from an ongoing medication trial for marijuana dependence. A power calculation was performed to estimate the number of MD participants that needed to be enrolled to conduct this analysis with acceptable power. To allow for missing baseline values in the CD study, a range of sample sizes from 140 to 170 was considered during power estimation. An effect size of 0.5 (e.g., Cohen's d) was established, and the statistical error rates were set at 0.05 and 0.20 for the type 1 and 2 errors (alpha=.05, beta=.2), respectively. Using the power limit of n=140 for CD subjects, 80% power to detect an effect size of 0.5 would be obtained using 42 MD subjects. The power was estimated at 85% if the analysis was conducted when the marijuana treatment study enrolled 50 participants. Thus, a sample size of 50 was selected for the marijuana treatment study to allow for the potential for missing data.

Baseline characteristics including demographic information of all subjects were summarized using descriptive statistics. Specifically, proportions and percentages were reported for categorical data. The mean, median, standard deviation and interquartile range were reported for continuous data. To compare these characteristics across studies, analyses were conducted using Pearson's chi-square for categorical outcomes (e.g., presence of clinically significant anxiety) or the Wilcoxon rank sum tests for interval-scaled data (e.g., amount of alcohol units consumed in the past 30 days). A Bonferroni correction has not been applied to p-values. A total of 15 statistical tests were performed. Therefore, if the reported p-value is multiplied by 15, one obtains a Bonferroni adjusted p-value. Using a traditional α=0.05, and a Bonferroni correction, unadjusted p-values less than 0.003 would still be statistically significant; however, given that many of the comparisons would not be considered statistically independent, the Bonferroni correction may be overly conservative for these analyses (van Belle et al, 2004). As such, unadjusted p-values ranging from 0.05 to 0.01 are interpreted as a strong trend; p-values less than 0.01 are regarded as statistically significant.

3. RESULTS

3.1 Demographic characteristics

Demographic characteristics of the study groups are summarized in Table 1. Marijuana-dependent (MD) subjects were more likely to be Caucasian (86%) than cocaine-dependent (CD) subjects (43%) ($p<.01$). MD subjects presenting for treatment were younger than CD subjects (mean ± sd = 31.9 ± 9.6 years vs. mean ± sd = 35.4 ± 7.2 years, $p<.005$). MD subjects were also more likely to have completed more than 12 years of education than CD subjects (70% vs. 25%, $p<.01$). No differences in marital status were seen between the two groups.

3.2 Substance use

Time-Line Follow Back data from the 30 days prior to study entry found that CD subjects were abstinent from use approximately mean(sd)=18.5(8.3) days while MD subjects were abstinent approximately mean(sd)=4.3(5.0) days ($p<.01$). No difference in number of cigarettes smoked in the previous 30 days between MD and CD subjects was found, as well as no difference in the number of subjects who were smokers in each group (CD, 65%; MD, 54%). There were also no group differences in the number of days within the past 30 days on which alcohol was used or in the number of years alcohol was used when the analysis was controlled for age (see Table 2).

A comparison of past 30 day use of opioids, barbiturates, sedatives/anxiolytics, amphetamines, and hallucinogens was conducted. MD subjects were more likely to have used hallucinogens in the past 30 days than CD subjects (4% vs. 0%; $p=0.01$). No other significant differences were found. Percentages of subjects reporting at least one year of regular use of a substance are presented in Table 3. Statistical comparisons were not conducted on this data, as a standard definition of regular use could not be applied to both studies.

The mean(sd) craving using the visual analog scale in CD subjects was 24.84(28.85). Similarly, the mean(sd) craving using the MCQ in MD subjects was 45.55(15.09). A comparison of tertiles of low, moderate, or severe craving ratings yielded differences. CD subjects were more likely to report low craving (67% vs. 14%; $p<.01$), while MD subjects were more likely to report moderate or high levels of craving (moderate: 64% vs. 21%; high: 22% vs. 12%; $p<.01$). A craving comparison using the standardization method yielded differences that were less profound ($\chi^2(2)=8.18$, $p=.02$). CD subjects were more likely to report low craving (54% vs. 38%). MD subjects were more likely to report moderate levels of craving (30% vs. 14%). Finally, across both studies, the number of subjects who reported extreme high levels of craving was similar (33% vs. 32%).

3.3 Anxiety and Depression

CD subjects had higher levels of anxiety than MD subjects, with 38% of CD subjects having moderate to extreme anxiety compared to 12% of MD dependent subjects ($p<.005$). MD subjects were more likely to report a history of depression (42%) compared to CD subjects (17%, $p<.0005$). Table 4 summarizes the anxiety, depression, and craving comparisons.

3.4 Study retention

Both studies had high drop-out rates, with approximately 40% of subjects in the CD and MD groups discontinuing prior to randomization or not returning for at least one visit after receiving medication.

4. DISCUSSION

In this preliminary analysis, there were no between group differences on gender, marital status, and recent alcohol and most other drug use. However, there were differences in binge (cocaine) and daily (marijuana) use patterns as well as some demographic characteristics and psychiatric symptomatology. MD subjects were generally younger than CD subjects, more likely to be Caucasian, and completed more years of education. These results differ somewhat from those reported by Budney and colleagues (Budney et al, 1998), in which no differences were reported in age or ethnicity. These differences may in part be due to greater diversity in the geographic area in which this study was conducted as compared to the Budney study.

As previously reported, MD subjects reported significantly more days using than CD subjects. However, our sample did differ in that there were no between group differences in amount of

alcohol or cigarettes consumed. Lower alcohol use in both groups is likely a result of excluding alcohol dependent subjects from the current sample. MD subjects were more likely to have used hallucinogens in the preceding days than CD subjects. A similar finding was reported by Budney and colleagues.

MD subjects reported higher levels of craving than CD subjects. CD subjects reported more binge use compared to more chronic use as compared to MD subjects. As such, it is possible that MD subjects were experiencing some withdrawal symptoms during assessment, including craving. A previous report found that 93% of treatment-seeking MD individuals had mild cravings, and 44% had rated past cravings as severe (Budney et al, 1999).

Of interest, differing rates of psychiatric symptomatology were found between MD and CD subjects. CD subjects were more likely to report moderate to high levels of anxiety than MD subjects. It is possible that these anxiety symptoms were induced or exacerbated by cocaine use. In contrast, MD subjects were significantly more likely to report lifetime depression than CD subjects. A increased risk of depression in marijuana users has been previously reported (Bovasso, 2001; Troisi et al, 1998). However, it should be noted that depression was assessed using different assessments (ASI and SCID). As the SCID is a more in depth psychiatric interview, lifetime depression may have been more thoroughly assessed in MD subjects.

The MD subjects in the current analysis appear to be similar in demographic and substance use characteristics to participants in the one published pharmacotherapy trial for marijuana dependence (Levin et al, 2004). Although data is not provided on retention from initial screening to randomization by Levin and colleagues, a significant percentage of subjects did not complete the trial. Retention in treatment appears to be a significant challenge with MD as well as CD individuals.

This comparison has several limitations. The analysis was conducted when approximately 70% of the total planned sample size for the marijuana treatment trial had been enrolled. However, assuming the subjects subsequently enrolled into the marijuana treatment study would have been comparable to the first 50 subjects, the potential for selection bias should be minimal. Related to this consideration is limited power due to unequal sample sizes; however, the power analysis indicated that given an effect size of .5 and an alpha of .05, 50 subjects for the MD group provided adequate power. While these studies were conducted at the same university, some measures (e.g., anxiety scales) differed between the two studies as they were conducted as separate protocols at different times. Therefore comparisons had to be made based on categorizations of the data. Furthermore, the studies were not controlled for time, and some changes in population use patterns may have occurred during the time the cocaine treatment study ended and when the marijuana treatment study began.

However, to our knowledge, this comparison is the first to utilize data from individuals dependent on only cocaine or marijuana, and not other substances. Also, this is the first comparison of MD individuals presenting for treatment in a medication treatment trial with another substance using population. These results highlight the significant impairments associated with marijuana and cocaine dependence, as well as the difficulty in retaining substance using individuals in clinical trials.

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Table 1

Sociodemographics of Participants

Sociodemographic Characteristic	Statistic	Marijuana Group	Cocaine Group	Test Statistic, p-value
Age	N	50	158	
	Mean (SD)	31.86 (9.63)	35.42 (7.17)	WRS=4030, p=.001
	Median (IR)	28.5 (11)	35.74 (11.03)	
Gender (male)	N	50	167	
	Frequency (%)	42 (84)	134 (80.24)	$X^2(1)=.4$, p=.55
Marital Status (married)	N	50	151	
	Frequency (%)	15 (30)	46 (30.46)	$X^2(1)=.0$, p=.95
Ethnicity (caucasian)	N	49	167	
	Frequency (%)	42 (85.71)	72 (43.11)	$X^2(1)=27.6$, p<.001
Education Status	N	50	154	
7th-12th Grade	Frequency (%)	6 (12)	39 (25.32)	
High School Graduate	Frequency (%)	9 (18)	76 (49.35)	$X^2(2)=32.7$, p<.001
Higher Education	Frequency (%)	35 (70)	39 (25.32)	

WRS=Wilcoxon Rank Sum

Table 2

Primary Substance Use Between Groups

Substance	Statistic	Marijuana Group	Cocaine Group	Test Statistic, p-value
Marijuana Use in Past 30 Days	N	50	153	
	Mean (SD)	27.26 (6.5)	3.51 (7.57)	WRS=8657, p<.001
	Median (IR)	30 (0)	0 (2)	
Marijuana Years	N	50	153	
	Mean (SD)	16.78 (9.4)	11.13 (9.07)	WRS=6297, p=.001
	Median (IR)	13 (12)	10 (17)	
Cocaine Use in Past 30 Days	N	50	153	
	Mean (SD)	.28 (1.16)	9.48 (7.7)	WRS=1714, p<.001
	Median (IR)	0 (0)	8 (8)	
Cocaine Years	N	50	153	
	Mean (SD)	1.12 (1.9)	10.8 (6.8)	WRS=1666, p<.001
	Median (IR)	0 (2)	10 (10)	
Alcohol Use in Past 30 Days	N	50	154	
	Mean (SD)	5.9 (6.94)	7.14 (8.12)	WRS=4893.5, p=.52
	Median (IR)	4 (8)	4 (11)	
Alcohol Years: Controlling for Age	N	50	154	
	LSMeans (SE)	14.26 (1.08)	15.64 (.52)	ANCOVA, Z=1.15, p=.25[1]

WRS=Wilcoxon Rank Sum

[1] Z-value for the Wald test using generalized estimating equations to correct the standard error for heteroscedasticity in the residuals

Table 3

Percentage of Subjects Who Reported Lifetime Years of Substance Use

Substance	Statistic	Marijuana Group	Cocaine Group
	N	50	153
Marijuana	% (n)	100 (50)	83.01 (127)
Cocaine	% (n)	40 (20)	100 (153)
Alcohol	% (n)	88 (44)	94.16 (145)
Heroin	% (n)	0 (0)	8.5 (13)
Methamphetamine	% (n)	0 (0)	.65 (1)
Opiates	% (n)	10 (5)	8.5 (13)
Barbituates	% (n)	2 (1)	9.15 (14)
Sedatives/Anxiolytics	% (n)	14 (7)	12.42 (19)
Amphetamines	% (n)	14 (7)	16.34 (25)
Halucinogens	% (n)	30 (15)	21.57 (33)
Inhalants	% (n)	2 (1)	4.58 (7)

Table 4

Psychiatric Symptoms

Symptom	Statistic	Marijuana Group	Cocaine Group	Test Statistic, p-value
Current Depression	N	50	151	
	Frequency (%)	1 (2)	6 (3.97)	Fisher's Exact Test, p=.64
Lifetime Depression	N	50	151	
	Frequency (%)	21 (42)	25 (16.56)	$X^2(1)=13.8$, p<.001
Anxiety	N	50	184	
No Symptoms	Frequency (%)	44 (88)	115 (62.5)	
Moderate Symptoms	Frequency (%)	4 (8)	61 (33.15)	$X^2(2)=12.7$, p=.002
Severe Symptoms	Frequency (%)	2 (4)	8 (4.35)	
Craving: MCQ Total vs.Cocaine VAS	N	50	185	
No Symptoms	Frequency (%)	7 (14)	124 (67.03)	
Moderate Symptoms	Frequency (%)	32 (64)	39 (21.08)	$X^2(2)=46.7$, p<.001
Severe Symptoms	Frequency (%)	11 (22)	22 (11.89)	