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COMPARISON OF SUBSTANCE USE MILESTONES IN CANNABIS- AND COCAINE-DEPENDENT PATIENTS

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Abstract

Objectives—To compare the progression of substance use milestones between cocaine- and cannabis-dependent patients.

Methods—Using data gathered from two separate clinical studies for treatment of cocaine dependence and cannabis dependence, 130 cannabis-dependent and 112 cocaine-dependent individuals were compared on milestones related to their substance use.

Results—In cannabis- vs. cocaine-dependent patients, the mean age of first use, regular use and first treatment contact differed significantly. No statistically significant differences were found between the two groups for other measured milestones.

Conclusions—These results differ from most epidemiologic studies that suggest cocaine users progress more rapidly to regular use and treatment contact.

Keywords

Cocaine dependence; marijuana dependence; substance abuse milestones

INTRODUCTION

Substance use disorders continue to represent a significant public health problem in the United States. The 2008 National Survey on Drug Use¹ reports that 20.1 million Americans aged 12 years and older were current (past month) users of illicit drugs, which represents 8.0% of the population aged 12 years and older. Of these illicit drugs, marijuana was the most commonly used substance, with 15.2 million past-month users, compared with cocaine, with 1.9 million past-month users. Various epidemiologic studies have found lifetime prevalence for substance dependence (excluding alcohol) to be between 3% and 7.5%,^{2–5} with 1.3%–1.4% and 1.0% lifetime prevalence for marijuana⁶ and cocaine⁷ dependence, respectively. A significant amount of research has identified various risk factors associated with the development of substance use disorders, including early onset of substance use,⁸ male sex,^{9–11} the use of gateway drug as suggested by the “gateway theory,”¹² and other risk factors specific to particular substances.¹³ However, been limited research has been done on the progression of substance use disorders from initial use to regular use or dependence. Greater understanding of the underlying biologic and psychosocial factors that

contribute to the progression of substance use disorders could lead to more effective primary and secondary preventive strategies.

It is generally held in both the scientific and lay community that cocaine is a more dangerous drug than marijuana in terms of both morbidity and mortality. Epidemiologic studies are consistent in showing that cocaine abusers follow a more aggressive course to regular, problematic use and treatment than marijuana users.^{12,14–16} However, clinical studies are significantly fewer in number and inconsistent in their results with respect to the progression of cocaine versus marijuana substance use disorders.^{9,17–19} If the course of marijuana use disorders is more aggressive than commonly believed, it would be of public health interest because cannabis use and the treatment of cannabis use is often de-emphasized in clinical settings.

In the current study, we evaluated the progression of cocaine and marijuana use disorders from initial use to regular use to first treatment contact in two separate groups of outpatient clinical trial participants. Our hypothesis was that cocaine use disorders would display a “telescoping” phenomenon, where the time course from first use to regular use to treatment contact would be accelerated compared with cannabis use disorders.

METHODS

Participants

All participants enrolling from 2000 to 2007 in a university-based research clinic offering two separate pharmacotherapy clinical trials for cannabis dependence and cocaine dependence were included in the analysis. Research protocols were approved by the New York State Psychiatric Institute Institutional Review Board and all patients gave written informed consent. Recruitment methods for both trials were similar and consisted primarily of paid advertising and clinical referrals. Patients with criminal justice system involvement (e.g., probation or parole status) were not excluded. Potential participants for both trials were screened during the same general time period by the same clinical staff. Both trials were similar in design because they were conducted exclusively in the outpatient setting for similar duration of time with similar financial compensation (e.g., small reimbursements for time and travel). There were also similar in methodology; all patients received manual-guided cognitive behavioral therapy and were randomly assigned to either study medication (nefazodone or bupropion for the cannabis trial and gabapentin for the cocaine trial) or placebo under double-blind conditions.

Data Collection

A total of 242 outpatients (cocaine, $n = 112$; cannabis, $n = 130$) enrolled in 2 clinical trials underwent standardized assessments, including the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) and structured histories of their substance use milestones. Together, these instruments inquired about age at first use of alcohol and illicit drug use, age at regular use of these substances (defined as 3 or more times per week), and age at first treatment contact regarding each substance. These data were then used to compare patients with regard to time from first use to regular use, first use to first treatment, and regular use to first treatment.

Data Analysis

Patient demographics and clinical characteristics between marijuana users and cocaine users were compared using t tests for continuous variables and chi-square tests for categorical variables. Substance use milestones (time from first use to regular use, time from first use to first treatment contact, and time from regular use to first treatment contact) between

marijuana and cocaine users were compared using Cox-proportional hazard models. Age at first use, chronological age, and addiction rate (defined as time from first use to regular use) were set a priori as potential predictors of outcomes and included as covariates in the models. All analyses were two-sided, with a significance level set at 0.05, and conducted using SAS version 9.1 software (SAS Institute, Inc., Cary, NC).

RESULTS

Sample demographic and clinical characteristics are presented in Table 1. Cocaine patients were older ($P < .001$) and composed of more African Americans than marijuana patients ($P = .04$). Age at first use, age at regular use, and age at first treatment were statistically later for cocaine patients than marijuana patients ($P < .001$).

Results from Cox-proportional hazard models showed that there statistically significant differences existed in the time from first use to regular use, from first use to treatment, and from regular use to treatment between cocaine and marijuana users ($P > .05$). Results remained non-significant even after controlling for covariates that were set a priori: first use age, chronological age, and addiction rate (i.e., time from first use to regular use) (Table 2) ($P > .05$). Nonetheless, all three covariates were found to be predictive of the outcomes. Patients who started substance use at an older age were more likely to transition from first use to regular use ($P = 0.05$) and treatment ($P < .001$). Patients who were older were less likely to transition from first use to regular use ($P = .01$) and from first and regular use to treatment ($P < .001$). Furthermore, patients who had a more delayed progression to regular use were less likely to transition from first use to treatment ($P = 0.04$) but were more likely to transition from regular use to treatment ($P < .001$). Two-way interactions between covariates and treatment were explored and found to be not significant. Final models did not include interaction terms.

DISCUSSION

The purpose of this study was to compare the substance abuse milestones of first use, regular use, and first treatment contact for patients seeking treatment for cocaine and marijuana substance use disorders. Our results did not support our initial hypothesis that cocaine users would progress more rapidly toward regular use and treatment for their disorder. This contrasts epidemiologic data suggesting that cocaine use disorders develop more rapidly than do marijuana disorders.

The theory that cocaine users are more likely to progress more quickly to dependence than marijuana users is largely based on animal studies that indicate that cocaine has a higher “addiction liability” than marijuana.^{13,20} This theory is also supported by various epidemiological studies, which would necessarily reflect not only the biologic contributors to a higher “addiction liability” suggested by animal studies, but also potential socioeconomic contributors. An analysis of the National Comorbidity Study data published by Anthony et al.¹⁴ found that cannabis was the most frequently used illicit drug, with 46.3% of responders indicating they had used cannabis at least once, but only 9.1% of users developing cannabis dependence. In comparison, 16.2% of the study population had tried cocaine at least once, with 16.7% of users developing cocaine dependence. A later analysis of the National Comorbidity Study data by Wagner and Anthony¹² reported that cocaine dependence among users appeared earlier and more explosively than cannabis or alcohol, with 5%–6% of cocaine users becoming cocaine dependent in the first year of use compared with 1.5% of cannabis users. In addition, 15%–16% of cocaine users had developed cocaine dependence within 10 years of first cocaine use, whereas approximately 8% of cannabis users developed cannabis dependence during the 10 years after their first use. O'Brien and Anthony¹⁵ have

also used National Household Survey on Drug Abuse (NHSDA) data to show that between 5% and 6% of cocaine users develop dependence over the first 24 months after first use. Kessler et al.¹⁶ reported pooled data indicating that cocaine and heroin users were more likely to seek treatment than other substance users (odds ratio, 2.1), including marijuana. These community-based epidemiologic data suggest that cocaine use disorders follow a more rapid and aggressive course than cannabis use disorders.

Clinical studies determining the timeline of substance use disorder development show mixed results. Haas and Peters¹⁷ retrospectively examined court-mandated substance abuse program participants with respect to age at substance initiation of alcohol or marijuana versus cocaine and progression to “problematic use.” They found a significant difference in latency from first use to problematic use among male and female cocaine users. However, their data also suggest that for both men and women the latency from first use of alcohol or marijuana to problematic use was shorter than for cocaine users (1.89 and 2.19 years for male and female alcohol or marijuana users, respectively, and 4.31 and 9.83 years for male and female cocaine users, respectively). Ridenour et al.¹⁸ presented prospective, longitudinal data from adolescent substance users that suggested that the time course from first use to dependence (as defined by DSM III-R) is significantly shorter for cocaine than for marijuana. However, the time from first use to first problem with substance abuse (defined as meeting one of the DSM III-R dependence criteria) showed no significant difference nor did time from first use to regular use (defined as at least one use per month during a phase of consumption).

Few studies have examined the progression from initial substance use to dependence in substance use disorder treatment settings. A study by Zinkernagel et al.¹⁹ examined 184 patients in an opiate maintenance program and asked them about the age at which they had first started using a particular substance and when, if ever, they began using the substance regularly. In contrast to many of the aforementioned epidemiological studies, in the current study the progression from the initiation of drug use to regular drug use was shorter for marijuana (0.7 years) than it was for cocaine (3.1 years), although substance dependence as defined by the DSM IV criteria was not evaluated. Hernandez-Avila et al.⁹ retrospectively examined gender effects on progression from regular use of cocaine, opioids, cannabis, or alcohol and entry into an index substance abuse treatment program. These data suggest that cocaine users entered treatment sooner than marijuana users after the onset of regular use.

The results of this study raise the possibility that there are significant differences between epidemiologic populations of cocaine and marijuana users and treatment-seeking populations. One contributing factor may be that marijuana users in the current study were used marijuana more frequently than those in epidemiologic studies. This may put these patients at higher risk for developing symptoms of dependence (such as physical withdrawal, see Hasin et al.²¹), as well as personal and legal consequences of their disorder, causing them to seek treatment more readily. Another factor to consider is the tetrahydrocannabinol (THC) concentration in marijuana, which has increased from 2.0% in 1980 to 4.5% in 1997 and 8.5% by 2006 in the United States.^{22–24} Although some question the importance of this increase in potency as it relates to public health effects,²⁵ the increasing connection between psychosis and cannabis raises the possibility that increased potency may influence the psychogenic effects of cannabis. Some also suggest that although THC concentrations are increasing, cannabidiol concentrations (which offsets many of the anxiogenic effects of THC) has remained unchanged, which may result in an increase in morbidity due to cannabis intoxication²⁶.

Even with these different contributing factors, the question of why the marijuana users seeking treatment in our study progressed as rapidly as cocaine users requires further study.

Perhaps treatment-seeking populations represent a subgroup of substance users at higher risk of developing dependence on any substance of abuse. Alternatively, those cannabis users who sought pharmacologic treatment represent a population of users in whom addiction developed more rapidly than among the general population of cannabis users.

Future studies comparing clinical and non-clinical populations could examine biological, psychological, and socioeconomic differences between these two populations to help determine what variables influence the time course of their substance abuse disorders. For example, the earlier age of onset or presence of additional substance use and psychiatric comorbidities may identify subpopulations at risk for rapid disease progression. Identifying these variables may have important public health implications because identifying those at risk for developing cannabis dependence may allow for targeted preventative strategies for this population. The marijuana-dependent patients in this study began using marijuana at an earlier age than cocaine-dependent patients began using cocaine, which is consistent with community-based epidemiological studies.^{12,18,27}

One important limitation of this study is its retrospective nature, which relies on patient recall for events that, often, happened many years ago. We may also be missing important variables that could be included in a prospective study, including measuring the time at which patients met criteria for dependence by DSM-IV criteria. Another major limitation of this study is combining two different clinical trial populations that could introduce differential selection bias because each clinical trial had unique eligibility criteria. These clinical trial patients may not be representative of patients seeking substance use disorder treatment in the community. Another limitation of this study is that the time at which patients met full DSM-IV criteria for marijuana or cocaine dependence was not evaluated. Instead, we relied on regular use and treatment contact as indicators of a substance use disorder. Our population was also largely male, which limits the generalizability of these findings to women.

Further research would ideally involve prospective studies that would record these milestones as they occur rather than relying on patients' recollection. This would allow for a more accurate understanding of the progression of these disorders and presumably more valid conclusions about the factors that contribute to this progression. These studies should also involve a wider range of clinical treatment settings and focus on identifying variables that differentiate treatment-seeking populations from substance users in the general population.

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TABLE 1

Distribution of Demographic and Clinical Characteristics by Substance of Use (N=202)

	Marijuana (n=122)	Cocaine (n=80)	P Value
<i>Demographic</i>			
<i>characteristics</i>			
Age, mean (SD)	32.1 (9.2)	38.3 (6.9)	<.001
Male, no. (%)	96 (78.7)	71 (88.8)	.06
Race, no. (%)			
Caucasian	41 (33.6)	18 (22.5)	.04
Hispanic	36 (29.5)	24 (30.0)	
African American	33 (27.1)	35 (43.8)	
Other	12 (9.8)	3 (3.8)	
<i>Clinical characteristics, mean (SD)</i>			
Age at first use	15.1 (3.8)	20.9 (5.7)	<.001
Age at regular use	18.2 (4.4)	23.8 (7.0)	<.001
Age at first treatment	29.0 (8.3)	34.3 (7.4)	<.001

TABLE 2

Observed and Modeled Effect of Substance on Substance Use Milestones

Observed	Time From First Use to Regular Use		Time From First Use to Treatment		Time From Regular Use To Treatment	
	Marijuana	Cocaine	Marijuana	Cocaine	Marijuana	Cocaine
Mean (SD)	3.0 (3.4)	2.9 (3.7)	13.8 (8.4)	13.4 (6.6)	10.8 (8.1)	10.5 (6.1)
Modeled	HR (95% CI)	P Value	HR (95% CI)	P Value	HR (95% CI)	P Value
Unadjusted						
Cocaine *	1.02 (0.77, 1.36)	0.87	1.12 (0.84, 1.50)	0.44	1.12 (0.83, 1.49)	.46
Adjusted **						
Cocaine *	1.00 (0.70, 1.44)	0.99	1.07 (0.74, 1.56)	0.71	1.06 (0.74, 1.52)	.76
Age at first use	1.03 (1.00, 1.07)	0.05	1.22 (1.17, 1.27)	<.001	1.21 (1.17, 1.27)	<.001
Chronological age	0.97 (0.95, 0.99)	0.01	0.84 (0.81, 0.86)	<.001	0.84 (0.82, 0.87)	<.001
Time from first use to regular use	NA	NA	0.96 (0.92, 1.00)	0.04	1.19 (1.14, 1.25)	<.001

Abbreviations: HR, hazard ratio; CI, confidence interval; NA, not applicable

* Marijuana was selected as the reference group.

** Models are adjusted for cocaine, age at first use, chronological age, and time from first use to regular use (i.e., addiction rate).