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Prior use of alcohol, cigarettes, and marijuana and subsequent abuse of prescription opioids in young adults

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Abstract

Purpose—There has been an increase in the abuse of prescription opioids, especially in younger individuals. The current study explores the association between alcohol, cigarette, and/or marijuana use during adolescence and subsequent abuse of prescription opioids during young adulthood.

Methods—We used demographic/clinical data from community-dwelling individuals in the 2006–2008 National Survey on Drug Use and Health. We used logistic regression analyses, adjusted for these characteristics, to test whether having antecedent alcohol, cigarette, or marijuana use was associated with an increased likelihood of subsequently abusing prescription opioids.

Results—12% of the survey population of 18–25 year olds (n=6496) reported current abuse of prescription opioids. For this population, prevalence of prior substance use was 57% for alcohol, 56% for cigarettes, and 34% for marijuana. We found prior alcohol use was associated with the subsequent abuse of prescription opioids in young men but not young women. Among both men and women, prior marijuana use was 2.5 times more likely than no prior marijuana to be associated with subsequent abuse of prescription opioids. We found that among young boys, all prior substance use (alcohol, cigarettes, and marijuana) but only prior marijuana use in young girls was associated with an increased likelihood of subsequent abuse of prescription opioids during young adulthood.

Conclusions—Prior alcohol, cigarette and marijuana use were each associated with current abuse of prescription opioids in 18–25 year old men but only marijuana use was associated with subsequent prescription opioids in young women. Prevention efforts targeting early substance abuse may help to curb the abuse of prescription opioids.

The authors have no potential conflicts of interest.

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Keywords

Substance-related disorders; adolescent; alcohol drinking; cigarettes; marijuana; opioid-related disorders; narcotics; prescription drugs

Introduction

The "gateway" hypothesis describes the progression of substance abuse during adolescence from licit drugs (alcohol and/or cigarettes) and illicit drugs (marijuana) to "harder" drugs (heroin and cocaine) in young adulthood [1–5]. This hypothesis contains three interrelated conditions: *sequencing* which implies that there is a static relationship between the two substances and that one is initiated before the other; *association* which implies that there is a relationship between starting to use one substance and starting to use the second; and *causation* which implies that use of one substance actually causes the use of the second. While the final condition of causation is controversial, evidence of the sequencing and association aspects of this hypothesis are borne out by a number of studies, including one twin study demonstrating that individuals who used marijuana before age 17 were two to five times more likely than their co-twin to engage in subsequent other drug use, abuse or dependence [6]. However, a second study found that of the 50% of high school students who initiated licit drug use, only 15% progressed to marijuana and only three percent progressed to harder drugs [7].

These patterns of behavior are variable [8] and alternative hypotheses exist. For example, the "common-factor model" supports the concept that if an individual has a propensity to use one drug, he/she has an increased propensity to use another drug [9]. In addition, there is evidence supporting a longitudinal pattern of drug use that is part of a genetically influenced developmental trajectory [10]. Despite ongoing debate between the gateway hypothesis and other theories such as the common-factor model [9, 11], there is growing evidence supporting the existence of the gateway hypothesis [8, 12, 13] and that it is present in both genders [14, 15]. However, studies examining the issue of gender have found conflicting results. One demonstrated that early use of alcohol or cigarettes was associated with higher risk of drug use among males but not females [15]. In turn, another study found that neither gender nor race was associated with subsequent illicit drug use in those with prior licit drug use [7].

Another important issue is the availability of and access to specific drugs as this may also have an impact on which earlier drugs used may be associated with subsequent drug use. The Monitoring the Future study reported in 2011 that between 38% and 59% of 8th graders, 68% and 78% of 10th graders, and 82% and 89% of 12th graders perceived marijuana, cigarettes and alcohol as being fairly or very easy to get (perceived availability of cigarettes by 12th graders) [16]. A second survey revealed that teens described prescription medicine as being generally available with an estimated 65% coming from their friends, family, or home [17]. Similarly a recent study demonstrated that 77% percent of survey participants ages 18 to 25 years who reported abusing prescription opioids had received them only from nonmedical sources [18]. While the gateway hypothesis has been explored for the relationship between marijuana and heroin or cocaine use, it has not been investigated for the subsequent abuse of prescription opioids or for potential differences based on gender with respect to prescription opioids.

While overall adolescent drug use has been decreasing significantly in the U.S. in recent years, there has been an increase in prescription drug abuse in adolescents and young adults

[16]. Strikingly, abuse of prescription opioids among teens is only exceeded by marijuana use and there are comparable numbers of initiates of prescription opioids as there are of marijuana [19]. For the purposes of this study, we define the term 'abuse' as the use of prescription opioids for the experience or feeling it causes, or use of opioids prescribed for someone else. In 2010, an estimated five million people aged 12 or older were current abusers of pain relievers. Two million were recent initiates with the average age at first use of pain relievers among recent initiates aged 12 to 49 being 21 years. In 2010, according to the National Survey on Drug Use and Health and the Monitoring the Future study, among young adults aged 18-25 years and 19-24 years, respectively, the prevalence of past year use ranged from 9–11% [16, 19]. Thirteen percent of young adult men and 10% of young adult women reported past-year abuse of prescription opioids [20]. An astounding increase in prevalence the abuse of prescription opioids has been seen in both adolescents and young adults. The prevalence of past-year abuse of prescription opioids in 12 to 17 years olds increased from 3.2% in 1994 to 6.2% in 2010 and in 18 to 25 year olds from 4.7% in 1994 to 11.1% in 2010 [19]. These percentages represent an estimated 1.55 million youths and 3.4 million young adults with past-year abuse of prescription opioids in 2010. In addition, an estimated 463,000 individuals aged 18-25 years met criteria for opioid dependence [20]. Finally, the number of persons receiving specialty substance use treatment within the past year for abuse of pain relievers more than doubled from 2002 to 2010 from 199,000 to 406,000. In 2010, over 105,000 of these individuals were 18 to 25 years.

Given the increasing prevalence of abuse of prescription opioids in both young adult men and women, the purpose of the current study is to evaluate the association, not necessarily causality, between the prior use of alcohol, cigarettes, and marijuana and the subsequent abuse of prescription opioids in young adults and assess the role that gender may play in this relationship.

Methods

Data Sources and Respondents

We used data pooled from the 2006, 2007, and 2008 National Survey on Drug Use and Health (NSDUH) conducted by the Substance Abuse and Mental Health Services Administration, Office of Applied Studies. The NSDUH is an annual, self-report survey of civilian, non-institutionalized U.S. citizens, age 12 years and older, that collects information on use of alcohol, cigarettes, and illicit drugs. Data was collected using a multistage area probability sample for each of the 50 states and the District of Columbia; respondents were paid \$30 for a completed interview [21]. For the years 2006, 2007 and 2008, strategies for ensuring high participation rates resulted in weighted screening response rates ranging from 89-91% and weighted interview response rates for the computer-assisted interviewing portion in the range of 74%. Youths were oversampled in order to create equal sample sizes among the following age strata: 12–17 year olds, 18–25 year olds, and 26 and older. Data for the current analysis includes only those respondents aged 18 to 25 years. We divided the sample into four discrete age groups: 18–19 years, 20–21 years, 22–23 years, and 24–25 years. We chose to separate out near adolescents (18-19) from young adults (20-24) so as to investigate the unique characteristics associated with these ages and developmental stages. The final sample size for our analysis after combining the three surveys and restricting to 18-25 year olds was 55,215 respondents.

Survey Validation and Administration

The NSDUH used a combination of both a computer-assisted in-person interview and a computer-assisted audio self-interview, a survey administration platform that has been extensively validated for accuracy [21]. NSDUH questions are evaluated for accuracy and

reproducibility of results, with a specific focus on non-ambiguity of syntax [22]. The NSDUH has undergone multiple validations over the past 30 years, including a recent analysis of test-retest reliability of key measures [23]. Questions concerning past illicit drug use are tested for precision of answers, and non-response is studied for patterns and homogeneity of non-responders [24].

Substance Use Initiation

To examine the timing and sequence of substance use, we examined the effect of age of first use of alcohol, cigarettes, and marijuana on past year abuse of prescription opioids. As alcohol, cigarettes and marijuana are the most widely-available and abused substances by young people, we defined alcohol, cigarette or marijuana use as "prior use" if it was initiated prior to age 18 and preceded the age of first abuse of prescription opioids, if the latter was present. If abuse of prescription opioids did not occur, we still considered alcohol, cigarette or marijuana use prior to age 18 "early" use. For the purposes of our analyses, we hypothesized that antecedent use of alcohol, cigarettes, or marijuana was associated with subsequent abuse of prescription opioids and that this relationship represents a specific sequencing of drug use. In the analysis described below, we sought to test whether having antecedent use of alcohol, cigarettes, or marijuana increased the likelihood of subsequently abusing prescription opioids.

Selection of Variables for Analysis

Past year (current) use of prescription opioids among respondents age 18–25 years old was our outcome of interest. For the purposes of this study, we define "abuse" of prescription opioids (or what the survey terms "non-medical use") as a positive response to the following question asked on the survey: 'Have you ever, even once, used any type of prescription pain reliever that was not prescribed for you or that you took only for the experience or feeling that it caused?' In an effort to minimize the effect of confounding and mediation, we chose demographic and substance use variables that could not be viewed as part of the causal pathway between prior use of substances and the outcome of interest. Gender, race and age were chosen as our main demographic variables. As indicated above, respondents were defined as having prior use of a specific substance (alcohol, cigarettes or marijuana) if the age of first use of that substance was before age 18 and before age of first use of prescription opioids.

According to the survey, those substances considered prescription opioids included the following: Darvon, Darvocet, Tylenol with codeine, Percocet, Percodan, Tylox, Vicodin, Lortab, Lorcet, codeine, Demerol, Dilaudid, Fioricet, Fiorinal, hydrocodone, methadone, morphine, OxyContin, propoxyphene, SK65, Stadol, Talacen, Talwin, TalwinNX and tramadol/Ultram. In order to create homogeneity in our analyses, we excluded respondents whose only abuse of analgesic medications in the past year was Fioricet and Fiorinal (n=2) since these medications are not opioids.

Statistical Analyses

All analyses were performed using SAS version 9.1 (SAS Institute Inc, Cary, NC) and SAScallable SUDAAN version 9.0.3 (Research Triangle Institute, Research Triangle Park, NC). We utilized study calculated weights and SUDAAN software to adjust for the complex sampling design and non-response.

We performed unadjusted odds ratios between all independent variables and past-year abuse of prescription opioids. We then examined bivariate associations between all possible sequences of substances, gender, race, age and the dependent variable. We conducted a modified, backwards, stepwise logistic regression model of past-year abuse of prescription

opioids with gender, age and race. Once the most parsimonious model was obtained, interactions were tested between substance use variables and both gender and race to examine if the associations between a substance's use and the abuse of prescription opioids were similar in men and women. While there were no statistically significant interactions found, we considered gender groups to be clinically different in a meaningful way and stratified the models in order to present the associations separately in men and women.

Results

Table 1 shows the characteristics of the 55,215 individuals in the study cohort. Fifty percent were men, 62% were white, 13% were black, 18% were Hispanic and 7% were other races/ ethnicities. They were relatively evenly divided between the four different age groups (18–19, 20–21, 22–23, 24–25 years). Twelve percent (6496/55215) reported current abuse of prescription opioids. Prevalences of prior substance use were notable and associated with a two to three times increased likelihood of subsequent abuse of prescription opioids: 57% for alcohol (OR 2.29, 95% CI 2.10–2.49), 56% for cigarettes (OR 2.28, 95% CI 2.13–2.43), and 34% for marijuana (OR 3.16, 95% CI 2.91–3.43).

Table 2 shows that on logistic regression, prior alcohol use, cigarette use, and marijuana use were each independently associated with the subsequent abuse of prescription opioids (AOR 1.23, 95% CI 1.11–1.36 for alcohol; AOR 1.25, 95% CI 1.16–1.36 for cigarettes; and AOR 2.44, 95% CI 2.22–2.67 for marijuana). On the full model, female gender was inversely associated with subsequent abuse of prescription opioids (AOR 0.78, 95% CI 0.73–0.84), while white race was associated with the outcome (AOR 2.12, 95% CI 1.88–2.39) when adjusting for other variables. Additionally, ages 18-19, 20-21, and 22-23 (compared with age 24-25) were all associated with abuse of prescription opioids. When examining the findings stratified by gender, alcohol use was associated with the subsequent abuse of prescription opioids in young men but not young women (AOR 1.29, 95% CI 1.14-1.47 for men versus AOR 1.16, 95% CI 1.00-1.33 for women). Antecedent cigarettes and marijuana use were both significantly associated with the subsequent abuse of prescription opioids in both young men and young women. For both young men and young women, prior marijuana use was nearly two and half times more likely to be associated with subsequent abuse of prescription opioids compared with no marijuana use. (AOR 2.53; 95% CI 2.22-2.85 for men; AOR 2.34; 95% CI 2.07-2.66 for women). The interaction terms were tested and found to not be significant, indicating that the association between antecedent use and later abuse of prescription opiods was similar in men and women.

Table 3 further examines gender differences in the association between antecedent substance use and subsequent abuse of prescription opioids. Compared to young men without prior substance use, (for all three substances) young men with prior alcohol use, cigarette use and marijuana use were significantly more likely to have subsequent abuse of prescription opioids (OR 1.23; 95% CI1.11–1.36 for alcohol; OR 1.25; 95% CI 1.16–1.36 for cigarettes; OR 2.44; 95% CI 2.22–2.67 for marijuana). In contrast, only prior marijuana use in young women, and not prior alcohol or cigarette use was associated with an increased likelihood of subsequent abuse of prescription opioids (OR 1.92; 95% CI 1.74–2.11).

Discussion

Our findings, we believe, are the first to demonstrate that reported antecedent alcohol, cigarette, and marijuana use are all associated in bivariate analysis with a two to three times greater likelihood of subsequent abuse of prescription opioids in this sample of 18 to 25 year olds. When adjusting for other variables and stratifying by gender, this relationship persists for young men but is only found with marijuana use in young women. While prior cigarette

use does increase a woman's risk for subsequent abuse of prescription opioids, our stratified analyses suggest that the effect may be stronger in men but this finding would need to be tested for robustness in future studies. Young women, in general, were less likely to endorse abuse or prescription opioids than young men. This finding was similar to a previous study our group conducted specifically examining gender and abuse of prescription opioids in a population 12 years and older [25]. The earlier study found that in women only, later initiation of illicit drugs, serious mental illness, and cigarette smoking were associated with past-year abuse of prescription opioids. It is not clear why marijuana was the only substance associated with subsequent abuse of prescription opioids in young women in the current study but this finding may be related to the specific age group of young adults. Therefore, in the current study, marijuana appears to be the substance most closely associated with the abuse of prescription opioids for the entire group as well as for both young men and young women. Given the increase in the abuse of prescription opioids, greater insights into potential associations of antecedent behaviors in youth including the use of specific substances such as marijuana may provide areas for targeted screening and intervention.

The concept of the sequencing of drug use has been evaluated in a number of studies. One study found a two to twenty fold increased risk of subsequent drug use in individuals with early-onset drug use with the greatest association between those with early-onset cigarettes at less than 12 years of age and subsequent alcohol use (OR 19.9, 95% CI 16.2-24.5) and early onset marijuana use at less than 16 years of age and subsequent illicit drug use (OR 16.33, 95% CI 3.9–30.2) [14]. Notably, the increased level of risk in this study was seen in specifically in those with earlier onset of initiation of drug use (those 14 years or younger). The magnitude of this association was significantly reduced in later-onset individuals (maximum increased risk of one and a half fold in those ages 17-18 years), which is more in the range of our study's findings. Additional studies have demonstrated compelling evidence of the sequencing effect of the gateway model. One study revealed that while most marijuana users do not progress to cocaine or heroin use, 90% of cocaine users report prior marijuana use [26]. While the existence of this association and its temporal relationship with other substance use has been well-established, the exact nature of that mechanism is unclear. [27] The well-established theory of drug priming may as well play a role. This theory states that exposure to one drug increases the likelihood for subsequent abuse of another drug [28– 30] and therefore this priming effect may be an important component of the sequencing of drug use. Furthermore, a recent study found that 80% of high school seniors who abused prescription opioids and who reported an earlier history of legitimate medical use, had abused the prescribed opioid [31]. This finding demonstrates that earlier receipt of prescribed opioids may also be an antecedent of subsequent abuse of prescription opioids.

Our study has several limitations. Because of the cross-sectional nature of this study, we were only able to examine an association and not establish a causal relationship. In addition, we relied on subject recall rather than collecting data on substance use serially. We were limited in the confounding variables we could examine to those variables that would not be viewed as being part of the pathway between the prior substance use and subsequent prescription opioid abuse. We examined the "abuse" of prescription opioids based on their specific positive response to the aforementioned survey question and not based on formal diagnostic criteria for opioid abuse or dependence. We acknowledge that many subjects who report early use of alcohol, cigarettes or marijuana do not ultimately abuse prescription opioids. Finally we were not able to examine the degree of early use. Dependent upon whether a subject's first use was within a year of when they were first surveyed or beyond that time, quantity/frequency data was not routinely available, preventing us from addressing this question using the NSDUH.

There is ongoing debate regarding the underlying mechanism for the association between early drug use and subsequent illicit drug use. Whether it is a "gateway" phenomenon or another theoretical construct such as the common-factor model or a priming effect, our data is the first to demonstrate that the relationship that has been previously described between reported antecedent use of a substance such as marijuana and other substances such as heroin and cocaine similarly exists with prescription opioids. Whether there is a causal relationship present still requires further investigation, but an association between these two entities is clear. Given the rapidly growing epidemic of abuse of prescription opioids in the general population and particularly in adolescents and young adults, prevention and treatment efforts targeting these individuals is critical. In addition to monitoring the availability of substances of abuse as well as that of medically prescribed opioids, attention to the early use of all substances but certainly marijuana in these specific populations may have an important impact on curbing the growing number of young abusers of prescription opioids.

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Implications and Contribution

Five million people abuse prescription opioids. We found that prior alcohol, cigarette and marijuana use in boys and girls but only marijuana use in girls was associated with abuse of prescription opioids in young adults. Prevention efforts targeting early substance abuse may help to curb the abuse of prescription opioids.

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Table 1

Demographic and Substance Use Characteristics: Sample restricted to 18–25 year olds 2006–2008 (N=55,215)

	Past-year a	buse of prescrip	tion opioids		
Characteristic	Total	Yes	No	OR	95% CI
Gender					
Male % (n)	50.33 (26,381)	13.54 (3539)	86.46 (22,842)	1	
Female % (n)	49.67 (28,834)	10.49 (2957)	89.51 (25,877)	0.82	0.73-0.92
Race					
White % (n)	61.75 (33,745)	14.83 (4770)	85.17 (28,975)	2.44	2.17-2.76
Black % (n)	13.86 (7281)	7.67 (473)	93.35 (6808)	1	
Hispanic % (n)	17.67 (9400)	8.07 (758)	91.93 (8642)	1.23	1.02 - 1.4
Other % (n)	6.72 (4789)	7.75 (495)	92.25 (4294)	1.18	0.97-1.43
Age (years)					
18–19 % (n)	27.60 (15,079)	12.55 (1916)	87.45 (13, 163)	1.21	1.07-1.37
20–21 % (n)	24.79 (13,602)	12.78 (1696)	87.22 (11,906)	1.24	1.08-1.42
22–23 % (n)	24.22 (13,363)	12.05 (1534)	87.95 (11,829)	1.16	1.03-1.31
24–25 % (n)	23.39 (13,171)	10.57 (1350)	89.43 (11,821)	1	
Prior alcohol use					
Yes % (n)	56.90 (31,638)	15.51 (4774)	84.49 (26,864)	2.29	2.10-2.49
No % (n)	43.10 (23,577)	7.43 (1722)	92.57 (21,855)	1	
Prior cigarette use					
Yes % (n)	55.58 (10439)	15.29 (1530)	84.71 (8909)	2.28	2.13—2.43
No % (n)	44.42 (7898)	7.77 (576)	92.23 (7322)	1	
Prior marijuana use					
Yes % (n)	34.50 (19,662)	20.52 (3908)	79.48 (15,754)	3.16	2.91 - 3.43
No % (n)	65.50 (11229)	7.55 (2588)	92.45 (32,965)	1	
* Results are reported a	s unweighted n and	1 weighted perce	atages using SUDA	AAN.	

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Table 2

Likelihood of subsequent abuse of prescription opioids: Full model and model stratified by gender: Sample restricted to 18–25 year olds 2006–08 (N=55,215)

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	Ful	Model	Men (n=26,381)	Women	ı (n=28,834)
	AOR	95% CI	AOR	95% CI	AOR	ID %56
Gender			NA		NA	
Male	Ref					
Female	0.78	0.73-0.84				
Race						
White	2.12	1.88–2.39	2.44	2.042.92	1.81	1.46-2.24
Black	Ref		Ref		Ref	
Hispanic	1.19	0.98-1.45	1.34	1.02-1.75	1.06	0.80 - 1.40
Other	1.23	1.01 - 1.49	1.43	1.05-1.95	1.03	0.79-1.35
Age (years)						
18–19	1.26	1.11-1.43	1.25	1.06 - 1.46	1.29	1.10 - 1.51
20–21	1.27	1.11 - 1.46	1.21	1.02 - 1.43	1.35	1.14–1.61
22–23	1.16	1.03 - 1.30	1.19	1.00 - 1.41	1.12	0.96 - 1.30
24–25	Ref		Ref		Ref	
Prior alcohol use	1.23	1.11-1.36	1.29	1.14–1.47	1.16	1.00 - 1.33
Prior cigarette use	1.25	1.16–1.36	1.21	1.06 - 1.37	1.33	1.17-1.51
Prior marijuana use	2.44	2.22–2.67	2.52	2.22-2.85	2.34	2.07–2.66

Interactions:

OR for prior marijuana is 0.92X higher in women than in men with 95% CI of 0.79–1.08 OR for prior cigarettes is 0.99X higher in women than in men with a 95% CI 0.83–1.18 OR for prior alcohol is 0.88X higher in women than in men with a 95% CI of 0.76–1.03

Table 3

Gender and the association between prior substance use and subsequent abuse of prescription opioids. (N=55,215)

Additive variable	OR	95% CI
Women with prior marijuana	1.92	1.74–2.11
Women without prior marijuana	0.78	0.73–0.84
Men with prior marijuana	2.44	2.22-2.67
Men without prior marijuana	Ref	
Women with prior alcohol	0.97	0.70-1.34
Women without prior alcohol	0.78	0.73–0.84
Men with prior alcohol	1.23	1.11-1.36
Men without prior alcohol	Ref	
Women with prior cigarettes	0.99	0.89–1.11
Women without prior cigarettes	0.78	0.73–0.84
Men with prior cigarettes	1.25	1.16-1.36
Men without prior cigarettes	Ref	