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Days with Pain and Substance Use Disorders: Is There an Association?

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Abstract

OBJECTIVES—We investigated possible associations between pain frequency and the five most common substance use disorders: alcohol abuse/dependence, cocaine abuse/dependence, methamphetamine abuse/dependence, opioid abuse/dependence, and marijuana abuse/dependence.

METHODS—We used data from the Rural Stimulant Study (RSS), a longitudinal (7 waves), observational study of at-risk stimulant users (cocaine and methamphetamine) in Arkansas and Kentucky (n=462). In fixed effects logistic regression models, we regressed our measures of substance use disorders on the number of days with pain in the past 30 days and depression severity.

RESULTS—Time periods when individuals had 1 to 15 days (OR=1.85, p<0.001) or 16+ days (OR=2.18, p<0.001) with pain in the past 30 days were more likely to have a diagnosis of alcohol abuse/dependence, compared to time periods when individuals had no days with pain. Compared to time periods when individuals had no pain days in the past 30 days, time periods when individuals had 16+ pain days were more likely to have a diagnosis of opioid abuse/dependence (OR=3.32, p=0.02). Number of days with pain was not significantly associated with other substance use disorders.

DISCUSSION—Pain frequency appears to be associated with an increased risk for alcohol abuse/dependence and opioid abuse/dependence in this population, and the magnitude of the association is medium to large. Further research is needed to investigate this in more representative populations and to determine causal relationships.

Keywords

pain; alcohol abuse/dependence; cocaine abuse/dependence; methamphetamine abuse/dependence; opioid abuse/dependence; marijuana abuse/dependence; depression

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1. INTRODUCTION

Self-medication of distress, including physical pain, is often cited as a reason for substance abuse by patients and clinicians.[1, 2] This relationship between pain relief and substance abuse is most obvious for opioids, as individuals attempt to self-medicate their pain with opioid analgesics. Cannabinoids also have a pain modulating effect in animals and have been shown to relieve neuropathic pain in humans.[3, 4] Sativex, which contains tetrahydrocannabinol and cannabidiol, has recently been approved in Canada for the treatment of neuropathic pain. A review from the Institute of Medicine concluded "The available evidence from animal and human studies indicate cannibinoids can have a substantial analgesic effect." [3]

On the other hand, the relationship between pain frequency and cocaine abuse, or pain frequency and methamphetamine abuse, or pain frequency and alcohol abuse, has received less attention, although there are theoretical reasons to expect a positive association. Alcohol may have analgesic effects,[5] although the evidence is not completely consistent. Cocaine is well known as a local anesthetic, is used in animal analgesia models,[6] and has been used as an intrathecal analgesic for over 100 years.[7] Amphetamine has a long record of use as a potentiator of opioid analgesia.[8] Further, the euphorogenic effects of opioids, alcohol, cocaine, marijuana, and methamphetamines are well known, and these substances might be used to self-medicate negative psychological sequelae of pain.

In studies from clinical settings, patients in substance use treatment have often been found to have higher rates of pain than the general population,[9, 10] and patients in treatment for pain have been found to have higher rates of SUDs than the general population.[11] One study found similar rates of substance abuse among methadone maintenance patients with and without pain but higher rates of mental health disorders among those with pain.[12] Analyses of survey data from the World Mental Health Surveys showed a non-linear relationship between alcohol use disorders and number of pain disorders in the U.S. sample; among individuals with 0 pain disorders, 1 pain disorder, and 2+ pain disorders rates of alcohol use disorders were 3.5%, 1.8%, and 3.9% respectively.[13] However, in another report from this study, among the U.S. sample with back pain, the rate of an alcohol use disorder was higher among those with back pain, compared to those with no back pain.[14] Similarly, those with arthritis were more likely to have an alcohol use disorder, compared to those with no arthritis.[15]

Generally these studies controlled for sociodemographic factors, but not mental health status, which is a potential limitation, as mental health status might be an important confounder in the relationship between pain and SUDs. Pain is associated with common mental health disorders, such as depression and anxiety,[13, 16–20] and common mental health disorders are associated with SUDs.[21–24] Thus, even if SUDs and pain were not causally associated, a statistical association between pain and SUDs might be expected, due to their common association with mental health disorders. This highlights the importance of controlling for mental health in models analyzing the association between pain and SUDs.

The focus of this paper is the association between frequency of pain and the five most common substance use disorders (SUDs) in the U.S.:[21] alcohol abuse/dependence, cocaine abuse/dependence, methamphetamine abuse/dependence, opioid abuse/dependence, and marijuana abuse/dependence. Thus we hypothesized a positive association between pain frequency and each of the SUDs, as individuals try to self-medicate their physical pain, in much the same way they have been posited to self-medicate psychological symptoms.[25] In this paper we assessed the relationship between pain frequency and: (i) alcohol use disorders (i.e., abuse and dependence), (ii) cocaine use disorders; (iii) methamphetamine use

disorders, (iv) opioid use disorders, and (v) marijuana use disorders. We hypothesized that individuals with greater pain frequency would be more likely to have SUDs, and that the magnitude of the relationship would be especially strong for opioid abuse/dependence. We used data from the Rural Stimulant Study (RSS), a longitudinal (7 waves), observational study of at-risk stimulant users (cocaine and methamphetamine) living in Arkansas and Kentucky. In addition to its longitudinal design, the RSS has several important features that make it an excellent data source for this analysis. Because RSS respondents had high rates of SUDs, the study is adequately powered to investigate the association of pain with individual SUDs. Further, the RSS has measures of pain frequency, as well as excellent measures of the individual SUDs and depression, the most common mental health disorder.

2. METHODS

2.1 Sample

Data are from a natural history study of 462 at risk stimulant users (cocaine or methamphetamine use in the past 30 days) residing in rural counties of Arkansas and Kentucky [26–31]. Counties were classified as rural according to the U.S. Office of Management and Budget definition of a non-metropolitan county, or a county with a population of 50,000 or fewer persons. Participant eligibility criteria included being 18 years of age or older, using crack or powder form cocaine and/or methamphetamine by any route of administration in the past 30 days, receiving no formal drug abuse treatment within the past 30 days, and having a verifiable address within one of the study counties. Along with cocaine and methamphetamine, respondents had high rates of other SUDs (Table 1).

For the six counties, the 2000 United States Census data indicates a range of county characteristics in terms of socioeconomic status. The three Arkansas counties were 49–57% African-American, compared to 0–2% in Kentucky. The Arkansas and Kentucky counties had high rates of household incomes under $10,000 (14–24%), and correspondingly high rates of families living below the federal definition of poverty (11–29%) and a wide range in overall employment rates (43–69%, lowest in Arkansas). The study was approved by the relevant institutional review boards and received a Certificate of Confidentiality from NIDA.

Participants were recruited using Respondent-Driven Sampling (RDS), a variant of snowball sampling.[31–35] Such non-probabilistic sampling methods are critical for recruiting community “hidden populations” such as illegal drug users or those with HIV. Theoretically, RDS can generate a sample that is much more representative of the hidden population under study than can snowball or targeted sampling.[32] One advantage of RDS over other targeted or referral sampling strategies is that initial “seeds” for sampling are not required to be random samples of the target population because RDS has been shown to “converge” to stable characteristics of the population following successive recruitment waves.[33, 34, 36]

In all counties, preliminary ethnographic methods were used to identify seeds who met study criteria.[37] Ethnographic methods included “hanging out” in propitious locations such as bars and county fairs, talking to community members about their knowledge of drug use, meeting with treatment providers, and handing out study “business” cards to anyone who knew drug users who might contact the study. Study seeds who completed the baseline interview were asked to give referral coupons to people they knew used drugs. If referrals resulted in study contact, the seeds received $10 per contact for up to three contacts but up to six referrals were allowed. Subsequent participants also followed the same procedures. Confidentiality was maintained by requiring that potential study participants initiate study contact.

Recruitment was conducted between June 2003 and September 2004. Written informed consent was obtained prior to the baseline interview.

Trained research assistants conducted baseline interviews using computer-assisted personal interview technology on a laptop computer. At each six-month follow-up interview, the majority of questions contained in the baseline interview were repeated and urinalysis was conducted to help assure the veracity of self-reported drug use.[38–40] Extensive tracking information was obtained at the baseline interview and throughout all follow-up interviews so that participants could be re-located, culminating in 79% follow-up participation rate at the 36-month interview. The RSS sample is shown in table 1.

2.2 Measures

2.2.1 Dependent Variables

Substance Abuse/Dependence Disorders: The five individual SUDS (alcohol use disorders (i.e., abuse and dependence), cocaine use disorders, methamphetamine use disorders, opioid use disorders, and marijuana use disorders) were measured using the Substance Abuse Outcomes Module (SAOM), for the previous 6 months. The SAOM has undergone extensive reliability and validity examinations and demonstrates reasonable reliability (internal reliability coefficient alpha 0.58–0.90, test-retest reliability 0.56–0.99) and validity (concurrent validity generally 0.5–0.8, predictive validity 0.5–0.9).[41] Concurrent validity for the SAOM was based on longer key instruments such as a structured diagnostic interview for substance use disorders, the CIDI-SAM, [42] and the Addiction Severity Index (ASI).[43] The SAOM has shown a 90–93% agreement with the CIDI-SAM on DSM-IV substance use diagnosis (present/absent).[41]

2.2.2 Independent Variables

Pain Frequency: The main independent variable of interest was the number of days in the past 30 days with pain. At each wave respondents were asked “How many days in the last 30 days have you had bodily pain (either recent or long-standing pain)?” To ease interpretation of the data and to allow for non-linear effects we coded this into three groups: 0 days, 1 to 15 days, and 15+ days. The RSS also contains data on the number of days that pain interfered with work activities, and number of days that pain interfered with social interactions; as might be expected these were highly correlated with the number of days with pain, and therefore not included in the final models. (The regression of number of days with pain on number of days that pain interfered with work activities pain had an R^2=0.41 ($p<0.001$), and the regression of number of days with pain on number of days that pain interfered with social activities had an R^2=0.39 ($p<0.001$)). In preliminary models we also investigated the effects of pain severity (0–10 scale), but these effects were statistically not significant when controlling for number of days with pain and depression, and not included in the final models.

Depression Severity: Depression severity was measured with the PHQ-9.[44] We divide the full sample into four groups based on PHQ-9 scores: 0 to 4 (no depression), 5 to 9 (mild depression), 10 to 14 (moderate depression) and 15+ (moderately severe or severe depression).[44]

2.3 Analysis

We utilized five logistic regressions, one for each SUD as the dependent variable, and each regression included the number of days with pain, and depression severity, as independent variables. We utilized fixed effects logistic regressions, which we believe are particularly well-suited for statistical analysis of longitudinal, non-experimental data.[45] In these models,

if there are no missing data, the total number of observations in a regression equals the number of individuals multiplied by the number of time periods. In our case, while there were was a theoretical possibility of 3234 observations, in actuality there were 2862 observations (89%). Fixed-effects models control for respondent characteristics that are stable over time, such as personality traits, thus possibly eliminating one potential source of omitted variable bias. This is done by including a separate dummy variable for each individual in the sample. As fixed effects models control for stable characteristics, variables such as gender and race are not (and cannot be) included in such models. Since the individual's level of education and income were also stable over the time period of our study, we did not include these variables in our models. The interactions between time and time-variant variables (pain frequency and depression) were also tested and were not included in the models due to non-significance.

We tested models that used both lagged predictors, (e.g., regressing six month substance use outcomes on baseline predictors, regressing 12 month substance use outcomes on six-month predictors, etc.) and models that used simultaneous predictors (e.g., regressing baseline outcomes on baseline predictors, etc.) These models produced similar results; in this paper we report the results from models using simultaneous predictors, that is regressing the baseline substance use disorder outcome on baseline predictors, regressing the 6 month substance use disorder outcome on predictors measured at 6 months, etc.

3. RESULTS

3.1 The RSS Sample

Characteristics of the RSS sample at baseline are shown in Table 1. Thirty percent of the RSS sample had no days with pain in the past 30 days, 43.2% had 1 to 15 days, and 26.6% percent had 16+ days. Among those with 1 to 15 days with pain in the last 30 days, 59.6% reported a chronic source of pain, and among those with 16+ days, 81% reported a chronic source. While the RSS was designed to study at-risk stimulant users, the other SUDS were also common. At baseline 50.6% had alcohol abuse/dependence, 51.7% had cocaine abuse/dependence, 34.2% had methamphetamine abuse/dependence, 5.0% had opioid abuse/dependence, and 36.4% had marijuana abuse/dependence. Approximately half were from Kentucky, half from Arkansas. Mean age was 34, and reflecting gender differences in rates of substance abuse, the majority were male (58%). Almost all were either African-American (39.6%) or white (57.6 %). Reflecting the disadvantaged population, only 40.7% had graduated high school and only about 3 in 10 were employed. At baseline, 26.6% percent had 16+ days with pain, while 43.2% had 1 to 15 days. Twenty-six percent had mild depression, 23.4% had moderate depression, and 15.4% had moderately severe or severe depression.

3.2 Pain Frequency and SUDs

The results of our fixed effects logistic regression models are shown in Table 2, with each column representing a separate regression. Time periods when individuals had 1 to 15 days with pain (OR=1.85, p=0.0002) or 16+ days (OR=2.18, p=0.0003) were more likely to have a diagnosis of alcohol abuse/dependence, compared to time periods when individuals had no days with pain in the past 30 days. Compared to time periods when individuals had no pain days, time periods with 16+ pain days were more likely to have a diagnosis of opioid abuse/dependence (OR=3.32, p=0.02); but the OR for 1 to 15 days, while large (OR=2.25) just missed being significant at the 0.05 level (p=0.06) as a predictor of opioid abuse/dependence. Number of days with pain was not significantly associated with cocaine abuse/dependence, methamphetamine abuse/dependence, or marijuana abuse/dependence.

3.3 Depression and SUDS

Compared to time periods when individuals had no depression, time periods when individuals had mild, moderate and moderately severe/severe depression were significantly associated with higher rates of cocaine abuse/dependence, and marijuana abuse/dependence. Results for the other SUDs were less consistent. While generally the odds ratios were positive, the only other significant findings were that periods with moderate depression were associated with opioid abuse/dependence (OR=2.67, p=0.04) and methamphetamine abuse/dependence (OR=2.35, p=0.006).

4. DISCUSSION

In separate analyses we investigated the relationship between pain frequency and the five most common SUDs. This allows us to investigate the relationship between a given SUD and pain frequency, and compare the magnitude of the associations across the five SUDs, which, to our knowledge, has never been done before. We found that the number of days with pain in the past 30 days was significantly associated with alcohol abuse/dependence and opioid abuse/dependence, and the strength of the association was moderate to strong (e.g., OR's of 1.85 to 3.32). Although we utilized longitudinal data, we emphasize that these results should be viewed as measures of association, and do not necessarily imply causality. The relationship between the number of days with pain in the past 30 days and cocaine abuse/dependence, methamphetamine abuse/dependence, and marijuana abuse/dependence were not statistically significant.

The results for alcohol use disorders are potentially important. Alcohol use disorders are the most common substance use disorders, occurring in 4 to 9% of the U.S. population in a given year,[21, 23, 46, 47] and cause substantial morbidity,[48] accounting for about 5% of all disability in Western industrialized countries.[49] The negative social and health consequences associated with alcohol use disorders are protean [50] and include increased suicidal behaviors,[51, 52] high rates of criminal justice involvement and violence,[53] and substantial medical/physical consequences.[50, 54] The medical consequences of alcohol use disorders, such as cirrhosis and premature death, are particularly high among Hispanics, Native Americans, and African Americans compared to whites.[55, 56]

Because of the high prevalence and societal costs of alcohol abuse/dependence, the identification of risk factors for these disorders is important, particularly if the risk factor identified is strongly associated with the disorder, occurs commonly, and is potentially modifiable. Notably, we found that the magnitude of the association between alcohol use disorders and pain frequency was comparable to, or even larger than, the magnitude of association between alcohol abuse/dependence and depression, a well established risk factor for alcohol use disorders. Further, chronic pain occurs commonly, significantly affecting approximately 37% of the general population.[57] By comparison, depressive disorders affect approximately 9% of the population in a given year.[21, 23] Given this, it is interesting to view our results in terms of the population-attributable risk for alcohol abuse/dependence (that is, the proportion of alcohol abuse/dependence disorders that can be attributed to various factors), which is a function of both the strength and the prevalence of the risk factor. Because pain disorders are more prevalent than depression, the population-attributable risk for alcohol abuse/dependence from pain may actually be as great, or greater, than population-attributable risk for alcohol abuse/dependence from depression.

Improved detection and treatment of chronic pain disorders might decrease the onset of alcohol abuse/dependence, and careful assessment and appropriate treatment of pain in individuals with alcohol abuse/dependence might facilitate the treatment of an existing disorder. Chronic pain can be successfully treated with medications,[58] cognitive-behavioral

therapy, and multidisciplinary pain treatment.[59] Treatment of chronic pain in the presence of SUDs is complicated,[60] but our findings suggest that among individuals with comorbid pain and SUDs concurrent treatment of chronic pain and SUDs might be more successful than treatment of only the SUD, or only the pain condition. Unfortunately, there is limited data on evidence based programs to simultaneously treat chronic pain and SUDs remain to be developed.[61–64]

Besides being a possible risk factor for alcohol abuse/dependence, the link between pain and alcohol abuse is important for other reasons. First, use of alcohol by patients on opioid therapy for chronic pain increases the risks of overdose and death.[65] Second, alcohol interferes with the efficacy of antidepressant treatment of depression,[66] and likely pain. Third, persistent pain reduces the effectiveness of treatment for alcohol disorders.[67]

We observed an interesting trend, to our knowledge not discussed in the literature previously. In models which contain measures of both pain frequency and depression as independent variables, depression is most strongly associated with cocaine abuse/dependence and marijuana abuse/dependence, while pain frequency is most strongly associated with alcohol abuse/dependence and opioid abuse/dependence. To a certain degree, this makes sense from a self-medication perspective. Although opioids are the oldest known anti-depressants, their analgesic effects are likely greater than their effects on mood, in most individuals. In contrast, the effects of cocaine on mood are likely greater than the analgesic effects. On the other hand, we expected a statistically significant positive association between marijuana abuse/dependence and number of days with pain, given the established analgesic properties of cannabinoids. However, not only was the relationship not statistically significant, the magnitude of the relationship was modest, with OR's ranging from 1.17 to 1.25.

As mentioned, our results should be viewed as measures of association, and do not necessarily imply causality, due to possible complex, bi-directional effects. Besides self-medication, there are other possible explanations for our significant results. For example, because of potential hyperalgesia, opioids and alcohol may worsen pain over time, although this is controversial for opioids and to our knowledge, has never been investigated for alcohol.

Our use of longitudinal data, with multiple data points for each individual, allowed us to use fixed-effects models, which we view as a distinct advantage in our study. In particular, fixed-effects models control for all stable characteristics of the individual. This is important, as potentially important, stable factors, such as personality, and personality disorders have generally not been controlled for in previous analyses. Thus, the potential for biased coefficients resulting from omitted confounders is decreased.

Several limitations deserve discussion. First, the measures of pain in the RSS have not been validated. Second, we utilized a sample of individuals in rural Arkansas and Kentucky who were at risk for stimulant use disorders, and who had extensive use of other substances. The extent to which results from this population can be generalized to the U.S population is unknown, and our results need to be replicated and validated in other studies with more representative populations. We would note however that future studies that investigate these issues might also have to use non-representative samples, as statistical power considerations necessitate the investigation of outcomes that are relatively infrequent, such as opioid abuse/dependence, or methamphetamine abuse/dependence, in samples that are significantly enriched for these disorders. Third, while we controlled for depression severity, the RSS did not contain measures of other common mental health disorders, such as anxiety disorders. Fourth, our data do not allow us to determine whether and individual with an opioid use

disorder was using the opioid solely for the opioid use disorder, or for the opioid use disorder and pain.

5. CONCLUSIONS

Pain frequency appears to be associated with increased risk for both opioid abuse/dependence and alcohol abuse/dependence. The population-attributable risk for alcohol abuse/dependence from frequent pain may be greater than that associated with depression, as chronic pain is more prevalent than depression. Pain is also known to impede treatment for depression, so that risk may be magnified when both pain and depression are present.[68] Further research is needed to investigate the relationship between alcohol abuse/dependence and pain frequency in more representative samples.

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Table 1

The Rural Stimulant Study (n=462): Baseline Descriptive Statistics

Variable	n (%)
State	
Arkansas	237 (51.3)
Kentucky	225 (48.7)
Sex	
Male	270 (58.4)
Female	192 (41.6)
Age (mean/SD/range)	34.1 ± 10.6 (18–61)
Race	
African-American	183 (39.6)
White	266 (57.6)
Hispanic/Latino	3 (0.6)
Native American	2 (0.4)
Other	8 (1.7)
Marital Status	
Single	215 (46.5)
Married	247 (53.5)
High school graduate?	
Yes	188 (40.7)
No	274 (59.3)
Employment Status	
Employed	142 (30.7)
Unemployed	320 (69.3)
Income	
less than $10,000	108 (23.5)
$10,000 or more	354 (76.5)
Days with pain in the past 30 days	
0 days	138 (30.1)
1–15 days	198 (43.2)
16+ days	122 (26.6)
Depression severity	
No depression	161 (34.8)
Mild depression	122 (26.4)
Moderate depression	108 (23.4)
Moderately severe or severe depression	71 (15.4)
Dependent variables	
Alcohol abuse/dependence (past 6 months)	234 (50.6)
Cocaine abuse/dependence (past 6 months)	239 (51.7)
Methamphetamine abuse/dependence (past 6 months)	158 (34.2)
Opioid abuse/dependence (past 6 months)	23 (5.0)

Variable	n (%)
Marijuana abuse/dependence (past 6 months)	168 (36.4)

Table 2

Pain Frequency and Depression Severity as Predictors of Substance Use Disorders in Fixed Effects Models

	Alcohol abuse/dependence		Cocaine abuse/dependence		Methamphetamine abuse/dependence		Opioid abuse/dependence		Marijuana abuse/dependence	
Independent Variables	**OR**	**p-value**	**OR**	**p-value**	**OR**	**p-value**	**OR**	**p-value**	**OR**	**p-value**
Days with bodily pain in past 30 days										
1–15 days vs. 0 day	1.85	0.0002	1.25	0.24	1.44	0.14	2.25	0.06	1.25	0.23
16+ days vs. 0 day	2.18	0.0003	1.50	0.09	1.57	0.13	3.32	0.02	1.17	0.50
Depression severity										
Mild depression vs. No depression	1.18	0.33	1.91	0.0006	1.34	0.23	1.11	0.79	1.62	0.008
Moderate depression vs. No depression	1.34	0.19	2.71	<.0001	2.35	0.006	1.31	0.57	2.38	0.0003
Moderately severe or severe depression vs. No depression	1.29	0.33	3.45	<.0001	1.56	0.21	2.67	0.04	1.97	0.01