

RATES OF PSYCHIATRIC COMORBIDITY AMONG U.S. RESIDENTS WITH LIFETIME CANNABIS DEPENDENCE

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ABSTRACT

Cannabis is the most widely used illegal drug in the U.S. population. Surveys have estimated that the lifetime prevalence rate for cannabis dependence is approximately 4%. Though the presence of a psychiatric disorder increases the likelihood of developing substance dependence, the field lacks data regarding the association between mental disorders and cannabis dependence. The aim of this study is to describe the prevalence of psychiatric disorders among individuals with cannabis dependence. The National Comorbidity Survey was used to obtain these data. We found that 90% of respondents with cannabis dependence had a lifetime mental disorder, compared to 55% without cannabis dependence. Alcohol dependence, antisocial personality disorder, and conduct disorder had the strongest

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associations with cannabis dependence, followed by anxiety and mood disorders. A large proportion of respondents with internalizing disorders developed mood or anxiety disorders prior to onset of their first cannabis dependence symptom. Data regarding the prevalence of comorbid mental disorders underscore the importance of thorough and systematic evaluation of patients seeking treatment for cannabis dependence. The failure to identify comorbidity may lead to inadequate treatment, and a poorer prognosis.

Key Words: Cannabis dependence; Comorbidity; Prevalence

INTRODUCTION

Epidemiological studies in the United States have repeatedly found that cannabis is the most commonly used illegal drug in the United States.^[1,2] The National Comorbidity Survey (NCS) observed a 4.2% lifetime prevalence rate for cannabis dependence.^[1]

Among populations treated for substance abuse, the magnitude of cannabis dependence is substantial. A national survey of substance abuse treatment facilities, conducted in 1996, found that 13% of admissions were for cannabis dependence, a rate similar to opiate dependence (14%).^[3]

A significant public health concern regarding the adverse consequences of habitual cannabis use on cognitive functioning. In a literature review, early adolescent marijuana use was a risk factor for poor educational outcomes and, in particular, early school leaving and reduced educational attainment.^[4] Heavy cannabis users appear to have impairments in mental flexibility, working memory, attention, and abstraction.^[5-7]

There are several reasons why a greater understanding of comorbidity may be relevant to our field. As indicated above, it is highly prevalent. Second, a history of psychiatric disorder is a risk factor for developing substance dependence.^[8]

Third, the presence of a mental disorder has prognostic significance in the treatment of substance dependence. Numerous studies^[9-11] found that severity of co-occurring psychiatric symptoms predicted worse outcomes. Patients with co-occurring mental disorders are generally more difficult to treat because continued use of substances interferes with treatment of the mental disorder; they also are at risk of dropping out prematurely.^[12,13]

Fourth, the extent of comorbidity among individuals with substance dependence is considerable in the general population. The NCS observed that 54% of individuals with a substance dependence disorder had a coexisting mental disorder.^[14]

Cannabis use is a considerable public health problem because it is highly prevalent; typically begins in adolescence—when the brain is still maturing—and is often a precursor to the use of other illicit substances.^[15] Though comorbidity is a risk factor for developing substance dependence, sparse epidemiological data exist regarding the extent to which comorbidity is a risk factor for developing cannabis dependence.

Longitudinal studies have also found a significant association between chronic cannabis use, mental disorders, and social morbidity. In study of large cohort ($N = 1325$) of adolescents who experimented with cannabis, Kandel^[16] found that those who remained regular users at age 24–25 had more psychopathology, and used other illicit drugs more frequently than those who stopped using cannabis. More recently, Fergusson and Horwood,^[17] in a study of 935 18-year-old New Zealanders, reported that those who used cannabis 10 or more times, between age 15 and 16, had high rates of major depression (46%) and anxiety disorders (31%). These rates were approximately twice as high as those who had never used cannabis.

Investigators have observed that psychiatric disorders substantially increase the likelihood of developing a variety of substance dependencies.^[18–22] However, the field lacks data regarding how comorbidity affects the prevalence and course of cannabis dependence.

We only found one epidemiological study that reported the link between cannabis dependence and comorbidity. The National Longitudinal Alcohol Epidemiologic Survey (NLAES)^[23] found a strong association (odds ratio = 7.0) between cannabis dependence and major depression during a 12-month period. Since the NLAES only assessed one nonsubstance psychiatric disorder (major depression), the field lacks data regarding the affiliation between cannabis dependence and a wide breadth of other mental disorders exhibited during the present and past. Hence the aim of this study is to describe the prevalence of psychiatric disorders among individuals with cannabis dependence in the NCS.^[24]

METHODS

Sample

These data were downloaded from the NCS database (see NCS homepage at www.hcv.harvard.med.edu^[25]). The NCS was designed to measure the prevalence of Diagnostic and statistical manual of mental disorders (DSM-III-R) as well as to examine risk factors for psychiatric disorders in a nationally representative sample. The NCS was based on a national probability sample of individuals, 15–54 years of age, in the noninstitutionalized population of the United States. The NCS had two phases: a part 1 diagnostic interview ($N = 8098$)

and a part 2 risk factor interview administered to a subsample ($N = 5877$) because of budgetary constraints. The part 2 interview was administered to all part 1 subjects aged 15–24 years, to all other subjects in part 1 with a lifetime diagnosis, and to random subsample of the remaining subjects in part 1. For more detailed information, see Ref. [24].

The prevalence data were weighted for differential probabilities of selection and nonresponse. A weight was also included to adjust the sample to approximate the cross-classification of the population distribution on a range of sociodemographic characteristics. Bivariate comorbidities were obtained by estimating odds ratios using the SYTAB procedure in the STATA 7.0 for Windows software package.^[25]

Diagnostic Assessment

Psychiatric diagnoses were based on the DSM-III-R.^[26] The diagnostic interview used to generate these diagnoses is a modified version of the composite international diagnostic interview,^[27] designed to be used by trained interviewers who are not clinicians.

RESULTS

Ninety percent of respondents with cannabis dependence had a lifetime mental disorder, compared to 54.7% without cannabis dependence. Alcohol dependence, antisocial personality disorder (ASP), and conduct disorder (CD) had the strongest associations with cannabis dependence, followed by anxiety and mood disorders (Table 1).

The detection of concurrent disorders, rather than lifetime comorbidity, may be more relevant to clinicians treating cannabis dependence, therefore, we examined the prevalence of past-month comorbidity. Respondents with a lifetime diagnosis of cannabis dependence, who used cannabis during the past month (Group A), were approximately twice as likely to have a current mood ($OR = 2.2$; $CL = 1.1-4.7$) or anxiety disorder ($OR = 2.6$; $CL = 1.5-4.5$) than respondents without lifetime cannabis dependence (Group B).

Understanding the temporal sequencing of comorbidity may provide useful information regarding the variety of pathways leading to development of cannabis dependence. Since the NCS data set did not have an onset age variable for cannabis dependence, we used a proxy measure; i.e., the earliest age a cannabis dependence symptom was manifested. It is important to emphasize that this is not equivalent to onset of cannabis dependence because the latter requires a constellation of symptoms to have occurred during a 12-month period.

Table 1. Lifetime Comorbidity of Cannabis Dependence with Other Disorders

Lifetime Diagnosis	Cannabis Dependence (%)	Crude Odds Ratio	95% Confidence Limits
Major depression	32.7	2.42	1.84–3.2
Dysthymic disorder	13.3	2.3	1.54–3.3
Mania	6.9	0.86	0.11–6.2
Hypomania	4.4	2.86	1.54–5.4
Conduct disorder	44.4	6.0	4.6–7.9
Antisocial personality	21.4	11.2	7.9–15.8
Agoraphobia	11.3	1.8	1.2–2.7
Generalized anxiety	12.1	2.7	1.78–4.0
Panic disorder	6.9	2.3	1.54–3.3
Social phobia	29.0	3.3	2.37–4.5
Post-traumatic stress	18.5	2.98	2.13–4.17
Simple phobia	18.1	1.8	1.28–2.5
Alcohol dependence	70	17.8	13.4–23.6
Nonaffective psychosis	2.0	3.49	1.35–9.02

The onset of mood disorder or an anxiety disorder antedating the earliest onset of cannabis dependence symptom was defined as having a primary mood/anxiety disorder. The onset of a mood or anxiety disorder following the earliest onset of dependence symptom was classified as having a secondary mood/anxiety disorder.

We found that the rates for primary anxiety and primary mood disorders were 73.1 and 47.8%, respectively; the rates for secondary anxiety disorders and secondary mood disorders were 26.9 and 52.2%, respectively.

Given the strong association found between cannabis dependence, CD, and ASP, we sought to determine the extent of comorbidity among respondents with CD. Since a large proportion (approximately two-thirds) of population with CD do not develop ASP,^[28] we confined our analysis to the CD group without ASP. We observed that those with CD and cannabis dependence were twice as likely to have major depression (lifetime) and approximately five times as likely to have alcohol dependence (lifetime) than those with CD without cannabis dependence; the between-group risk for other mental disorders was generally much smaller.

DISCUSSION

This study found a high degree of psychiatric comorbidity among noninstitutionalized persons with cannabis dependence in the United States. Approximately 90% of respondents with cannabis dependence had a lifetime

comorbid disorder. The associations between cannabis dependence and comorbid disorders were also substantial both for past-month assessment periods.

ASP and CD had the strongest relationship to lifetime cannabis dependence. This finding was not surprising, since studies^[14,29] have confirmed that ASP and CD are correlated with very high rates of substance dependence. We found that lifetime cannabis dependence with CD was strongly associated with the lifetime major depression and lifetime alcohol dependence.

Few prospective, community-based, longitudinal epidemiological studies of CD have measured cannabis use over time. Boyle et al.^[31] in a follow-up study of 726 12–16-year-olds from the general Ontario community found that CD made an independent contribution to predicting use of marijuana and “hard drugs” (amphetamines, stimulants, hallucinogens, heroin) 4 years later, even after prior drug use and coexisting emotional disorders were controlled. An 18-month longitudinal study of a national sample of Norwegian adolescents, also found a strong association between conduct disorder symptoms and subsequent cannabis initiation.^[32]

The robust link between cannabis dependence and alcohol dependence was not unexpected given that drug dependence is very common among populations with alcohol dependence.^[30,33]

Cannabis dependence was associated with an approximate two-fold risk of having a mood or anxiety disorder for both lifetime and past month assessments. The NLAES^[23] also found a strong 12-month association between cannabis dependence and major depression in the NLAES. Though the prevalence estimates in the NLAES and this study were for different time periods, and therefore they cannot be regarded as similar, these results generally confirm the strong link between mood or anxiety disorders and cannabis dependence across different time periods.

The finding that a high proportion of population dated the onset of their anxiety and mood disorders prior to the earliest manifestation of cannabis dependence symptoms, suggests that a portion of the population may be using cannabis to self-medicate their depression. Caution is urged in interpretation of this finding because our proxy measure should not be construed as equivalent to onset of cannabis dependence disorder because the latter requires that a constellation of symptoms to have occurred at the same time during a 12-month period.

The NCS observed that 55.5–84% of respondents reported that their mood or anxiety disorder occurred prior to the onset of a drug dependent disorder.^[14] These results indirectly confirm the NCS findings regarding the direction of temporal sequencing with respect to cannabis dependence.

Though marijuana has been the most widely used illicit drug in the United States for the past several decades, a paucity of studies have tested the efficacy of interventions for cannabis dependence. We were only able to locate relatively

few controlled treatment studies of cannabis dependence.^[34–37] The lack of controlled treatment studies is notable given the extensive treatment literature for alcohol dependence, cocaine dependence, and opiate dependence.

Furthermore, though studies targeting treatments of co-occurring mental disorders among patients with alcohol, cocaine, or opiate dependence have been conducted in recent years, similar studies have not been undertaken for cannabis dependence.^[38]

Data regarding the prognostic significance and social morbidity associated with marijuana dependence underscore the importance of a thorough and systematic diagnostic evaluation of patients seeking treatment for substance dependence. However, this is often not done in general clinical settings.^[39] King et al.,^[41] in a large sample of adolescents treated for substance abuse, found that 53% of cases with a mental disorder were not detected by a traditional mental health care service delivery system. The failure to identify mental disorders among patients seeking treatment for cannabis dependence may lead to inadequate treatment, and a poorer prognosis.

It is important to emphasize that the association between cannabis dependence and other psychiatric disorders does not imply causality. Longitudinal studies delineating the timing and sequencing of psychiatric disorders are clearly needed to gain a better understanding of the linkage between various disorders.^[41]

There are several significant limitations of this study. It only relied upon self-reports of substance use; informants and urine test results were not used to validate these reports. Lifetime diagnoses were assessed cross-sectionally; retrospective self-reports may not be accurate, especially with respect to events in the distant past.

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REFERENCES

1. Anthony, J.C.; Warner, L.A.; Kessler, R.C. Comparative Epidemiology of Dependence on Tobacco, Alcohol, Controlled Substances, and Inhalants: Basic Findings from the National Comorbidity Survey. *Exp. Clin. Psychopharmacol.* **1994**, 2 (3), 244–268.

2. Robins, L.N., Regier, D., Eds. *Psychiatric Disorders in America: The Epidemiological Catchment Area Study*; Free Press: NY, 1991.
3. Substance Abuse and Mental Health Services Administration: Treatment Episode Data Set (TEDS). www.samsha.gov (accessed 9/25/2001).
4. Lynskey, M.; Hall, W. The Effects of Adolescent Cannabis Use on Educational Attainment: A Review. *Addiction* **2000**, 95 (11), 1621–1630.
5. Pope, H.G.; Gruber, A.J.; Hudson, J.I.; Huestis, M.A.; Yurgelun-Todd, D. Neurological Performance in Long-Term Cannabis Users. *Arch. Gen. Psychiatry* **2001**, (58), 909–915.
6. Pope, H.G.; Yurgelun-Todd, D. The Residual Cognitive Effects of Heavy Marijuana Use in College Students. *J. Am. Med. Assoc.* **1996**, 275 (7), 521–527.
7. Fletcher, J.M.; Page, J.B.; Francis, D.J.; Copeland, K.; Naus, M.J.; Davis, C.M.; Morris, R.; Krauskopf, M.; Satz, P. *Arch. Gen. Psychiatry* **1996**, 53, 1051–1057.
8. Weiss, R.D. The Role of Psychopathology in the Transition from Drug Use to Abuse and Dependence. In *Vulnerability to Drug Abuse*; Glantz, M., Pickens, R., Eds.; A.O.A.: Washington, DC, 1992; 137–148.
9. LaPorte, D.J.; McLellan, A.T.; O'Brien, C.P.; Marshall, J.R. Treatment Response in Psychiatrically Impaired Drug Abusers. *Comp. Psychiatry* **1981**, 22 (4), 411–419.
10. McLellan, A.T.; Luborsky, L.; Woody, G.E.; O'Brien, C.P.; Druley, K.A. Predicting Response to Alcohol and Drug Abuse Treatments: Role of Psychiatric Severity. *Arch. Gen. Psychiatry* **1983**, 40, 620–625.
11. Osher, F.C.; Kofoed, L.L. Treatment of Patients with Psychiatric and Psychoactive Substance Abuse Disorders. *Hosp. Community Psychiatry* **1989**, 40, 1025–1030.
12. Bukstein, O.G.; Brent, D.A.; Kaminer, Y. Comorbidity of Substance Abuse and Other Psychiatric Disorders in Adolescents. *Am. J. Psychiatry* **1989**, 40, 1025–1030.
13. McCarick, A.K.; Manderscheid, R.W.; Bertolucci, D.E. Correlates of Acting-Out Behaviors Among Adult Chronic Patients. *Hosp. Community Psychiatry* **1985**, 36, 848–853.
14. Kessler, R.C.; Crum, R.M.; Warner, L.A.; Nelson, C.B.; Schulenberg, J.; Anthony, J.C. Lifetime Co-occurrence of DSM III-R Alcohol Abuse and Dependence with Other Psychiatric Disorders in the National Comorbidity Survey. *Arch. Gen. Psychiatry* **1997**, 54, 313–321.
15. Kandel, D.B.; Yamaguchi, K.; Chen, K. Stages of Progression in Drug Involvement from Adolescence to Adulthood: Further Evidence for the Gateway Theory. *J. Stud. Alcohol* **1992**, 53, 447–457.
16. Kandel, D.B. Marijuana Users in Young Adulthood. *Arch. Gen. Psychiatry* **1984**, 41, 200–209.

17. Fergusson, D.M.; Horwood, L.J. Early Onset Cannabis Use and Psychosocial Adjustment in Young Adults. *Addiction* **1997**, *92* (3), 279–296.
18. Burke, J.D.; Burke, K.C.; Rae, D.S. Increased Rates of Drug Abuse and Dependence After Onset of Mood or Anxiety Disorders in Adolescence. *Hosp. Community Psychiatry* **1994**, *45*, 541–555.
19. Christie, K.A.; Burke, J.D.; Regier, D.A.; Rae, D.S.; Boyd, J.H.; Locke, B.Z. Epidemiologic Evidence for Early Onset of Mental Disorders and Higher Risk of Drug Abuse in Young Adults. *Am. J. Psychiatry* **1988**, *145* (8), 971–975.
20. Deykin, E.Y.; Levy, J.C.; Wells, V. Adolescent Depression, Alcohol and Drug Abuse. *Am. J. Public Health* **1987**, *77*, 178–182.
21. Giaconia, P.R.; Parker, A.M. A Six-Year Prospective Study of Pathways Toward Drug Use in Adolescent Boys with and without a Family History of Substance Use Disorder. *J. Stud. Alcohol* **2001**, *62*, 166–178.
22. Nelson, C.B.; Little, R.J.; Heath, A.C.; Kessler, R.C. Patterns of DSM-III-R Alcohol Dependence Symptom Progression in a General Population Survey. *Psychol. Med.* **1996**, *26*, 449–460.
23. Grant, B.F.; Pickering, R. The Relationship Between Cannabis Use and DSM-III-R Cannabis Abuse and Dependence: Results from the National Longitudinal Alcohol Epidemiologic Survey. *J. Subst. Abuse* **1998**, *10*, 255–264.
24. Kessler, R.C.; McGonagle, K.A.; Zhao, S.; Nelson, C.B.; Hughes, M.; Eshleman, S.; Wittchen, H.; Kendler, K.S. Lifetime and 12-Month Prevalence of DSM-III-R Psychiatric Disorders in the United States: Results from the National Comorbidity Survey. *Arch. Gen. Psychiatry* **1994**, *51* (1), 8–19.
25. *Stata Reference Manual: Release 7.0*; Stata Corp.: College Station, TX, 2000.
26. National Comorbidity Homepage. www.hcv.harvard.med.edu (accessed 5/1/2000).
27. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*; American Psychiatric Association: Washington, DC, 1987.
28. World Health Organization. *Composite International Diagnostic Interview*; World Health Organization: Geneva, Switzerland, 1991.
29. Robins, L.N. Sturdy Childhood Predictors of Adult Antisocial Behavior: Replications from Longitudinal Studies. *Psychol. Med.* **1978**, *8*, 611–622.
30. Regier, D.A.; Farmer, M.E.; Rae, D.S. Comorbidity of Mental Disorders with Alcohol and Other Drug Abuse: Results from the Epidemiologic Catchment Area (ECA) Study. *J. Am. Med. Assoc.* **1990**, *264*, 2511–2519.

31. Boyle, M.H.; Offord, D.E.; Racine, Y.A.; Fleming, J.E.; Link, P.S. Predicting Substance Use in Late Adolescence: Results from the Ontario Child Health Study Follow-Up. *Am. J. Psychiatry* **1992**, *149*, 761–767.
32. Pedersen, W.; Mastekaasa, A.; Wichstrom, L. Conduct Problems and Early Cannabis Initiation: A Longitudinal Study of Gender Differences. *Addiction* **2001**, *196*, 415–431.
33. Schuckit, M.A. *Drug and Alcohol Abuse: A Clinician's Guide to Diagnosis and Treatment*, 5th Ed.; Kluwer Academic/Plenum Publishers: New York.
34. Kessler, R.C.; Nelson, C.B.; McGonagle, K.A.; Edlund, M.J.; Frank, R.J.; Leaf, P.J. The Epidemiology of Co-occurring Addictive and Mental Disorders: Implications for Prevention and Service Utilization. *Am. Ortho. Psychiatric* **1996**, *66*, 17–31.
35. Stephens, R.S.; Roffman, R.A.; Curtin, L. Comparison of Extended Versus Brief Treatments for Marijuana Use. *J. Consult. Clin. Psychol.* **2000**, *68*, 8908–8989.
36. Stephens, R.S.; Roffman, R.A.; Simpson, E.E. Treating Adult Marijuana Dependence: A Test of the Relapse Prevention Model. *J. Consult. Clin. Psychol.* **1994**, *62*, 92–99.
37. Budney, A.J.; Higgins, S.; Radonovich, K.J.; Novy, P.J. Adding Voucher-Based Incentives to Coping Skills and Motivational Enhancement Improves Outcomes During Treatment for Marijuana Dependence. *J. Consult. Clin. Psychol.* **2001**, *68*, 1051–1061.
38. Levin, F.R.; McDowell, D.; Evans, S.; Akerele, E.; Donovan, S. Utility of Divalproex Sodium for Marijuana Dependence: A Double-Blind Placebo-Controlled Pilot Study. *Am. J. Addict.* **2002**, in press.
39. Rosenthal, R.N.; Westreich, L. Treatment of Persons with Dual Diagnosis of Substance Use Disorder and Other Psychological Problems. In *Addictions: A Comprehensive Guidebook*; McCrady, B.S., Epstein, E.E., Eds.; Oxford University Press: New York, 1999; 439–476.
40. Clark, D. Identifying Anxiety Disorders in Adolescents Hospitalized for Alcohol Abuse or Dependence. *Psychiatr. Serv.* **1995**, *46*, 618–620.
41. King, R.D.; Gaines, L.S.; Lamber, E.S.; Summerfelt, W.T.; Bickman, L. The Co-occurrence of Psychiatric and Substance Use Diagnoses in Adolescents in Different Service Systems: Frequency, Recognition, Cost, and Outcomes. *J. Behav. Health Serv. Res.* **2000**, *27*, 417–430.
42. Kessler, R.C. Epidemiology of Psychiatric Comorbidity. In *Textbook in Psychiatric Epidemiology*; Tsuang, M.T., Tohen, M., Zahner, G., Eds.; Wiley-Liss: New York, 1995; 179–197.