

Subtypes of Illicit Drug Users: A Latent Class Analysis of Data From an Australian Twin Sample

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This article applies methods of latent class analysis (LCA) to data on lifetime illicit drug use in order to determine whether qualitatively distinct classes of illicit drug users can be identified. Self-report data on lifetime illicit drug use (cannabis, stimulants, hallucinogens, sedatives, inhalants, cocaine, opioids and solvents) collected from a sample of 6265 Australian twins (average age 30 years) were analyzed using LCA. Rates of childhood sexual and physical abuse, lifetime alcohol and tobacco dependence, symptoms of illicit drug abuse/dependence and psychiatric comorbidity were compared across classes using multinomial logistic regression. LCA identified a 5-class model: Class 1 (68.5%) had low risks of the use of all drugs except cannabis; Class 2 (17.8%) had moderate risks of the use of all drugs; Class 3 (6.6%) had high rates of cocaine, other stimulant and hallucinogen use but lower risks for the use of sedatives or opioids. Conversely, Class 4 (3.0%) had relatively low risks of cocaine, other stimulant or hallucinogen use but high rates of sedative and opioid use. Finally, Class 5 (4.2%) had uniformly high probabilities for the use of all drugs. Rates of psychiatric comorbidity were highest in the polydrug class although the sedative/opioid class had elevated rates of depression/suicidal behaviors and exposure to childhood abuse. Aggregation of population-level data may obscure important subgroup differences in patterns of illicit drug use and psychiatric comorbidity. Further exploration of a 'self-medicating' subgroup is needed.

A recurrent finding in the literature is that individuals who use one type of drug are also considerably more likely to use other drugs (Darke et al., 2003; Degenhardt et al., 2001; Hasin et al., 1988; Kendler et al., 2003; Leri et al., 2003; Tsuang et al., 1998; Zinkernagel et al., 2001). While polydrug use is common, it is not the case that all individuals who have used one drug class have also used all — or any — other classes of drug. Differences in polydrug use may simply reflect differences in availability and opportunity to use (Lillie-Blanton et al., 1993; Morral et al., 2002). It may also be possible, however, to

subtype drug users on the basis of different patterns of polydrug use. There have been only limited prior attempts to classify individuals on the basis of different patterns of drug use, despite numerous previous attempts to subtype alcohol and other drug use on the basis of various factors including age of onset (Clark et al., 1998), personality (Cloninger, 1987) and psychiatric comorbidity (Schuckit et al., 1969), and to develop multidimensional typologies (Babor et al., 1992). These efforts have largely been confined to consideration of aspects of abuse/dependence on single drug categories. There has been relatively little consideration of the extent to which different patterns of use across multiple drug classes may identify subgroups of individuals with distinct patterns of drug use and comorbidity.

One approach to studying this issue involves the use of latent class analysis (LCA; McCutcheon, 1987). A major advantage of LCA is that it assigns individuals to classes on a probabilistic basis, allowing comparison of rates of comorbid psychopathology and other correlates across classes. We have been unable to identify any previous published work applying these techniques to measures of illicit drug use in the general population. Thus, in this article we report on the results of a series of LCAs to assess the extent to which patterns of lifetime use of eight different drug categories (cannabis, cocaine, stimulants, sedatives, opioids, solvents, inhalants) identify different subtypes of illicit drug user. We further explore the extent to which such groups may differ in respect to psychiatric comorbidity.

While illicit drug use has been shown to be associated with increased risks for a range of psychiatric comorbidities, including antisocial behavior, mood disorders and suicidal behaviors (e.g., Degenhardt et al., 2003; Kidorf et al., 2004; Kranzler & Rounsaville, 1998; Rey & Tennant, 2002), it is not the case that all

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individuals who use drugs meet criteria for these disorders. It is therefore possible that different subgroups of illicit drug users may be distinguished by qualitatively distinct patterns of psychiatric comorbidity, although such a possibility has been largely neglected by the common practice of contrasting rates of psychiatric morbidity between users and nonusers of specific drug classes. Thus, a second aim of this study is to explore the extent to which subgroups of lifetime illicit drug users, identified on the basis of LCA, exhibit distinct patterns of psychiatric comorbidity. Such analyses have the added advantage of providing an external validation of the extent to which LCA may have identified qualitatively distinct subgroups of illicit drug user.

Methods

Sample

Interviewees were members of the young adult cohort of the Australian Twin Registry, a volunteer twin panel who were born between 1964 and 1971. Nearly all were first registered with the panel between 1980 and 1982 by their parents in response to approaches either through Australian school systems or via mass media appeals. Twins were first contacted as adults in 1989 by means of a mailed questionnaire. The data presented in this report are derived from responses to a telephone interview conducted by lay interviewers during the period 1996 to 2000. Informed consent was obtained from participants prior to administering the interviews, as approved by the institutional review boards of Washington University-St Louis and the Queensland Institute of Medical Research.

The initial panel recruited between 1980 and 1982 comprised 4262 twin pairs. Of these, 5.9% of pairs could not be located even after extensive efforts to locate family members. Diagnostic interviews were conducted during 1996 to 2000 with 6265 individuals, which comprised 78.1% of the remaining 8020 twins. Allowing for individuals who could not be located; who were deceased, incapacitated or otherwise unable to complete a telephone interview; or who were not assigned for interview by the end of the study, the individual response rate increases to 84.2%. The median age at assessment of respondents was 30 (range = 24–36).

Assessments

A structured diagnostic interview designed for genetic studies on alcoholism, the SSAGA (Bucholz et al., 1994), was adapted for telephone use and updated for *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.; DSM-IV; American Psychiatric Association, 1994) diagnostic criteria.

Psychiatric disorders. The modified SSAGA collected information on full DSM-IV criteria for major depressive disorder as well as separate information on whether subjects had ever contemplated or attempted suicide. DSM-IV conduct disorder, alcohol dependence and nicotine dependence were assessed using the modified SSAGA and diagnoses were assigned by

computer algorithm. The prevalence of these disorders in the entire sample were (a) major depressive disorder, 22.9% of males and 33.0% of females; (b) suicidal ideation, 26.3% of males and 26.4% of females; (c) suicide attempt, 3.4% of males and 4.8% of females; (d) conduct disorder, 20.0% of males and 7.8% of females; (e) nicotine dependence, 32.8% of males and 29.0% of females; (f) alcohol dependence, 30.6% of males and 15.6% of females.

Symptoms of illicit drug abuse/dependence. Individuals reporting any use of cannabis, sedatives, cocaine/other stimulants or opioids on at least a monthly basis were asked additional questions concerning the extent to which they may have experienced symptoms of drug abuse (use in physically hazardous situations, use interfering with major role obligations) or dependence (using more frequently or for longer periods than intended, needing larger amounts to achieve an effect [tolerance], continued use despite use causing emotional problems, recurrent desire to cut down on use). For the current analysis, a measure of abuse/dependence symptomatology was constructed by classifying an individual who reported any of these symptoms as showing symptoms of abuse/dependence for that drug class.

Childhood sexual abuse. Respondents were also asked a series of questions concerning their exposure to unwanted sexual contact, sexual molestation or rape. A composite measure was constructed that classified respondents who reported any such experiences before the age of 18 years as having a history of childhood sexual abuse (Nelson et al., 2002). Reported exposure to childhood sexual abuse was 5.7% for males and 17.0% for females.

Childhood physical abuse. Respondents were asked a series of questions concerning whether they had been physically abused as a child. An individual was classified as being exposed to childhood physical abuse if he/she reported (a) sometimes or often being physically punished so hard that they hurt the next day, (b) being physically injured on purpose by an adult relative, or (c) being physically abused as a child. Reported exposure to childhood physical abuse was 2.9% for males and 4.2% for females.

Statistical Analyses

LCA assumes that symptom (in this case drug use) frequency can be explained by the existence of a small number of mutually exclusive classes, with each class having a distinct profile of item endorsement probabilities (i.e., patterns of drug use). A critical implication of this assumption is that the observed variables are statistically independent conditional on class membership.

A series of models (2–8 class) were fitted to the data from both members of the twin pair by LCA using Mplus (v3.1; Muthén & Muthén, 2004). Standard errors were adjusted to account for familial clustering of data by employing a maximum likelihood ratio (MLR) sandwich estimator, which is robust to nonindependence of observations. MLR uses random starting

values to optimize the parameters. In the initial stage, 500 random sets of starting values were used and a maximum of 100 iterations were allowed for each initial stage. In the final stage, 10 optimizations were allowed. The conservative Bayesian Information Criterion (BIC) was used to select the most parsimonious model that also provided a good fit to the data. These models were fitted to the data from all individuals studied, including those who reported no lifetime illicit drug use.

To investigate the discriminant validity of our preferred LCA solution, we tested for associations between class membership and (a) lifetime rates of substance dependence including DSM-IV-based nicotine and alcohol dependence, (b) measures of psychiatric illness including lifetime history of DSM-IV major depressive and conduct disorders, suicidal ideation, suicide attempt and a nondiagnostic measure of social anxiety, (c) exposure to sexual and physical abuse during childhood, (d) symptoms of abuse or dependence on cannabis, cocaine/other stimulants, sedatives or opioids. Each individual was assigned the most probable class membership associated with their self-report drug use profile under the preferred latent class model. Dummy predictor variables were created for membership in Classes 2 ... *n*, using the first (no/minimal use) class as the reference group, and multinomial logistic regression models were fitted in STATA (StataCorp, 1999), using the Huber-White robust variance estimator to correct for nonindependence of observations on twin pairs.

To further explore the influence of trauma on latent class membership, we selected four covariates: gender (0 = female, 1 = male), conduct disorder, childhood sexual abuse and physical abuse for inclusion in the latent class modeling. The multinomial logistic

regression of the latent class on each individual covariate was estimated in a full model (the best-fitting solution from LCA). Next, we fit a reduced model where regression coefficients were independently estimated for each of the four covariates but were constrained across latent classes. A series of intermediate models, where constraints were imposed across latent classes with similar regression coefficients, were also fit and the change in the -2 loglikelihood fit of the models was compared. Model fitting was done in Mplus using a standard numerical integration algorithm.

Results

Associations Between the Use of Different Illicit Drugs

Table 1 shows the odds ratios and their associated 95% confidence intervals (CI) between measures of lifetime use of eight classes of illicit drugs including cannabis, stimulants, hallucinogens, sedatives, inhalants, cocaine, opioids and solvents. The table also shows the prevalence of drug use among males and females. The results in this table show consistently high associations between the lifetime use of different drug categories with odds ratios (OR) ranging from 4.2 to 51.2. There were particularly strong associations between cocaine use and both cannabis (OR = 51.2, 95% CI = 22.8–114.8) and stimulant use (OR = 39.3, 95% CI = 28.9–53.3) and between hallucinogen use and the use of cocaine (OR = 34.0, 95% CI = 26.6–43.4), stimulants (OR = 25.5, 95% CI = 21.3–30.7) and cannabis (OR = 49.9, 95% CI = 29.3–84.8).

Latent Class Analysis of Lifetime Use of Different Drug Classes

A 5-class model was identified as giving the best fit to the data, by BIC. Specifically, the 5-class solution had the lowest BIC (28,395.2 compared with 28,397.0 for

Table 1
Odds Ratios (95% Confidence Intervals) Between Measures of Lifetime Drug Use

	Cannabis	Stimulants	Hallucinogens	Sedatives	Inhalants	Cocaine	Opioids	Solvents
Cannabis								
Stimulants	12.2 (9.8–15.2)							
Hallucinogens	49.9 (29.3–84.8)	25.5 (21.3–30.7)						
Sedatives	4.6 (3.6–5.9)	7.6 (6.4–9.2)	7.8 (6.4–9.4)					
Inhalants	11.5 (8.1–16.2)	12.7 (10.4–15.4)	15.6 (12.9–19.0)	7.5 (6.1–9.2)				
Cocaine	51.2 (22.8–114.8)	39.3 (28.9–53.3)	34.0 (26.6–43.4)	8.5 (6.8–10.6)	18.8 (15.1–23.5)			
Opioids	4.2 (3.2–5.5)	8.8 (7.1–10.9)	9.5 (7.7–11.7)	14.7 (11.8–18.3)	8.2 (6.6–10.2)	11.1 (8.8–14.1)		
Solvents	14.1 (6.6–30.3)	6.3 (4.6–8.9)	7.4 (5.3–10.3)	8.4 (6.0–11.8)	8.1 (5.8–11.4)	5.0 (3.4–7.4)	5.8 (4.0–8.5)	
Prevalence								
Males	68.8	25.9	18.6	9.2	13.1	8.8	8.1	3.5
Females	53.2	16.8	9.1	9.0	5.6	4.9	5.5	1.5

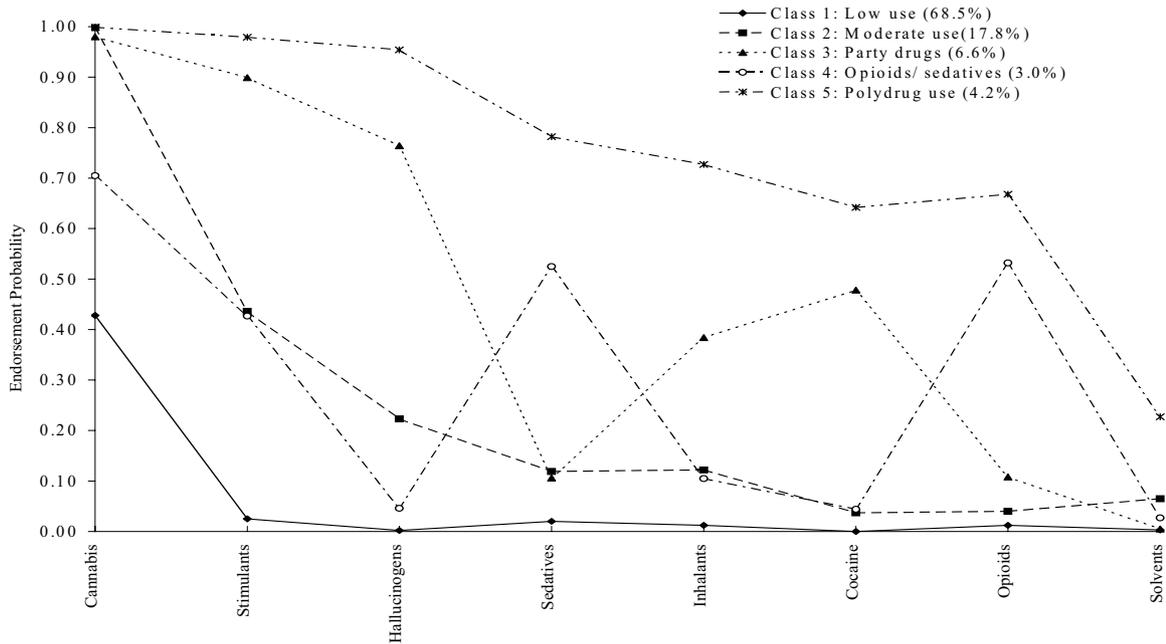


Figure 1
Symptom endorsement profiles by class membership.

the 4-class solution and 28442.9 for the 6-class solution). The symptom endorsement probabilities (SEPs) for each of the eight drug use measures derived from the 5-class model are displayed in Figure 1. Consideration of the SEPs for each item, along with class prevalence, provides a substantive interpretation of each of the five classes:

1. Individuals in the first class (68.5%) had near zero probabilities of the use of all drug classes except cannabis. The probability of cannabis use (42.8%) in this class was substantial, reflecting the high prevalence of cannabis use in this sample.
2. The second class (17.8%) had high probabilities of cannabis use (99.8%), stimulant use (43.6%) and hallucinogen use (22.3%) but relatively low probabilities of the use of other drug classes, with these probabilities ranging from 3.7% for cocaine to 12% for sedatives. Thus, they could be characterized as individuals with moderate rates of lifetime illicit drug use, with most of their drug use being confined to cannabis, stimulants and hallucinogens, the three most commonly used drug classes in this sample.
3. The third group consisted of 6.6% of the sample and, in addition to near universal rates of cannabis use, were characterized by increased risks of stimulant use (89.9%), cocaine use (47.8%), hallucinogen use (76.4%) and, to a lesser extent, inhalant use (38.4%). In contrast, probabilities of solvent (0.5%), sedative (10.6%) and opioid use (10.8%) by this group were low. Thus, members of this group can best be characterized as having high rates of cannabis, cocaine, other stimulant and hal-

lucinogen use but low rates of use of sedatives and opioids.

4. In contrast, members of the fourth group, which comprised 3.0% of the sample, had elevated probabilities of sedative use (52.5%) and opioid use (53.2%) but relatively low risks of the use of other drugs. In fact, their probability of hallucinogen use (4.6%) and cocaine use (4.4%) approximated those for Latent Class 1 and they had the second lowest prevalence of cannabis use (70.5%). It would appear that members of this group are best characterized as having elevated risks for the non-medicinal use of prescription drugs but relatively low rates of other drug use.
5. The fifth class (4.2%) showed the highest probabilities of the use of each drug class, with these probabilities ranging from 22.7% for solvents to 99.9% for cannabis. These individuals are best characterized as extreme polydrug users with high risks for the use of all drug classes.

Perhaps the most striking feature of this graph is the extent to which the lines cross, indicating that the analysis has identified classes within the sample who have qualitatively distinct patterns of drug use rather than simply reflecting differences in the extent of drug use.

Rates of Lifetime Symptoms of Illicit Drug Abuse/Dependence and Latent Class Membership

Figure 2 shows the percentage of individuals in each latent class experiencing at least one symptom of abuse or dependence on cannabis, cocaine/other stimulants, sedatives or opioids. There were dramatic differences between latent classes in rates of illicit drug

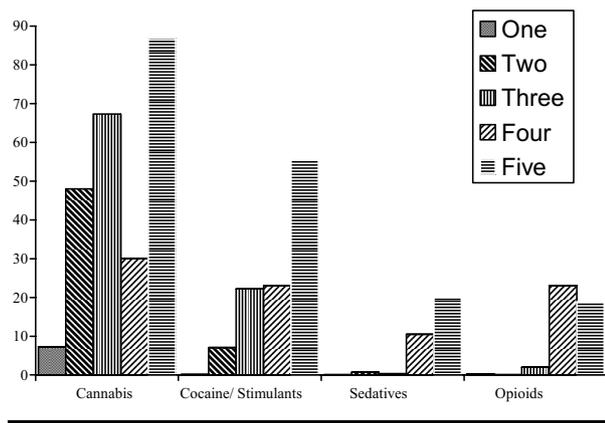


Figure 2

Rates (%) reporting at least one symptom of abuse or dependence on cannabis, cocaine/other stimulants, sedatives and opioids by class membership.

abuse/dependence symptoms. Of particular note, there was evidence that members of Latent Class 4, who were characterized by high rates of lifetime sedative and opioid use, had elevated rates of symptoms of both sedative and opioid abuse/dependence. This indicates that individuals in this class were characterized not solely by lifetime use of these substances but were also at increased risks for symptoms of abuse/dependence. Conversely, members of Latent Class 3, who had been characterized by high rates of cocaine/other stimulant and hallucinogen use, did not have elevated symptoms of sedative or opioid abuse/dependence. They did, however, have elevated rates of symptoms of cannabis and cocaine/other stimulant abuse or dependence.

LCA was successful in identifying a group with high probabilities of experiencing drug-related problems. Although members of Latent Class 5 comprised only 4.2% of the sample, they accounted for 47.9% of all those experiencing opioid-related problems and 45.9% of all those experiencing cocaine/other stimulant problems.

Rates of Exposure to Traumatic Events and Psychiatric Disorders Across Latent Classes

The results of a series of multinomial logistic regression models are summarized in Table 2, which shows the OR describing the risks of each of the substance abuse/dependence and mental health outcomes relative to members of the first group. There were significant differences in the gender composition of the five latent classes with Classes 2 (moderate use), 3 (party drugs) and 5 (polydrug) having a significantly higher proportion of males, relative to the first latent class. In addition the proportion of males in the polydrug class (65.4%) was significantly higher than the corresponding proportions in Classes 2 (52.2%) or 3 (58.6%). In contrast, the majority of Class 4 (sedatives/ opioids) were female (65.5%). Relative to members of the first latent class, exposure to traumatic events (childhood sexual abuse, physical abuse) was elevated in all four

drug use classes, and was particularly high in members of the sedative/opioid and extreme polydrug use classes.

Table 2 also shows that rates of substance dependence and psychiatric disorders were significantly elevated for members of Latent Classes 2, 3, 4 and 5 relative to the first latent class. However, there were also important differences between groups 2 to 5 in risks of these outcomes. Specifically, while members of Latent Class 2 (moderate drug use) generally had the lowest profile of risk, members of Class 4 (sedative, opioid use) had risks of several outcomes that were equivalent to (nicotine dependence, alcohol dependence, conduct disorder, social anxiety) or significantly lower than (cannabis dependence) risks of these outcomes in Group 2. In contrast, members of Latent Class 4 had dramatically elevated risks of major depressive disorder, suicidal ideation and suicide attempt.

Members of Latent Class 3, who were characterized by high probabilities of cocaine and other stimulant and hallucinogen use, had rates of these outcomes that were elevated relative to members of the first latent class but were generally similar to risks in the moderate use group (Latent Class 2). However, while they had greatly elevated odds of meeting criteria for cannabis dependence (OR = 25.22, 95% CI = 18.76–33.90), their odds of social anxiety did not differ significantly from those among members of Group 1 (OR = .86, 95% CI = 0.66–1.22) and were, in fact, significantly lower than the corresponding risks among members of Latent Classes 2, 4 and 5.

Finally, members of the ‘polydrug use’ group had dramatically elevated rates of each of the substance dependence and mental health outcomes: relative to members of the no use/cannabis only group odds of these outcomes were 1.6 to 12.1 times higher in members of the polydrug use group.

The regression of each latent class (with the first latent class serving as the reference group) on physical abuse, childhood sexual abuse, gender and conduct disorder was significant across a majority of the latent classes ($-2LL = 13,413.01$ with 60 estimated parameters). The reduced model where the influence of each covariate was equated across latent classes did not fit the data well ($-2LL = 13,515.45$ for 48 parameters, $\Delta\chi^2 = 102.44$ for $\Delta df = 12$). The best fitting model ($-2LL = 13,428.67$ for 52 parameters, $\Delta\chi^2 = 15.75$ for $\Delta df = 8$) allowed us to (a) constrain the regression coefficients for gender across Latent Classes 2, 3 and 5 ($\beta = 1.054$, $SE = 0.1$) but not Class 4 ($\beta = -0.38$, $SE = 0.3$), (b) constrain the regression coefficients for conduct disorder across Latent Classes 2, 3 and 4 ($\beta = 1.94$, $SE = 0.2$) but not Class 5 ($\beta = 3.36$, $SE = 0.2$), (c) constrain the regression coefficient for childhood sexual abuse across Classes 4 and 5 ($\beta = 1.70$, $SE = 0.2$) and across Classes 2 and 3 ($\beta = 0.96$, $SE = 0.2$), (d) constrain the nonsignificant regression coefficient for physical abuse across Classes 3 and 5 ($\beta = 0.20$,

Table 2

Odds Ratios (95% Confidence Intervals) Between Lifetime Substance Abuse/Dependence, Major Depression and Suicidal Behaviors and Latent Class Membership

	Class 2	Class 3	Class 4	Class 5
Gender (male)	1.6 ^a (1.3–1.8)	2.0 ^{a,b} (1.6–2.6)	.8 ^c (.5–1.1)	2.7 ^b (2.0–3.6)
Physical abuse	2.2 ^a (1.8–2.8)	2.4 ^a (1.7–3.5)	3.8 ^a (2.8–5.3)	4.9 ^b (3.2–7.7)
Sexual abuse	2.0 ^a (1.7–2.5)	2.2 ^a (1.6–3.0)	4.0 ^a (2.6–6.2)	4.1 ^b (3.1–5.5)
Substance dependence				
Nicotine	3.3 ^a (2.8–3.8)	3.8 ^a (3.0–4.9)	2.8 ^a (1.9–4.1)	6.9 ^b (5.3–9.0)
Alcohol	3.4 ^a (2.9–3.9)	4.2 ^a (3.3–5.3)	2.7 ^a (1.8–4.1)	7.6 ^b (5.8–9.9)
Mental health				
Conduct disorder	3.7 ^a (3.1–4.4)	3.7 ^a (2.7–4.9)	2.7 ^a (1.6–4.4)	12.1 ^b (9.3–15.9)
Social anxiety	1.2 ^a (1.1–1.4)	0.9 ^b (0.7–1.1)	1.6 ^a (1.1–2.4)	1.6 ^a (1.2–2.1)
Major depressive disorder	1.7 ^a (1.5–2.0)	1.8 ^a (1.4–2.3)	3.5 ^b (2.4–5.1)	3.4 ^b (2.6–4.4)
Suicidal ideation	2.4 ^a (2.1–2.8)	2.3 ^a (1.8–3.0)	5.1 ^b (3.5–7.5)	6.1 ^b (4.7–7.9)
Suicide attempt	3.7 ^a (2.7–5.0)	2.1 ^a (1.2–3.8)	7.1 ^b (4.1–12.5)	9.3 ^b (6.4–13.5)

Note: Odds ratios with the same superscript are not significantly different from each other.

$SE = 0.4$) and across Classes 2 and 4 ($\beta = 3.35$, $SE = 0.2$) where these coefficients were significant.

Discussion

In this article we have examined patterns of polydrug use in a large sample of young adult twins recruited from the general population. We confirmed previous findings (Darke et al., 2003; Degenhardt et al., 2001; Hasin et al., 1988; Kendler et al., 2003; Leri et al., 2003; Tsuang et al., 1998; Zinkernagel et al., 2001) that the use of one drug is associated with dramatically elevated risks for the use of other drugs, with these odds ratios ranging from 4.2 to 51.2. LCA identified a 5-class solution in which three classes were distinguished by quantitative differences in the probabilities of all drug use: Class 1 had low risks of the use of all drugs (with the exception of cannabis), Class 2 had moderate risks of the use of all drugs and Class 5 was distinguished by uniformly high probabilities for the use of all drugs. The analysis also identified two further latent classes that showed qualitatively distinct patterns of drug use: Class 3 had high rates of cocaine use, other stimulant use and inhalant use but lower risks for the use of sedatives or opioids. In contrast, Class 4 had relatively low risks of cocaine, other stimulant or inhalant use but high rates of sedative and opioid use.

Further analysis revealed marked differences between the five latent classes in risks of substance abuse/dependence symptomatology and mental health problems. In particular, while all substance use groups had generally elevated rates of these outcomes relative to the nonuse/cannabis only class, distinct patterns of comorbidity emerged. Most strikingly, members of Latent Class 4, who had been characterized by high rates of opioid and sedative use, had dramatically elevated rates of major depressive disorder, suicidal ideation and suicide attempt but only moderately elevated risks of other disorders. This pattern of results is consistent with the interpretation that members of this group may have been experimenting with — and later experiencing abuse/dependence symptomatology as a result of — the nonmedicinal use of prescription drugs in an attempt to self-medicate aversive mental states. Further analyses indicated a moderate degree of within-twin pair concordance for membership of Latent Class 4 among monozygotic female twin pairs only, suggesting some heritable influences on risks of membership of this group among females.

The differential pattern of comorbidity observed across classes highlights potential heterogeneity in mechanisms underlying comorbidity and may also help to partially explain apparently contradictory and controversial findings in the research literature regarding such mechanisms as the self-medication hypothesis (Khantzian, 1985, 1997; Markou et al., 1998). Specifically, they suggest that such mechanisms may indeed play an important role in the etiology of comorbidity for some individuals but that such individuals may form a relatively small proportion of the general population and findings and processes unique to such groups may be obscured in analyses which fail to consider potential within-population sources of heterogeneity.

Importantly, the two groups characterized by high rates of sedative and opioid use (and symptoms of abuse and dependence on these drug classes; Latent Classes 4 and 5) also had high levels of exposure to childhood physical and sexual abuse. This is consistent with a growing body of literature demonstrating that childhood abuse plays a causal role in the development of substance use problems and other psychopathology (Fergusson et al., 1996; Nelson et al., 2002). Nonetheless, given our reliance on retrospective reports we cannot be certain whether depressive symptomatology preceded the onset of drug use, a necessary condition for our contention that drug use in this subgroup of the sample represents attempts at self-medication. While both the drug use characteristics of this sample (predominantly misuse of pharmaceuticals with relatively low rates of use of recreational drugs such as cocaine) and related factors (e.g., high rates of exposure to childhood abuse) support the contention that drug use for this group represents attempts at self-medication, it remains possible that drug use could, in fact, have preceded the onset of depressive symptomatology for this group. Thus further replication,

ideally within the context of a prospective design which addresses issues of temporal ordering, is needed to test whether the drug use in this subsample does genuinely reflect attempts at self-medication.

Further research is needed both to determine whether the latent drug use classes identified in this sample can be replicated in other samples and also to determine the associations between such latent classes and a broader array of potential covariates, including both measures of psychopathology and exposure to social/family disadvantage and dysfunction. A further potential limitation concerns our use of a twin sample and our analyses, that did not fully exploit the genetic informativeness of the sample, rest on the assumption that drug use and related processes are the same for twins as for singletons. Nonetheless, while we would like to see the current analyses replicated in a sample of unrelated individuals, the existing literature supports the assumption that analyses of twin and singleton samples are likely to lead to the same results (Kendler et al., 2002).

Finally, these results have implications for gene-hunting efforts that attempt to identify genes associated with or linked to increased risks for poly-substance abuse or dependence (Stallings et al., 2003; Uhl et al., 2001). Specifically, they suggest that, to the extent that the phenotype of polysubstance use/abuse may encompass several distinct subgroups differing in patterns of drug use, etiology and associated mental health problems, such efforts are likely to be compromised. Thus, further refinement of polysubstance use phenotypes may aid in the successful identification of genetic — and environmental — influences associated with these patterns of multiple drug use.

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