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Psychometric modeling of abuse and dependence symptoms across six illicit substances indicates novel dimensions of misuse

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Abstract

Aims—This study explored the factor structure of DSM III-R/IV symptoms for substance abuse and dependence across six illicit substance categories in a population-based sample of males.

Method—DSM III-R/IV drug abuse and dependence symptoms for cannabis, sedatives, stimulants, cocaine, opioids and hallucinogens from 4179 males born 1940-1970 from the population-based Virginia Adult Twin Study of Psychiatric and Substance Use Disorders were analyzed. Confirmatory factor analyses tested specific hypotheses regarding the latent structure of substance misuse for a comprehensive battery of 13 misuse symptoms measured across six illicit substance categories (78 items).

Results—Among the models fit, the latent structure of substance misuse was best represented by a combination of substance-specific factors and misuse symptom-specific factors. We found no support for a general liability factor to illicit substance misuse.

Conclusions—Results indicate that liability to misuse illicit substances is drug class specific, with little evidence for a general liability factor. Additionally, unique dimensions capturing propensity toward specific misuse symptoms (e.g., tolerance, withdrawal) across substances were identified. While this finding requires independent replication, the possibility of symptom-specific misuse factors, present in multiple substances, raises the prospect of genetic, neurobiological and

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Contributors

Drs. Clark and Neale designed the study. Drs. Clark and Gillespie conducted the statistical analysis. Drs. Adkins and Neale provided guidance for the statistical analysis. Dr. Kendler aided in the substantive interpretation of the statistical analyses. Dr. Clark wrote the first draft of the manuscript and all authors contributed to and approved of the final manuscript.

Conflict of Interest

The authors declare they have no conflicts of interest.

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behavioral predispositions toward distinct, narrowly defined features of drug abuse and dependence.

Keywords

Cannabis; cocaine; dependence; DSM; opioids; factor analysis

INTRODUCTION

Effective treatment of substance use disorder (SUD) depends on accurate models and measurement of the underlying psychopathological phenotypes. The importance of this issue has prompted extensive research examining the latent structure of substance misuse characteristics in dialogue with the models implicit in DSM diagnostic categories. Such research recently led to revising the long-standing DSM model of separate substance-specific SUD diagnoses for abuse and dependence, combining both criteria into single substance-specific SUDs in DSM-5 (1). This revision was supported by expert consensus that when considering substances individually, a single factor, known as *liability*, best explains the covariance between DSM abuse and dependence symptoms (2-11). However, less research has jointly considered misuse symptoms across multiple substance categories to examine the possibility of general poly-substance liability and/or more complex latent structures.

Among studies jointly considering misuse across multiple substance classes, results have been equivocal, primarily due to differing methodologies and substantive aims. Contrasting our current psychometric approach of modeling the latent structure of substance misuse phenotypes, previous studies have generally employed biometric approaches to decompose misuse phenotype variance into genetic and environmental components. Results from such research, including previous analyses of the present sample (12), have typically found a mix of substance-specific and general liability factors in both genetic and environmental risk (13-14). This conclusion has not received universal support, however, as other studies have found distinct, but correlated, genetic and environmental influences for cannabis versus other illicit substances (i.e., cocaine, sedatives, stimulants, hallucinogens or opioids) (15), as well as unique genetic liabilities toward illicit (cocaine and cannabis) versus licit (alcohol, nicotine and caffeine) substance dependence (16). Moreover, studies of illicit drug abuse/dependence using categorical, rather than dimensional, latent variable models have suggested distinct patterns of substance misuse (e.g., cannabis-only, prescription drugs), with truly general poly-substance misuse occurring rarely (17). Thus, while general liability to substance misuse has conceptual appeal and has received considerable empirical support, research on the topic has been inconclusive.

One major limitation of the studies described above is they rely on a count of dichotomous indicators to generate DSM diagnoses. For example, DSM V diagnosis of severe substance abuse requires at least 6 of 10 possible symptoms. This method may be sub-optimal because it assumes the symptoms function equivalently both within and between substances. Thus, all symptoms are implicitly assumed to be equally valid measures of SUD diagnosis, regardless of the substance in question. However, as shown by Gillespie *et al.* (18), identical

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symptoms measure different levels of liability across substances, suggesting that substance misuse symptoms do not function equivalently. Thus, condensing symptom data into binary diagnostic categories greatly decreases the amount of unique, relevant information compared to psychometric approaches directly modeling symptom-level data. The situation is only slightly improved in DSM-V, which sub-classifies SUDs into mild, moderate and severe. With symptom-level data it may be possible to identify novel latent dimensions of substance misuse, in addition to improved ability to adjudicate between substance-specific versus general misuse liability. Of particular interest, symptom-level data across a range of illicit substances allow the investigation of poly-substance liability to different misuse characteristics. For instance, there may exist a propensity to develop tolerance across multiple substances. The possibility of poly-substance liability was overlooked in previous analyses of the topic (e.g., Gillespie et al 2007) which only investigated liability structures within one specific substance at a time and not across substances. Identification of liability factors for specific misuse symptoms has the potential to yield novel targets for studies of, e.g., genetic association, neural substrates, prevention or treatment.

In this article, we build on previous research exploring SUD liability by jointly analyzing 13 individual DSM III-R/IV abuse and dependence symptoms across six inclusive illicit substance categories. This approach addresses limitations associated with examining substance categories independently, as well as those due to collapsing symptom data into binary diagnoses. Specifically, the study has two primary aims. The first is to determine whether there are substance-specific and/or misuse symptom-specific liability factors underlying DSM SUD symptom data. Second, we test whether the general SUD liability factor identified in previous research using diagnostic categories represents an accurate model of DSM illicit substance misuse symptoms when examining symptom-level data.

METHODS

Participants and measures

This study is based on data collected from Caucasian adult male twins in the Virginia Adult Twin Study of Psychiatric and Substance Use Disorders (VATSPSUD). Described in detail elsewhere (19), data came from a second wave of interviews between 1994 and 1998. Subjects were eligible for participation if they were successfully matched to birth records, a member of a multiple birth with at least one male, Caucasian, and born between 1940 and 1974 in Virginia, USA. Interviewers had a master's degree in a mental health-related field or a bachelor's degree in this area plus two years of clinical experience. Of 9,417 eligible individuals for the first wave (1993–1996), 6,814 (72.4%) completed the interview. The second interview was completed by 5,629 individuals (82.6%). Complete drug initiation data were available from 4,179 male subjects ranging in age from 20 to 58 years ($\mu = 36.9$ yrs, $\sigma^2 = 9.1$yrs). Unlike previous analyses (18), these data included an additional 1,602 males from opposite-sex and incomplete twin pairs. As recruitment focused on males, analyses of females were relatively underpowered in this sample. This fact, combined with previous research indicating gender differences in substance liability factor structure (20), led us to limit analyses to males only. Subjects were informed of the study's goals and

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provided informed consent. The project was approved by the Virginia Commonwealth University institutional review board

The interview included assessments of lifetime drug use, abuse and dependence across six categories of substances using an adaptation of the Structured Clinical Interview (SCID) (21). Categories (examples) included: cannabis (marijuana and hashish); sedatives (quaalude, Seconal and Valium); stimulants (speed, ecstasy and Ritalin); cocaine (intranasal and crack); opioids (heroin and morphine); and hallucinogens (LSD and PCP). For substances that could be obtained legally, we defined non-medical use as, 1) without a doctor's prescription, 2) in greater amounts or more often than prescribed, or 3) for any reason other than a doctor prescribed. For each substance, the abuse and dependence assessment comprised 13 symptoms listed in Table 1. Symptoms were structured this way to permit assignment of both DSM-III-R and DSM-IV diagnostic definitions. Initially, all 13 symptoms were measured on a three-point scale (definite/probable/no). Consistent with previous research in this sample (18), 'probable' responses were combined with 'definite' to minimize small cell optimization problems. The data were analyzed as dichotomous variables.

Statistical methods

We used Mplus V6.0 (22) to jointly model the diagnostic symptoms from the six substances. Specifically, the latent structure of SUD liability was modeled using confirmatory factor analysis. To handle twin clustering, we specified the "complex" analysis option, which implements a clustering corrected robust maximum likelihood estimator (23). This method uses a Huber/White/Sandwich clustered variance estimator to calculate standard errors (24-25), and has superior estimation properties for the analysis of dichotomous data with small cluster sizes (23), as observed here. Subjects not initiating use of a substance were considered missing for those symptoms.

Confirmatory factor analyses (CFAs)—A series of CFA models were fit to the symptom data for all six substances. Using CFA we were able to test specific hypotheses about the structure of factors underlying liability to SUD. Specifically, we considered models specifying only substance-specific liability factors, only misuse symptom-specific liability factors, or a combination of both, as well as a model specifying a general liability factor underlying all illicit drug abuse and dependence symptoms. Each of these types of factors is explained in more detail below.

Model M1 tests whether substance-specific liability factors best explain the relationship between diagnostic symptoms. M1 specifies a unique liability for developing SUD for each specific substance. Thus, in M1 there are six latent factors, one for each substance (Figure 1A). Each substance factor is defined by the 13 DSM symptoms measured for that substance. Conversely, model M2 (Figure 1B) assumes no distinction between substances and instead models how well latent misuse symptom-specific factors explain the relationship between diagnostic symptoms. Thus, M2 examines if there are unique liabilities associated with specific misuse symptoms across the range of substances considered. For example, the factor pertaining to the symptom of hazardous use models a dimension capturing propensity

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toward engaging in dangerous behavior during drug use, irrespective of the specific substance.

Model M3 combines M1 and M2 by modeling both substance and misuse symptom factors simultaneously. Under M3 (Figure 1C), there are 19 factors being modeled, six substance factors and 13 misuse symptom factors. This model specifies unique liabilities toward both substance-specific SUDs and misuse symptoms across substances. Model M4 (Figure 1D) tests whether there is a single overall liability for SUD across all substances and symptom types. Thus a single latent factor is measured by all 78 observed items (13 symptoms × 6 substances). Additional exploratory analyses were used to explore some minor modifications of these models, e.g., adding a second order poly-substance factor to model M3.

Choice of best fitting and most parsimonious model—All models were compared using omnibus fit indices. In addition to inspecting the difference in the chi-square statistics and traditional CFA model comparison indices, such as the Comparative Fit Index (CFI), Root Mean Square Error of Approximation (RMSEA) and the Akaike Information Criterion (AIC), we used the Bayesian Information Criterion (BIC) and sample-size adjusted BIC (saBIC) indices. For the CFI, values close to one are regarded as indicative of good model fit. For the RMSEA, values of 0.05 or less indicate good model fit, while values of 0.10 and greater are indicative of poor model fit. The lowest, most negative AIC, BIC and saBIC values are indicative of a superior balance of parsimony and explanatory power.

RESULTS

Table 1 displays the endorsement rates of the abuse and dependence symptoms by substance, as well as self-reported use of a substance. Cannabis had the highest self-reported use, while opioids had the lowest. The most frequently endorsed symptom across all drug categories was hazardous use. The two withdrawal symptoms had the lowest endorsement. When different substance users are compared, we see patterns consistent with the established illicit substance abuse literature (26). Cannabis and hallucinogen users reported experiencing fewer symptoms of withdrawal than did cocaine and opioid users. Stimulant users reported ‘using when doing something important’ more frequently than other substances, presumably because they are using the stimulant to enhance performance.

Model fit comparisons

As seen in Table 2, both M1, which specified only substance factors, and M2, which specified only misuse symptom factors, provided poor fit to the data compared to M3, which specified both substance and misuse symptom factors. Regarding omnibus indices, CFI was higher for M3, while RMSEA and all three parsimony indices were lower for M3, consistently indicating superior fit for M3 compared to M1 and M2 (Table 2). Thus, both substance and misuse symptom factors made unique, significant contributions to model fit. Next, to test for the presence of an overall liability to illicit SUD, M4, which specified one overall liability factor, was compared to M3, the best fitting model with substance and misuse symptom factors. These models were non-nested, prohibiting formal chi-square comparisons; however, across all omnibus measures of model fit M3 markedly out-

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performed M4 (Table 2), indicating that a simple, general SUD liability CFA failed to accurately model these symptom-level data.

Characterizing the preferred model M3

The factor loading estimates for the M3 substance factors are plotted with their 95% confidence intervals in Figure 2A, for the abuse symptoms, and in 2B for the dependence symptoms. Most of the symptoms loaded significantly on the substance factors with factors loadings ranging from 0.30-0.93 (See Supplementary Material Table S1). For each substance factor, D3 (Spend time using it or recovering from it) and D4 (Use instead of work or hobbies) had factor loadings greater than 0.70 suggesting that these two symptoms are particularly strong indicators of liability for these substances.

Examining each substance factor individually revealed unique features. The cannabis factor was moderately defined by the two withdrawal symptoms (D6, D7) and A6 (staying away from school/missed appointments). Hazardous use (A1) and having physical or psychological consequences (A4) were not good indicators of cannabis liability, having lower loadings than other symptoms. Liability for sedatives was highly defined by staying away from school and missing appointments (A6) and having social consequences (A3), but like cannabis, was not defined by hazardous use (A1). The stimulant factor had large loadings for legal consequences (A2) and staying away from school/missing appointments (A6). However, stimulant liability was not indexed highly by using when doing something important (A5), physical or psychological consequences (A4) or inability to stop using or quit (D2). Liability to cocaine SUD is highly defined by the tolerance (D5) and withdrawal symptoms (D6 and D7) as well as using longer than thought or planned (D1). It was not measured well by being unable to stop or cut-down on use (D2). Opioid liability was highly indexed by social (A3) and physical and psychological consequences (A4) and was moderately indexed by the tolerance and withdrawal symptoms (D5-D7). Hallucinogen liability was highly defined by using more or longer than intended (D1) and feeling sick when cutting down/stopping (D6), but was not defined well by hazardous use (A1) and physical or psychological consequences (A4). These findings must be interpreted in the light of the misuse symptom factor loadings.

The factor loading estimates and 95% confidence intervals for the misuse symptom factors are plotted in Figure 3A and 3B (See Supplementary Material Table S2 for the misuse factor loadings and standard errors). Their interpretation is that substances with higher loadings index the liability to the specific misuse symptom factor better than those substances with lower loadings. Cannabis tended to have lower loadings in comparison to the other substances on most of the misuse symptom factors and did not load significantly on any of the dependence misuse symptom factors with the exception of D2 (Loss of control). Several of the dependence misuse symptom factors (D1, D3, D4, D6 and D7) had opioids as the highest loading substance while several other misuse symptom factors had sedatives as the highest loading substance (A5, D1 and D5). Examining the factors individually yields additional interesting findings. Cocaine involvement was the strongest indicator of liability toward hazardous use (A1). Cannabis indexed the liability for legal consequences (A2) better than other substances. Use instead of work or hobbies (D4) had only one significant

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loading, from opioids. For the tolerance factor (D5), sedatives and stimulants had the highest loadings. The two withdrawal factors (D6 and D7) both had opioids as the best index of the underlying liability and cocaine as the worst.

DISCUSSION

Overall, results indicate that a model including both substance-specific and misuse symptom-specific factors provides superior fit for symptom-level data across illicit substances relative to the other models considered and in omnibus fit. Furthermore, the relevance of individual questionnaire items varied considerably across substance- and symptom-specific factors. Notably, misuse characteristics pertaining to using instead of work or hobbies (D4) and spending time using or recovering from the substances (D3) emerged as the best indices of symptom-specific SUD liability.

Perhaps the most controversial finding was the lack of support for a general poly-substance liability factor. Several potential explanations for this result exist. First, the general liability model tested here was specified as a single factor measured by all items (Figure 1D). While intuitive and parsimonious, this model is only one of a multitude of potential general liability specifications; so it is possible that other, more complex, poly-substance liability models that were not tested may have provided superior fit. Although comprehensive comparison of the full universe of possible latent structures is impractical and contrary to the aims of CFA, we did explore alternative models of general liability, including adding a second-order factor loading on all substance factors to M3. However, no tested model out-performed M3. The failure of these alternative models is clarified by considering the non-significant correlations observed between substance factors in M3 (See Supplementary Material Table S3), indicating little shared variance. Specifically, out of the 15 covariances modeled between substance factors in M3, only 3 were significant ($p < 0.05$)—opioids-cocaine ($p=0.037$), hallucinogens-stimulants ($p=0.018$) and hallucinogens-sedatives ($p=0.006$). The cannabis factor showed the lowest intercorrelation among substance factors, supporting previous research indicating greater uniqueness for cannabis liability compared to other illicit drugs (15). It is also important to note that substance-factor correlations were attenuated by modeling misuse symptom factors (i.e., comparing M1 v. M3), suggesting that a portion of the variance modeled as general liability in former studies may be more accurately modeled as symptom-specific poly-substance liabilities. However, given the indeterminate nature of latent variable modeling, we cannot claim to have definitively debunked general liability, only to have found no evidence among the models considered. In addition to the possibility of a superior, untested model of general liability, it is also possible that the population may be qualitatively heterogeneous. Thus, future research should test for subpopulations of individuals with distinct liability structures (e.g., factor mixture models) (17).

The findings of this study suggest several directions for future research. Since SUDs are heritable, with about 9-45% of phenotypic variation being explained by additive genetic effects (27-29), it is reasonable to investigate genetic variance in liability to symptom-specific factors. Beseler *et al.* (30) found that the 11 symptoms of the DSM-III-R for alcohol, cannabis, cocaine, opioids, sedatives and stimulants were heritable. Previous studies

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have found genomic regions associated with DSM abuse and dependence symptoms (31-32). Instead of using SUD diagnosis in genetic studies, as is common practice, we suggest using factor scores from the substance and symptom dimensions found here to better identify genetic factors underlying each component of liability and behaviors associated with addiction. The loss of control symptom may be particularly useful in this respect as all substances loaded highly on this factor, suggests that loss of control is a central poly-substance liability characteristic.

Liability structure implications by substance

The results of our liability structure analysis reveal that each substance and symptom indexes the liability of SUD differently. We review these results by substance.

Cannabis—The effects of cannabis use are among the least disruptive. Users were less likely to endorse using instead of work/hobbies, and were least likely to experience physical and psychological consequences. Along with hallucinogen users, they were also less prone to encounter legal consequences. Kosten *et al.* (33) have shown that cannabis use is associated with fewer dependence symptoms than the use of other drugs. The misuse symptom factors in our analyses confirm this result. Cannabis symptoms tended to have lower loadings on most of the misuse symptom factors and did not load significantly on any of the dependence symptom factors with the exception of loss of control. Notably, the cannabis-specific substance factor was moderately defined by the two withdrawal symptoms. While it is has been previously shown that withdrawal symptoms are commonly reported among cannabis users (7), it has been suggested that there is no evidence to support a clear cannabis withdrawal syndrome (34). In recent years, however, there has been increasing evidence in both the human and animal literature of physical and psychological effects associated with cannabis withdrawal (26). Our findings do not suggest that there is a definitive cannabis withdrawal syndrome, but instead suggest that those individuals who do experience withdrawal effects from cannabis have a greater risk of developing cannabis SUD.

Sedatives—Compared to other substances, sedative users were somewhat less likely to report misuse symptoms in this study. Liability for sedative SUD was highly defined by staying away from school/missing appointments and having social consequences. Notably, sedatives were one of the highest loading substances on several of the misuse symptom factors, including using when doing something important. Thus, while misuse is relatively uncommon among sedative users, when it does occur it is a superior indicator of liability for various poly-substance misuse symptoms.

Stimulants—Stimulants were comparatively frequently associated with several symptoms including physical and psychological consequences, using while doing something important and difficulty stopping or reducing. However, the most frequently endorsed stimulant symptoms were relatively poor indicators of the stimulant factor. Thus, characteristics like using when doing something important and physical and psychological consequences were more typical features of illicit stimulant use, while symptoms including social consequences and using instead of work/hobbies occurred rarely but were more indicative of

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psychopathology. This may reflect the fact that some stimulants (e.g., Ritalin, Adderall) may be used illicitly during work or school for cognitive enhancement in the absence of broader psychiatric dysfunction (35).

Cocaine—Cocaine users were comparatively most likely to report misuse, particularly dependence, symptoms. Dependence symptoms, including tolerance and withdrawal, also accurately indexed liability to cocaine SUD. Cocaine users are known to develop tolerance quickly, though there is differential tolerance to cocaine based on the route of administration(26). Oral administration is less likely to produce tolerance effects, presumably because of the lower absorption rate, than intravenous or smoking, which produce rapid acute tolerance(36). Cocaine withdrawal is associated with few physical symptoms, but is associated with psychological symptoms including dysphoria, depression and craving(26) due, in part, to remodeling of the mesolimbic dopaminergic pathway(37). However, cocaine misuse was generally a poor indicator of dependence symptom factors. This seems counterintuitive since cocaine is one of the more addictive substances under consideration here. Perhaps because it is so highly addictive, the endorsement rate is of these symptoms is very high, which increases the error of the factor loadings. Substances with lower rates of endorsement of dependence symptoms may serve as superior indices.

Opioids—Withdrawal symptom endorsement was comparatively frequent among opioid users, particularly for using to prevent sickness. Similarly, liability for opioid SUD was indexed by the dependence symptoms and physical and psychological consequences. Opioids also had the highest factor loadings on the two withdrawal symptom factors. These results are consistent with previous findings of both high mean levels of, and significant inter-individual variation in, opioid withdrawal severity(38). Thus, results highlight the centrality of physical dependence to opioid SUD and suggest that sensitivity to opioid withdrawal is an excellent indicator of poly-substance withdrawal liability.

Hallucinogens—Hallucinogen users generally had lower symptom endorsement rates than the other substances considered. Hallucinogen liability was highly defined by using more or longer than intended and feeling sick when cutting down/stopping. The strong loadings of these items seems counterintuitive because hallucinogens are typically not associated with physical dependence (39), but they may relate to nausea which is a common side-effect of many hallucinogenic compounds (e.g. mushrooms(40)). This anomaly may reflect study participants interpreting these items to mean that hallucinogenic experiences lasted longer than desired, perhaps related to the commonly occurring panic symptom colloquially known as a "bad trip"(41). Similar to cannabis, hallucinogens did not load significantly on the dependence symptom factors, with the exception of loss of control. This result is not unexpected given that hallucinogens are typically used in small doses and in recreational settings (42).

Limitations

Our findings must be interpreted in the context of a few limitations. First, as these data were restricted to white males, it is unclear whether these results will generalize to females or other races and ethnicities. Future research in other samples should test whether the same

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liability structure is seen in females and other races and ethnicities. Second, these analyses did not include cohort effects. However, preliminary analyses with age at interview and age of first drug use as covariates suggested no significant changes. Third, endorsement rates for several items were low. This may result in unreliable parameter estimates, but this uncertainty should be accurately quantified by robust standard error estimates. As a sensitivity analysis, the models were fit to the symptoms from only the three substances with highest reported use from Table 1—cannabis, stimulants, and cocaine. Results were similar to the full six substance analyses. Finally, the current study did not address the possibility of subpopulation-specific liability structures, as fitting factor mixture models to these data led to optimization problems due to model complexity and sparse data. Future research to address this line of inquiry might consider the use of clinical addiction case-control samples because they are likely to provide denser item endorsement to support the mixture models needed to investigate subpopulation-specific liability structures.

CONCLUSION

Results from the CFAs support a model of illicit substance misuse liability including substance specific factors, as well as factors capturing poly-substance symptom-specific liability. Inspection of the substance factors reveals that individual symptoms do not index the liability for misuse to the same degree across the six major illicit drug classes considered. These results also showed variation in the relevance of substances as indices of misuse symptom factors. We identified several symptoms as reliable, poly-substance features of SUD and recommend that they be investigated in genetic and neurobiological studies of substance misuse. Finally, in these symptom-level data, there is no support for a general liability to illicit substance misuse after modeling symptom-specific factors. Further research should consider the possibility of that SUD liability structure may vary across subpopulation classes. A potentially high impact application of these results would be to use the factor scores from the substance and symptom dimensions to better identify measured genetic variants in samples with genome-wide association study data.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- The liability to misuse illicit substance is drug class specific.
- There is no evidence to support a general liability for illicit substance misuse.
- We identified dimensions capturing propensity toward specific misuse symptoms.

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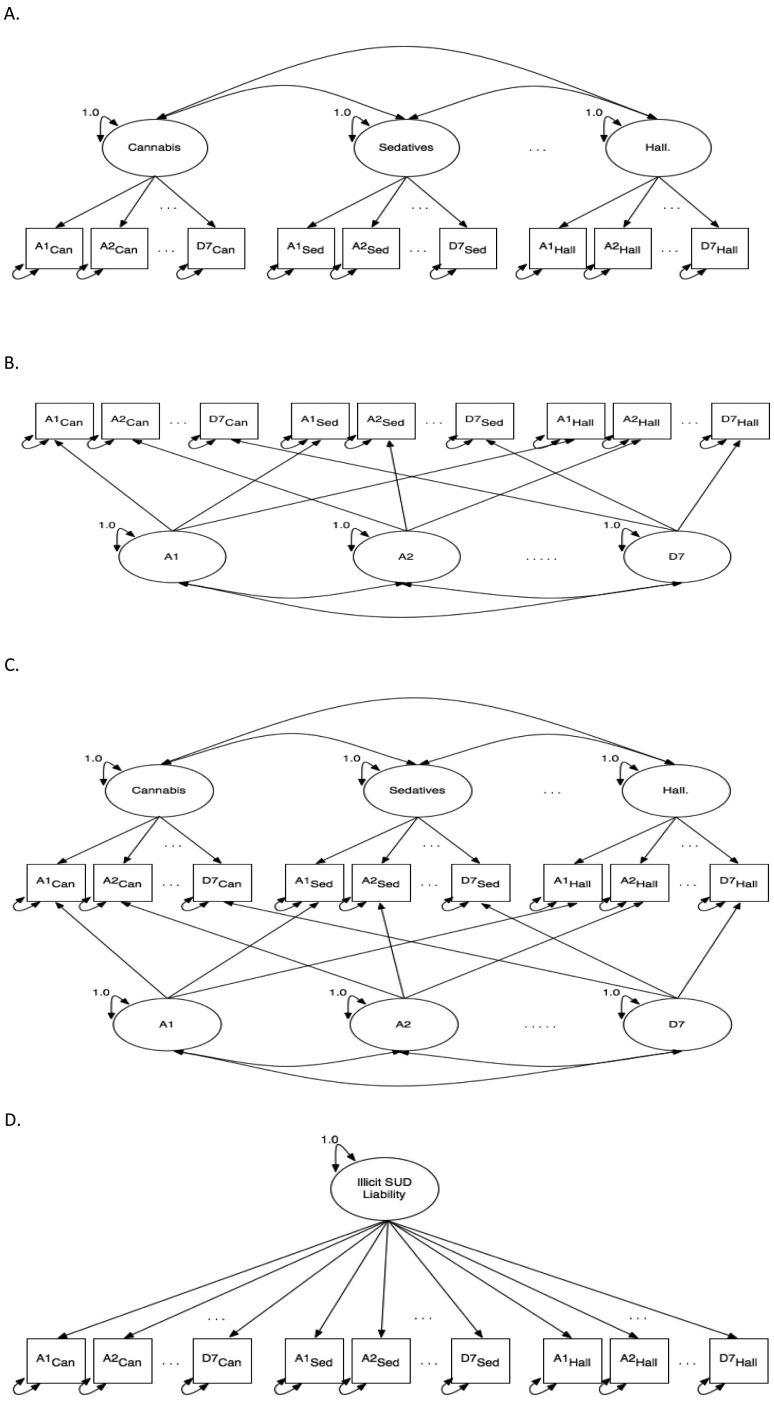

Figure 1.

Path diagrams for confirmatory factor analytic models. Circles represent unobserved latent factors for cannabis (Can), sedatives (Sed), and hallucinogens (Hall). Not shown, but included in the modeling, are cocaine, opioids and stimulants. Boxes represent the 13 observed DSM abuse (A1-A6) and dependence (D1-D7) diagnostic symptoms for each substance. A. Path diagram for M1, which had only substance factors. B. Path diagram for M2, which had only misuse characteristic factors in the model. C. Path diagram for M3,

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which combines M1 and M2 together by having both substance and misuse characteristic factors in the same model. D. Path diagram for M4, which has one latent factor for overall illicit drug use defined by the 13 abuse and dependence symptoms for each substance (13 symptoms × 6 substances = 78 symptoms)

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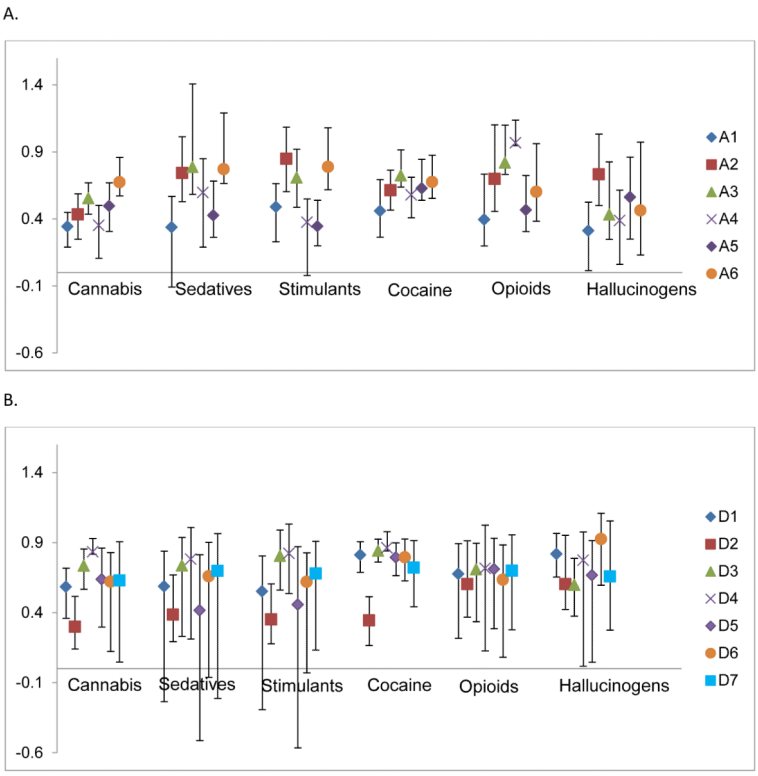

Figure 2.

Plot of substance factor loadings from Model 3 with 95% confidence intervals. A. Abuse symptom substance factor loadings. B) Dependence symptom substance factor loadings. Symptom meaning: A1= Hazardous use; A2 = Consequences: legal; A3 = Consequences: Social; A4 = Consequences: Physical and psychological; A5 = Used often when doing something …important; A6 = Stay away from school\miss appointments; D1 = Used more of longer than thought\planned; D2 = Loss of control: unable to stop\desire to stop; D3 = Spend time taking\using it, recovering from it; D4 = Used instead of work\hobbies; D5 = Need for larger amounts\doses (tolerance); D6 = Withdrawal symptoms: Feeling sick when cutting down\stopping; D7 = Withdrawal symptoms: After not using …use to prevent sickness.

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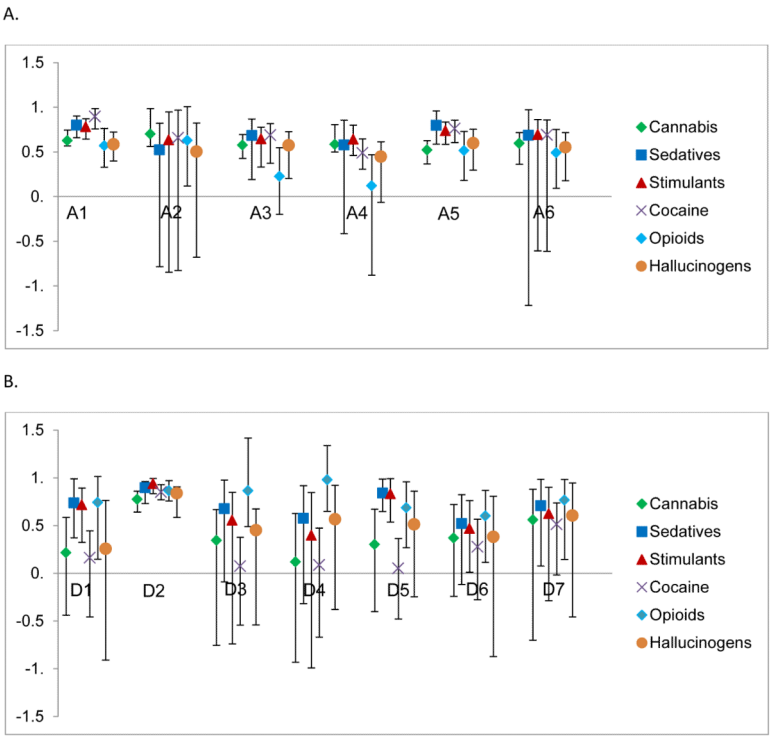

Figure 3.

Plot of misuse characteristic factor loadings from Model 3 with 95% confidence intervals. A. Abuse misuse characteristic factor loadings. B) Dependence misuse characteristic factor loadings. Symptom meaning: A1= Hazardous use; A2 = Consequences: legal; A3 = Consequences: Social; A4 = Consequences: Physical and psychological; A5 = Used often when doing something …important; A6 = Stay away from school\miss appointments; D1 = Used more of longer than thought\planned; D2 = Loss of control: unable to stop\desire to stop; D3 = Spend time taking\using it, recovering from it; D4 = Used instead of work \hobbies; D5 = Need for larger amounts\doses (tolerance); D6 = Withdrawal symptoms: Feeling sick when cutting down\stopping; D7 = Withdrawal symptoms: After not using … use to prevent sickness.

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Table 1

Percentage endorsement for abuse and dependence symptoms based on subjects who reported illicit drug use, experimentation or non-medical use of illicit substances. Symptoms that begin with an A are thought to measure abuse, while symptoms that begin with a D are thought to measure dependence.

	Cannabis		**Sedatives**		**Stimulants**		**Cocaine**		**Opioids**		**Halluc.**	
Have you ever taken any of these drugs?	**n = 2313**		**n = 539**		**n = 843**		**n = 767**		**n = 292**		**n = 636**	
Symptoms	Freq.	%	Freq.	%	Freq.	%	Freq.	%	Freq.	%	Freq.	%
A1-Hazardous use	583	25	114	21	204	24	200	26	67	23	130	20
A2-Consequences: Legal	64	3	15	3	16	2	34	4	11	4	6	1
A3-Consequences: Social	221	10	41	8	48	6	114	15	28	10	35	6
A4-Consequences: Physical and psychological	189	8	33	6	147	17	138	18	28	10	63	10
A5-Used often when doing something …important	352	15	50	9	210	25	78	10	41	14	36	6
A6-Stay away from school/ miss appointments	135	6	36	7	30	4	81	11	21	7	37	6
D1-Used more or longer than thought/planned	254	11	51	9	113	13	182	24	41	14	38	6
D2-Loss of control: Unable to stop/desire to stop, tried to cut down or stop using	428	19	87	16	208	25	210	27	53	18	89	14
D3-Spend time taking/using it, recovering from it, or doing whatever	220	10	36	7	63	7	123	16	37	13	42	7
D4-Used instead of work/hobbies	124	5	24	4	24	3	92	12	25	9	26	4
D5-Need for larger amounts/doses (tolerance)	305	13	40	7	98	12	141	18	32	11	36	6
D6-Withdrawal symptoms: Feeling sick when cutting down/stopping	56	2	26	5	67	8	102	13	27	9	13	02
D7-Withdrawal symptoms: After not using … use to prevent sickness	28	1	17	3	29	3	40	5	21	0.07	3	0.5

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Table 2

Confirmatory factor analysis model fit results. Model fit indices include: Comparative Fit index (CFI), Root Mean Square Error of Approximation (RMSEA), Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC) and sample size adjusted Bayesian Information Criterion (saBIC).

Model	χ^2	DF	*p*-value	CFI	RMSEA	AIC	BIC	saBIC
M1: Drug Factors Only	4175	2910	<0.001	0.78	0.017	4517	5431	4887
M2: Misuse Characteristic Factors Only	3647	2847	<0.001	0.86	0.013	4115	5365	4622
M3: Drug and Misuse Characteristic Factors	2966	2754	<0.001	0.96	0.007	3620	5367	4328
M4: General Liability Factor	4598	2925	<0.001	0.71	0.019	4910	5744	5248
M1 vs. M3	1209	156	<0.001					
M2 vs. M3	681	93	<0.001					