Stimulant use and symptoms of abuse/dependence: Epidemiology and associations with cannabis use—A twin study

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Abstract

Background: This paper explores the magnitude of– and extent of overlap between– additive genetic, shared environmental and non-shared environmental influences on lifetime stimulant use and on stimulant abuse/dependence symptoms; the associations between stimulant use and cannabis use and the extent to which these associations can be attributed to common or correlated genetic and environmental influences.

Methods: Self-report data on lifetime stimulant use, abuse/dependence symptoms and corresponding measures of cannabis involvement were collected from a sample of 6265 male and female Australian twins born 1964–1971.

Results: Approximately one in five study participants reported lifetime stimulant use while 5% reported experiencing at least one symptom of abuse/dependence. Multivariate genetic model fitting indicated moderate genetic influences on stimulant use (40%) and symptoms (65%) while there was no evidence of sex differences in the magnitude of these influences. Despite some overlap in genetic influences on these measures, approximately 60% of the genetic variance in symptoms was specific to this phenotype. There were also strong genetic and shared environmental correlations between the factors associated with stimulant use and those associated with cannabis use.

Conclusions: There were moderate genetic influences on stimulant use and stimulant abuse/dependence with moderate overlap between the genetic factors associated with these outcomes. Additionally, there were strong associations between measures of lifetime stimulant use and analogous measures of cannabis use which, importantly, could be largely attributed to shared familial risk factors predisposing to both stimulant and cannabis use.

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1. Introduction

After cannabis, stimulants are among the most commonly used illicit drugs. For example, in the US, it has been estimated that amphetamines (including methamphetamine and the non-medical use of prescribed pharmaceuticals (e.g., Ritalin)) are the second most commonly used illicit drug among 12th graders with 14.4% reporting lifetime use of amphetamines and 9.9% reporting past year use (Johnston et al., 2004). In addition, there is some recent evidence from the treatment episode data system (TEDS) of a dramatic rise in the number of people seeking treatment for stimulant related disorders. Specifically, between 1992 and 2002 there was a five-fold increase in the proportion of the adult population presenting for treatment whose primary drug population was classified as stimulants: from 10 admissions per 100,000 population in 1992 to 52 admissions per 100,000 population in 2002 (U.S. Department of Health and Human Services, 2004). However, there appears to have been relatively little published research focusing exclusively on the etiology of and patterns of stimulant use. Against this general background, the current paper focuses on several distinct issues relating to stimulant use. The first involves a description of lifetime rates of stimulant use and the correlates of such use. Available evidence, although based largely on the analysis of aggregate measures of illicit drug use, has suggested that such use is likely to be elevated in individuals characterized by early childhood disadvantage, exposure to childhood abuse, early conduct problems and related disadvantages (e.g., Hawkins et al., 1992).
A second goal is to fit a series of multivariate genetic models to data on lifetime stimulant use, symptoms of stimulant abuse or dependence and lifetime cannabis use. These models allow exploration of three substantive issues. Firstly, they will allow an examination of the extent to which lifetime patterns of stimulant use and symptoms of stimulant abuse/dependence are influenced by additive genetic, shared environmental and non-shared environmental influences. While several previous reports have documented significant heritable influences on lifetime stimulant use and related phenotypes, there has been considerable variability in these estimates, which have ranged from 0.16 to 0.69 (Agrawal et al., 2004; Karkowski et al., 2000; Kendler et al., 2000, 2003; McGue et al., 2000; Tsuang et al., 1998, 1999; Vanden Bree et al., 1998). In addition, at least one previous report has concluded that there are no significant heritables influences on lifetime stimulant use (Kendler et al., 1999).

Further, one issue which has yet to be explored and which we wish to focus on is the current study concerns the extent to which heritable influences on stimulant use and abuse/dependence symptoms may vary by gender. Although we are unaware of any study which has attempted to specifically test for possible sex differences in the heritability of stimulant use or abuse/dependence symptoms, there is at least some suggestive evidence that such influences may be more prominent in males than in females. Specifically, in a study of 1198 male same-sex twin pairs Kendler et al. (2000) reported that 69% (95% CI = 60–77) of variance in liability to stimulant use could be attributed to genetic influences while, in a sample of 1934 female twins, Kendler et al. (1999) reported no significant genetic influences on liability to stimulant use. While direct comparison of these results does not provide a formal test of possible sex differences, they do suggest the possibility of such differences.

Additionally, we are interested in exploring the extent to which any heritable influences on lifetime stimulant use and symptoms of abuse/dependence are specific to stimulants or overlap with and are correlated with the heritable influences associated with cannabis use. Cannabis is the most commonly used illicit drug in most developed societies and there appears to be consistent evidence of moderate to high heritabilities for cannabis use and related phenotypes, including abuse and dependence: estimates of the heritability of cannabis use have ranged from 13% to 85%, those for abuse have ranged from 72.4% to 76% and those for dependence have ranged from 44.7% to 62.3% (Kendler and Prescott, 1998; Kendler et al., 2000, 2002; Lyskey et al., 2002; Maes et al., 1999; McGue et al., 2000; Miles et al., 2001; True et al., 1999; Tsuang et al., 1998). The extent to which such heritable factors may be correlated or overlap has important implications, particularly given the common practice, noted above, of exploring combined categories of “any illicit drug use”.

Finally, a related goal is to explore the extent to which genetic and environmental influences on stimulant use overlap or are correlated with those factors associated with liability to stimulant abuse/dependence symptomatology. Specifically, while some lifetime use of stimulants is relatively common, only a minority of those who use stimulants transition to experiencing symptoms of abuse or dependence on these drugs, with some estimates suggesting that approximately 13.3% of those who use amphetamines develop abuse/dependence (Tsuang et al., 1999). While genetic factors have been implicated in both stimulant use and the liability to stimulant abuse/dependence, relatively little is known regarding whether the genetic influences on use are similar to or different from those factors associated with abuse/dependence.

These issues are explored using data from a young adult volunteer sample of Australian twins born 1964–1971. Full details of this study are provided below.

2. Methods

2.1. Sample

Interviewees were members of the young adult cohort of the Australian Twin Register, 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 (Heath et al., 2002). The data presented in this report are derived from responses to a telephone interview conducted by lay interviewers during the period 1996–2000 (Nelson et al., 2002; Knopik et al., 2004). Verbal 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. Subject to respondent consent, all interviews were audio taped for quality control. Separate interviewers interviewed each member of a twin pair, so that interviews were conducted without prior knowledge of the history of the twin or his or her co-twin or family members.

The initial panel recruited in 1980–1982 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 1996–2000 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).

2.2. 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 DSM-IV diagnostic criteria (American Psychiatric Association, 1994). Diagnostic assessments in the adapted SSAGA (SSAGA-OZ) included lifetime history of alcohol dependence, major depression and childhood conduct disorder as well as a non-diagnostic assessment of history of social anxiety.

2.3. Measures

2.3.1. Measures of stimulant use. Two measures of stimulant use were included in the analyses, as described below:

1. Lifetime stimulant use. Lifetime use was based on respondent report of having ever used stimulants in their lifetime.

2. Symptoms of stimulant abuse/dependence. Individuals reporting using stimulants 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 stimulant abuse/dependence.
Each of these measures referred only to illicit or non-prescribed use of stimulants and therefore excluded the use of prescribed medications for the treatment of ADHD or other conditions.

2.3.2. Lifetime cannabis use. Lifetime use was based on respondent report of having ever used cannabis in their lifetime.

2.3.3. Sociodemographic, family and individual factors. A range of social, family and individual factors were selected for inclusion in the analyses based on their availability within the data set and on previous research indicating putative relationships between these factors and risks of substance use and/or substance related problems.

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 which 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).

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.

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.

2.4. Statistical analyses

We first tested for sex differences in the prevalence of lifetime stimulant use and symptoms of abuse or dependence using the odds ratio and its associated 95% confidence intervals. Similarly, associations between lifetime measures of stimulant involvement (use and abuse/dependence symptomatology) and corresponding measures of lifetime cannabis involvement were assessed using the odds ratio and its associated 95% confidence interval.

The statistical significance of the association between lifetime stimulant use and co-twin’s stimulant use controlling for socio-demographic variables was tested using methods of logistic regression analysis. Next, standard genetic model fitting procedures (Eaves et al., 1978; Kendler et al., 1986; Neale et al., 1999) were used to fit a trivariate Cholesky model, described in detail by Neale and Cardon (1992), to the data. These models provide estimates of the additive genetic, shared environmental and non-shared environmental influences on lifetime stimulant use, lifetime cannabis use and symptoms of stimulant abuse/dependence. These models also allow for the estimation of the extent to which these sources of variation in stimulant use, cannabis use and symptoms of stimulant abuse/dependence are correlated and are illustrated diagrammatically in Fig. 1. These models were fitted to the data using methods of maximum likelihood estimation as implemented in the statistical package Mx (Neale et al., 1999).

3. Results

3.1. The prevalence and correlates of lifetime stimulant use

Approximately one in five study participants reported lifetime stimulant use with rates of use being higher among males (25.9%) than among females (16.8%; OR = 1.73, 95% CI 1.53–1.96). Table 1 shows, for males and females, the associations between stimulant use, psychiatric and other risk factors and co-twin’s history of lifetime stimulant use from multiple logistic regression models. Childhood conduct disorder was a strong predictor of stimulant use in both males (OR = 2.6, 95% CI = 2.1–3.3) and females (OR = 3.2, 95% CI = 2.4–4.4) as were major depression (males OR = 1.6, 95% CI = 1.3–2.1; females OR = 1.9, 95% CI = 1.6–2.4) and exposure to childhood sexual abuse (males OR = 2.2, 95% CI = 1.5–3.5; females OR = 1.6, 95% CI = 1.3–2.0). Among females only, not being raised by both biological parents to age 16 had a marginally significant protective effect on risks of stimulant use (OR = 0.8, 95% CI = 0.6–1.0).

After control for these variables significant associations remained between MZ co-twin’s stimulant use and risk of stimulant use: both women (OR = 6.4; 95% CI = 4.3–9.5) and men (OR = 3.2, 95% CI = 2.2–4.7) whose MZ co-twin had used stimulants had elevated odds of lifetime stimulant use. Conversely, risks of stimulant use were significantly reduced among men (OR = 0.5, 95% CI = 0.4–0.7) – but not women (OR = 0.9, 95% CI = 0.7–1.3) – whose MZ twin had not used stimulants. Additionally, for both women and men having a DZ twin who had used stimulants was associated with significantly increased risks for stimulant use. Comparison of odds ratios indicated that this

<table>
<thead>
<tr>
<th></th>
<th>Females</th>
<th></th>
<th>Females</th>
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<tbody>
<tr>
<td></td>
<td>Odds ratio</td>
<td>95% CI</td>
<td>Odds ratio</td>
<td>95% CI</td>
</tr>
<tr>
<td>MZ co-twin used stimulants</td>
<td>6.4</td>
<td>4.3–9.5</td>
<td>3.2</td>
<td>2.2–4.7</td>
</tr>
<tr>
<td>DZ female co-twin used stimulants</td>
<td>4.9</td>
<td>2.8–8.3</td>
<td>2.5</td>
<td>1.6–4.0</td>
</tr>
<tr>
<td>DZ male co-twin used stimulants</td>
<td>2.2</td>
<td>1.5–3.4</td>
<td>2.5</td>
<td>1.7–3.8</td>
</tr>
<tr>
<td>MZ co-twin unaffected</td>
<td>0.9</td>
<td>0.7–1.3</td>
<td>0.5</td>
<td>0.4–0.7</td>
</tr>
<tr>
<td>DZ male co-twin unaffected</td>
<td>0.9</td>
<td>0.6–1.3</td>
<td>0.7</td>
<td>0.5–1.0</td>
</tr>
<tr>
<td>Not raised by both parents up to age 16</td>
<td>0.8</td>
<td>0.6–1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Childhood sexual abuse</td>
<td>1.6</td>
<td>1.3–2.0</td>
<td>2.2</td>
<td>1.5–3.5</td>
</tr>
<tr>
<td>Childhood conduct disorder</td>
<td>3.2</td>
<td>2.4–4.4</td>
<td>2.6</td>
<td>2.1–3.3</td>
</tr>
<tr>
<td>Major depressive disorder</td>
<td>1.9</td>
<td>1.6–2.4</td>
<td>1.6</td>
<td>1.3–2.1</td>
</tr>
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</table>
increased risk of stimulant use was significantly higher among individuals with an MZ affected co-twin than among those with a DZ affected co-twin among women but not men. This set of results is consistent with the hypothesis that, even after control for observed covariates, there is a significant residual genetic influence on stimulant use among women and a significant residual shared environmental influence on risks in men.

3.2. Lifetime stimulant use, cannabis use and the transition from stimulant use to symptoms of abuse/dependence

While the majority of those who reported lifetime stimulant use reported using these drugs on only a few occasions a small minority (23.4% of users, 4.9% of entire sample) reported experiencing symptoms of stimulant abuse or dependence. Again there were significant gender differences with abuse/dependence symptoms more common among males than among females in the entire sample (6.5% versus 3.5%, OR = 1.90, 95% CI = 1.50–2.40).

There were also strong associations between lifetime cannabis use and both stimulant use and stimulant abuse/dependence symptoms: among females lifetime cannabis use was associated with a 11.4-fold (95% CI = 8.6–15.2) increase in the odds of lifetime stimulant use and an 11.8-fold (95% CI = 6.0–23.4) increase in the odds of experiencing at least one symptom of stimulant abuse/dependence. The corresponding odds ratios among males were 12.1 (95% CI = 8.6–16.8) and 18.0 (95% CI = 7.4–44.1).

3.3. Multivariate genetic modeling of cannabis use, stimulant use and symptoms of stimulant abuse/dependence

Next, a series of trivariate Cholesky models were fitted to the data on lifetime stimulant use, cannabis use and stimulant abuse/dependence symptomatology. This model fitting process is summarized in Table 2 and proceeded as follows. An initial model was fit to the data assuming that the proportion of variance of each of the three phenotypes that could be attributed to additive genetic, shared and non-shared environment differed between men and women. A series of models (2–4 in Table 2) then tested whether it was possible to equate A, C and E for men and women. The non-significant \( \chi^2 \) indicated no significant deterioration in model fit and therefore it was possible to equate each of these parameters individually. Next, we confirmed that it was possible to equate both A and C across men and women simultaneously (model 5). It was, however, not possible to equate all three parameters across males and females. The fourth step involved dropping parameters which were estimated at their lower bounds: removing shared environmental paths specific to stimulant use and to stimulant abuse/dependence symptoms resulted in a non-significant reduction in model fit (models 6–7). Finally, we conducted a series of tests of whether it was possible to equate thresholds across zygosity groups (models 8–15). This model fitting process indicated that for males the thresholds could be equated across zygosity groups (monozygotic, same sex dizygotic and males from opposite sex dizygotic twin pairs) for each of these measures. Similarly, thresholds could be equated for females across all zygosity groups for stimulant use and for stimulant abuse/dependence. The cannabis threshold for female dizygotic twins from opposite sex twin pairs could not, however be equated with the other groups, indicating that females from opposite sex twin pairs had a higher prevalence of lifetime cannabis use than females from either monozygotic or same sex dizygotic twin pairs. Finally, males were more likely to than females to have used cannabis, stimulants and to develop symptoms of stimulant abuse or dependence.

The parameter estimates from the preferred model (model 12 in Table 2) are shown in Table 3 and their substantive interpretation is given below.

This model estimated that, for both men and women 40% of the variance in stimulant use could be attributed to additive genetic factors (95% CI = 18–61%), 22% could be attributed

### Table 2

<table>
<thead>
<tr>
<th>Model</th>
<th>Comparison Model</th>
<th>( \Delta \chi^2 )</th>
<th>( \Delta \text{d.f.} )</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A, C, E estimated separately for men and women</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>2</td>
<td>Equate A for men and women</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>3</td>
<td>Equate C for men and women</td>
<td>1</td>
<td>4.636</td>
<td>6</td>
</tr>
<tr>
<td>4</td>
<td>Equate E for men and women</td>
<td>1</td>
<td>7.791</td>
<td>6</td>
</tr>
<tr>
<td>5</td>
<td>Equate A and C for men and women</td>
<td>1</td>
<td>3.178</td>
<td>5</td>
</tr>
<tr>
<td>6</td>
<td>No new C for stimulant use</td>
<td>2</td>
<td>5.883</td>
<td>6</td>
</tr>
<tr>
<td>7</td>
<td>No new C for stimulant dependence</td>
<td>5</td>
<td>0.43</td>
<td>2</td>
</tr>
<tr>
<td>8</td>
<td>Equate the thresholds for MZF and DZF</td>
<td>6</td>
<td>0.004</td>
<td>1</td>
</tr>
<tr>
<td>9</td>
<td>Equate the thresholds for MZM and DZM</td>
<td>7</td>
<td>0.619</td>
<td>3</td>
</tr>
<tr>
<td>10</td>
<td>Equate DZOM thresholds to MZM and DZM</td>
<td>8</td>
<td>2.534</td>
<td>3</td>
</tr>
<tr>
<td>11</td>
<td>Equate DZOF thresholds to MZF and DZF</td>
<td>9</td>
<td>3.379</td>
<td>3</td>
</tr>
<tr>
<td>12</td>
<td>Equate DZOF thresholds to MZF and DZF for cannabis use and stimulant use only</td>
<td>10</td>
<td>11.184</td>
<td>3</td>
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<tr>
<td>13</td>
<td>Equate cannabis threshold for DZOF and men</td>
<td>10</td>
<td>2.379</td>
<td>2</td>
</tr>
<tr>
<td>14</td>
<td>Equate stimulant use threshold for men and women</td>
<td>12</td>
<td>36.775</td>
<td>1</td>
</tr>
<tr>
<td>15</td>
<td>Equate stimulant problem threshold for men and women</td>
<td>12</td>
<td>75.860</td>
<td>1</td>
</tr>
</tbody>
</table>

\( a \) The nonshared environmental correlation between novel stimulant use effects and stimulant dependence was fixed to 0 in all models in order to have the model be identified.

\( b \) Final model.
to shared environmental factors (95% CI = 7–40%), and 38% could be attributed to non-shared environmental factors (95% CI = 31–46%). Similarly, the model estimated that for men and women the variance in liability to lifetime cannabis use could be attributed to additive genetic (60%, 95% CI = 45–72%), shared environmental (9%, 95% CI = 1–22%) and non-shared environmental factors (32%, 95% CI = 26–36% (men); 26–34% (women)). Additionally, the model estimated substantial heritable influences on symptoms of stimulant abuse/dependence with 65% (95% CI = 11–85%) of the variance in liability to abuse dependence attributed to additive genetic factors, 8% (95% CI = 0–42%) to shared environmental factors and 28% (95% CI = 14–47% (men); 14–44% (women)) to non-shared environmental factors.

Importantly, this model also provided estimates of the extent to which the genetic and shared environmental factors associated with cannabis use, stimulant use and symptoms of stimulant abuse/dependence were correlated. For men, the genetic correlation between stimulant use and each measure ranged from 0.63 to 0.74 while the genetic correlation between cannabis use and stimulant problems was non-significant (0.31). There were also significant non-shared environmental correlations between stimulant use and cannabis use for both genders and between cannabis use and stimulant problems for men only. These correlations indicate that there was moderate overlap in the genetic but only modest overlap in the environmental factors contributing to liability to cannabis use, stimulant use and stimulant abuse/dependence. The incomplete overlap between these factors indicated that there were outcome specific factors contributing to both genetic and environmental vulnerability. Thus, for example, the estimated genetic correlation between cannabis use and stimulant use (0.74) indicated that, while there was 55% overlap in the genetic influences on cannabis and stimulant use, 45% of genetic factors were specific to stimulant use. Importantly, these analyses also indicated that, while there was considerable overlap in the factors associated with stimulant use and those associated with the development of abuse/dependence symptomatology, there was also evidence of genetic and environmental factors specific to the development of abuse/dependence symptomatology: the model estimated that approximately 40% of the genetic variance in symptomatology was shared with use while 60% was specific to abuse/dependence. Because there were no shared environmental influences specific to either stimulant use or stimulant problems, the correlation was 1.00 for the modest C component.

4. Discussion

Although some lifetime use of stimulants was relatively common in this sample, only a small minority of the sample reported relatively frequent or problem use. Consistent with previous research on both cannabis and other substance use, each measure of lifetime stimulant involvement was more common among males than among females.

Other correlates of lifetime stimulant use identified in the multiple logistic regression models were again consistent with those previously identified in the literature. These included conduct disorder, exposure to childhood sexual abuse and lifetime affective disorders. Although consistent with previously identified correlates of substance use, our capacity to fully explore variables associated with lifetime stimulant use was limited by a number of features including: our reliance on retrospective reports of childhood events; a limited assessment of childhood sexual abuse and a constrained number of potential correlates available for examination. One controversial risk factor not included in our analyses was childhood attention deficit hyperactivity disorder (ADHD): while controversy remains as to whether ADHD, in the absence of conduct disorder, is independently associated with increased risks for the development of substance use and related problems (Lynskey and Hall, 2001), one ongoing concern particularly relevant to the current analyses is the extent to which the prescribed used of psychostimulants (commonly used to treat childhood ADHD) may heighten risks for the development, specifically, of stimulant use and abuse/dependence. However, the available literature suggests that the use of prescribed stimulants is, in fact, associated with decreased risks for the development of illicit stimulant use (Faraoe and Wilens, 2003; Wilens et al., 2003).

Multivariate genetic modeling indicated a moderate degree of heritability of both lifetime stimulant use and symptoms of stimulant abuse/dependence: additive genetic factors accounted for 40% of the variance in stimulant use and 65% of the variance in symptoms of abuse/dependence while shared environmental factors accounted for 22% and 8% of the variance, respectively, in these phenotypes. Hypothesis testing indicated no significant sex differences in the heritability of either stimulant use or abuse/dependence symptomatology. The apparent discrepancy between these results and the work of Kendler et al. (1999, 2000) may be due to a number of factors including cohort or cross-national differences in influences on stimulant use. Nonetheless, the extent that we were able to conduct formal tests of the hypothesis that there are sex differences in the heritability of

### Table 3

Trivariate genetic models for lifetime cannabis, stimulant use and symptoms of stimulant abuse/dependence

<table>
<thead>
<tr>
<th>Variance components</th>
<th>Correlations</th>
</tr>
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<tbody>
<tr>
<td>Cannabis use</td>
<td>Cannabis use-stimulant use</td>
</tr>
<tr>
<td>A</td>
<td>0.60 (0.45–0.72)</td>
</tr>
<tr>
<td>B</td>
<td>0.09 (0.01–0.22)</td>
</tr>
<tr>
<td>E – men</td>
<td>0.32 (0.26–0.36)</td>
</tr>
<tr>
<td>E – women</td>
<td>0.32 (0.26–0.34)</td>
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stimulant use, we have confidence in the conclusion that there are no sex differences in the relative contributions of genetic and shared environmental influences on stimulant use. Additionally, our results are consistent with a number of previous reports that have not reported sex differences in the heritability of stimulant or amphetamine use (Van den Bree et al., 1998), although it is not clear whether these reports specifically tested for such differences.

Importantly, our analyses, which simultaneously modeled influences on use and symptomatology, indicated that, while there was a moderate degree of overlap between the additive genetic factors associated with stimulant use and those associated with symptomatology, approximately 65% of the genetic influences on symptomatology were specific to the experience of these outcomes. While our use of a twin methodology has necessarily limited us to a consideration of the sum of latent genetic vulnerabilities, it seems probable that genetic factors related to a propensity to risk taking or novelty seeking may be primarily related to vulnerability to substance initiation (Agrawal et al., 2004) while factors related to drug metabolism may be specific to risks for the development of symptomatology (conditional on exposure).

Finally, our results indicated a high degree of overlap in both the genetic and the shared environmental influences associated with stimulant use and those associated with cannabis use, suggesting that a large proportion of the correlation or comorbidity between measures of stimulant and cannabis use could be explained by the influence of shared or correlated familial risk factors (both genetic and shared environmental) that predispose to the use of these drugs. These results parallel previous findings of a high degree of overlap in the genetic factors associated with abuse across a range of drug classes (Kendler et al., 2003; Tsuang et al., 1998).

Nonetheless, given the high degree of overlap or correlation between the genetic and shared environmental risk factors associated with stimulant use and cannabis use, it is of considerable interest to consider what distinguishes “pure” users of stimulants and cannabis both from each other and from polydrug (stimulant and cannabis) users. The high genetic and shared environmental correlations from the current results suggest that the sources of these exclusive stimulant/cannabis use paths are likely to lie in the non-shared environment and we would posit that they reflect aspects of peer and social networks that encourage the use of specific drug classes.

Acknowledgements

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