Title page

Associations Between Personality Disorders and Cannabis Use and Cannabis Use Disorder: A Population-Based Twin Study

N.A. Gillespie PhD[1], S.H. Aggen PhD[1], M.C. Neale PhD[1,2], G.P. Knudsen MD[3], R.F. Krueger PhD[4], S.C. South PhD[5], N. Czajkowski PhD[3,6], R. Nesvåg MD PhD[3,7], E. Ystrom PhD[3,8,9], K.S. Kendler MD[1,2]*, & T. Reichborn-Kjennerud MD[3,10]*

* Drs Kendler and Reichborn-Kjennerud are joint senior authors

[1] Virginia Institute for Psychiatric and Behavioral Genetics, Department of Psychiatry, Virginia Commonwealth University, Richmond, VA, USA
[2] Human and Molecular Genetics, Virginia Commonwealth University, Richmond, VA, USA
[3] Department of Mental Disorders, Norwegian Institute of Public Health
[4] Department of Psychology, University of Minnesota, Minneapolis, MN
[5] Department of Psychological Sciences, Purdue University, IN
[6] Department of Psychology, University of Oslo
[7] Department of Psychiatric Research, Diakonhjemmet Hospital, Oslo, Norway
[8] Section of Health, Developmental and Personality Psychology, Department of Psychology, University of Oslo, Norway
[9] PharmacoEpidemiology and Drug Safety Research Group, School of Pharmacy, University of Oslo, Norway
[10] Institute of Clinical Medicine, University of Oslo

Corresponding author
Nathan Gillespie, PhD
Virginia Institute for Psychiatric and Behavioral Genetics, Virginia Commonwealth University,
Box 980126, Richmond, VA 23298-0126 (USA).
E-mail: nathan.gillespie@vcuhealth.org

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This manuscript is original, not published elsewhere, and not under consideration elsewhere. There are no previous versions of this manuscript that have been submitted and rejected from any section of Journal of Addiction. All data used in this manuscript were collected in a manner consistent with ethical standards for the treatment of human subjects. We have no conflicts of interest.

Abstract

BACKGROUND AND AIMS: Individual differences in DSM-IV personality disorders (PDs) are associated with increased prevalence of substance use disorders. Our aims were to determine which combination of PDs trait scores best predict cannabis use (CU) and cannabis use disorder (CUD), and to estimate the size and significance of genetic and environmental risks in PD traits shared with CU and CUD.

DESIGN: Linear mixed effects models were used to identify PD traits for inclusion in twin analyses to explore the genetic and environmental associations between the traits and cannabis use.

SETTING: Cross-sectional data were obtained from Norwegian adult twins in a face-to-face interview in 1999-2004 as part of a population-based study of mental health.

PARTICIPANTS: Subjects were 1,419 twins (μ_{age}=28.2 years, range=19-36) from the Norwegian Institute of Public Health Twin Panel with complete PD and cannabis data.

MEASUREMENTS: PD traits were assessed using DSM-IV criteria. Lifetime CU and CUD were based on DSM-IV abuse and dependence criteria, including withdrawal and craving.

FINDINGS: After adjusting for age and sex, Antisocial (ß=0.23, 95% CI=0.19 - 0.28) and Borderline PDs (ß=0.20, 95% CI=0.14 - 0.26) were strongly associated with CU. Antisocial (ß=0.26, 95% CI=0.21 - 0.31) and Borderline PDs (ß=0.12, 95% CI=0.06 - 0.18) were also strongly linked to CUD. Genetic risks in Antisocial and Borderline PD traits explained 32-60% of the total variance in CU and CUD. Dependent and Avoidant PDs explained 11% and 16% of the total variance in CU and CUD respectively.

CONCLUSIONS: Individual differences in the liability to cannabis use and cannabis use disorder appear to be linked to genetic risks correlated with Antisocial and Borderline personality disorder traits.

Keywords

Cannabis use, cannabis use disorder, personality disorder traits, twin, genes, environment

Introduction

Cannabis use (CU) and cannabis use disorder (CUD) tend to manifest in late adolescence and early adulthood and can persist throughout adulthood (1). Personality disorders (PDs) have been linked to substance use and misuse (2-9) including cannabis (10). For example, analyses of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) data found that increased CU is associated with higher rates of schizotypal PD (11). One review of 29 cross-sectional studies reported that CU is associated with higher schizotypy scores (12). However, all ten DSM-IV PDs (13) have never been examined together to determine which subset of PDs correlates with CU and CUD, while also exploring the genetic and environmental etiology linking PDs to CU and CUD.

Individual differences in PDs are associated with an increased substance use disorders (5-7, 9). Among the DSM-IV PDs (13), Antisocial (14), Borderline (15), and Schizotypal (6, 11, 12) have been linked to CU and CUD. Together, these PDs account for high rates of comorbid substance use disorders (SUDs) (5, 6). Eaton and colleagues (16) have shown Antisocial PD, when compared to Borderline, is the stronger phenotypic indicator of the liability to externalising disorders that includes cannabis and other SUDs (16).

We are unaware of any study that has jointly analysed all ten PDs to identify which PDs are most strongly linked to CU and CUD within a genetic framework. Among the genetic studies linking PDs to CU and CUD, most have focused on single PDs such as Borderline (17), or Antisocial (18). We addressed this gap with two specific aims. First, we determined which

PDs are most strongly associated with the liability to CU and CUD. Second, we estimated the degree of genetic and environmental covariance shared between PD traits and CU and CUD.

Method

Sample

Subjects came from the Norwegian Institute of Public Health (NIPH) Twin Panel (19, 20) comprising twins born 1967-1979 identified through the Norwegian National Medical Birth Registry (see Supplement, Methods). Data came from an interview study (1999-2004) assessing DSM-IV Axis I and Axis II disorders. Among 3,221 eligible twin pairs, 1,391 complete pairs (43.2%) and 19 single twins (0.6% pairwise) totalling 2,801 twins participated (43.4%) (63% female). The average age at interview was 28.2 years (SD=3.9 years, range=19-36).

Ethical Standards

Interviewers were advanced psychology students or psychiatric nurses, who received standardised training, and supervision during data collection. Written informed consent was obtained from all participants who received stipends of $35. The Regional Committee approved the study for Medical and Health Research Ethics. The Norwegian Data Inspectorate approved the collection and storage of individual twin data.

Measures

Predictors

Lifetime DSM-IV (13) Axis II personality disorders were assessed using a Norwegian version of the Structured Interview for DSM-IV Personality (SIDP-IV) (21) comprising: Paranoid (7 criteria); Schizoid (8 criteria); Schizotypal (9 criteria); Histrionic (8 criteria);

Borderline (9 criteria); Obsessive-Compulsive (8 criteria); Dependent (8 criteria), Avoidant (7 criteria); Narcissistic (9 criteria); and Antisocial (7 criteria; conduct disorder criterion before age 15 not included). The SIDP-IV used non-pejorative questions organised into topical sections rather than by individual PD thereby improving the flow of the interview. The SIDP-IV interview was conducted after the Composite International Diagnostic Interview (CIDI) (22) to enable interviewers to distinguish stable behaviours from temporary states resulting from Axis I disorders. Each criterion was scored on a 4-point scale (absent, subthreshold, present, or strongly present), then dichotomized (0=absent, 1= sub-threshold or greater), and summed for each PD. Since few participants endorsed most criteria, each PD sum score was recoded onto a 3-point scale (0=0 criteria, 1=1-2 criteria, 2=≥3 criteria). We have previously tested the validity of this approach by examining the fit of the multiple threshold model to determine if the number of endorsed criteria reflected differences in severity on a single continuum of liability. This assumption was supported for all ten PDs (23-25).

Outcomes

Lifetime cannabis use (CU) and cannabis use disorder (CUD) were based on DSM-IV criteria for cannabis abuse and dependence assessed using a Norwegian version of the CIDI (13, 22). Used previously (26, 27), this CIDI has good test-retest and interrater reliability (28-30). Of the sample, 21% reported lifetime CU. Lifetime CU declines with age (9). However, CU assessment at age 28.2 years was close enough to the self-reported average age of most frequent CU (μ_{age}=19.1 years) thereby lessening possible recall biases. After responding to '*How often have you taken [hashish] on your own?*' when using most frequently, CU was coded using a 3-point scale (0=never tried, 1=1-4 times, and 2=≥5 times). This was then followed by 12 items assessing CUD based on DSM-IV (13) criteria for abuse, dependence

including withdrawal, and craving. Each criterion was assessed present or absent, summed, and recoded to derive a distribution approximating DSM-V CUD thresholds. For the linear mixed effects models, there were 1,116 twins with both PD and cannabis data following listwise deletion. For the bivariate twin analyses, there were 1,419 twins with combined cannabis and PD data.

Statistical Analyses

Overview

We used linear mixed effects models to identify which PD traits predict lifetime CU and CUD. Because data included correlated twin pairs, we modelled zygosity as a random effect to correct for clustering. CU and CUD were analyzed separately. In each case, PDs traits that significantly predicted CU and CUD were brought forward and biometrical twin models were fitted to estimate the proportion of genetic and environmental risks shared between each PD trait and CU and CUD.

Univariate and multiple mixed effects models

Given the number of PDs, we adopted a systematic approach to identify PD traits for inclusion in the twin models. We began with univariate linear mixed effects models to predict CU and CUD separately using the nlme() package in $R_{3.1.1}$ (31). Univariate results illustrate the strength of each predictor when other PDs are not considered. We then fitted two separate mixed effects models: (i) the regression of CU onto all ten PDs; and (ii) the regression of CUD onto all ten PDs. Having recoded each PD trait onto a common ordinal scale enabled direct comparison of beta regression coefficients (see Table S1 for variable distributions). All models included sex and age covariates.

Bivariate and multivariate twin modelling

Twin models were fitted using the Full Information Maximum Likelihood (FIML) raw ordinal data methods in the $OpenMx_{2.0}$ package (32) in $R_{3.1.1}$ (31). This approach assumes that the ordinal categories within each variable are an imprecise measure of a latent normal liability distribution. Thresholds can be conceived of as cut-points along a standard normal distribution that relate category frequencies to cumulative probabilities indicating increasing levels of risk. Thresholds were adjusted for the effects age and sex. By exploiting the expected genetic and environmental correlations between monozygotic (MZ) and dizygotic (DZ) twin pairs, standard bivariate biometrical genetic methods (33) were used to estimate the size and significance of the genetic and environmental risks shared between each significant PD and the CU and CUD. Our method decomposed the covariance between MZ and DZ twin pairs into additive (A) genetic, shared environmental (C), and non-shared or unique (E) environmental risks. Because MZ twin pairs are genetically identical, compared to DZ twin pairs who share on average half of their genes, the expected twin pair correlations for the genetic (A) effects are 1.0 and 0.5 respectively. The modelling assumes that common environments (C) are equal in MZ and DZ twin pairs and because non-shared environments (E) are uncorrelated, E must also reflect measurement error. To determine the best fitting bivariate and multivariate models, a fully saturated (A+C+E) model was used as a reference to compare models in which the C and A parameters were dropped to zero. Model comparisons were evaluated using the Akaike Information Criterion (34), which provides a balance between complexity and data misfit.

Results

Linear Mixed Effects Models

In the univariate linear mixed effects models predicting CU, seven PD traits were significantly and positively associated with lifetime CU (Table 1). In the multivariate model predicting CU, Paranoid, Antisocial, and Borderline PD traits each had significant positive beta coefficients for CU, whereas Schizoid and Dependent PD traits had significant negative beta coefficients. In the univariate model predicting CUD, eight of the ten PD traits were significantly associated with CUD. In multivariate model for CUD, the standardized beta coefficients for Antisocial, Borderline and Avoidant PD traits were significantly and positively associated with CUD.

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Twin Analyses

Bivariate Cholesky Decompositions

PD traits significantly associated with CU and CUD in the multivariate models were then examined in bivariate twin analyses. In each analysis, an additive genetic model from which the shared environmental component was removed provided the most parsimonious fit. See Supplement, Tables S2-3 for model fit comparisons.

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Cannabis Use

The phenotypic (r_P), additive genetic (r_A) and environmental (r_E) correlations between the PD traits and CU varied considerably (Table 2). There was very little phenotypic association between CU and either Schizoid or Dependent PD traits. The phenotypic correlation between Paranoid and CU was modest. However, the genetic correlation was non-significant. The highest phenotypic and genetic correlations with CU were with Antisocial and Borderline PD traits.

Table 2 summarises the proportions of variance in CU explained by additive genetic and environmental risks in each of the PD traits. None of the random environmental risks in any of the five PD traits was significantly shared with CU. In terms of genetic covariance, the genetic risks in Paranoid and Schizoid PD traits were unrelated to CU, whereas Dependent explained 11% of the additive genetic risks in CU. In contrast, the genetic risks in the Antisocial and Borderline PD traits were significantly and positively correlated and explained 40% to 48% of the total variance in CU respectively.

The Antisocial and Borderline PD traits included criteria referencing substance use. Therefore, to determine if the genetic correlations with CU were influenced by these criteria, the bivariate analyses were repeated after removing the '*Failure to conform to social norms with respect to lawful behavior as indicated by repeatedly performing acts that are grounds for arrest*' and '*Impulsivity in at least two areas that are potentially self-damaging (e.g., spending, sex, substance abuse, reckless driving, binge eating)*' from Antisocial and Borderline PD traits respectively. There was a change from 48% to 32% in terms of total variance in CU explained by genetic risks in Borderline. For Antisocial, the change was

smaller with a reduction in the total variance in CU explained by genetic risks from 40% to 32%.

Cannabis Use Disorder

Table 3 shows the phenotypic, additive genetic, and environmental bivariate correlations between each the three significant PD traits and CUD. Phenotypic correlations ranged from small (0.23) to modest (0.52 to 0.62). The additive correlation between Avoidant PD and CUD was 0.47, but given the small phenotypic association, the genetics of Avoidant PD explained only 16% of the total risks in CUD. In contrast, the additive genetic correlations between Borderline or Antisocial and CUD were higher. Commensurate with their phenotypic and additive genetic correlations, genetic risks in these PD traits explained 32% to 60% of the total variance in CUD.

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After removing the substance use criteria from the Antisocial and Borderline PD traits, the phenotypic correlations with CUD dropped (Table 3). Despite this, the total variance in CUD explained by the genetic risks in the Antisocial PD trait increased from 24% to 27%. For Borderline, the proportion of total variance in CUD explained by the genetic risks of this PD dropped from 60% to 45%.

Multivariate Cholesky Decompositions

A Cholesky Decomposition was fitted to the Paranoid, Schizoid, Antisocial, Borderline, and Dependent PD traits and lifetime CU. An AE model provided the best fit to the data (Table 4). Table 5 shows the additive genetic and non-shared environmental latent factor

correlations. The genetic and environmental correlations largely resembled the observed bivariate correlations. Although the genetic correlations between Antisocial and Borderline PD traits and CU are lower than those in the bivariate analyses, they remained high (0.68 to 0.69).

An AE model also provided the best fit to the Antisocial, Borderline, and Avoidant PD traits and CUD data (Table 6). Table 7 shows the additive genetic and non-shared environmental latent factor correlations. Again, the genetic and environmental correlations largely resemble the bivariate correlations. Of note is the high genetic correlation between Borderline PD and CUD.

Discussion

To our knowledge, this is the first study to investigate all ten personality disorders and to explore associations with CU and CUD within a genetically informative design. Among all ten PD traits, individual differences in Borderline and Antisocial emerged as the strongest phenotypic and genetic correlates of lifetime use *and* misuse of cannabis.

Our results are consistent with the known PD correlates of alcohol use and misuse. In findings recently reported by us using the same Norwegian twins, we found that Borderline and Antisocial PD trait scores were also the strongest correlates, within and across time, of the phenotypic and genotypic liability to lifetime alcohol use and alcohol use disorder (35). This suggests that lifetime alcohol and cannabis use and misuse are indexed by many of the same genetic and environmental risk factors. To test this hypothesis, we conducted *post-hoc* bivariate twin analyses in which we found very high phenotypic correlations between lifetime alcohol and cannabis use (0.55), as well as alcohol and cannabis use disorders (0.64) assessed

at the same interview. As shown in Supplement Table S6, the genetic correlation in each case was 0.84. These results are consistent with studies suggesting that comorbidity between licit and illicit substance use, and substance use disorders can be attributed to correlated genetic risks (36-38). Therefore, the genetic covariance between alcohol and cannabis use and misuse, including other psychoactive substances, is likely being captured in part by the same genetic risks in Borderline and Antisocial PD trait scores.

Previously, we have shown how CU and the progression to CUD fall along a single liability (39-41) and that large proportions of the genetic and environmental risks in CU covary with CUD criteria (39, 42). Because genetic risk factors in Borderline and Antisocial PD traits explained modest to large portions of the total variation in CU and CUD, this suggests that these two PD traits are genetically correlated with the same continuum of risk from use to misuse. However, twin studies have also shown that smaller portions of the genetic and environmental risks in CU and CUD are unshared (43-45). This is consistent with our findings of different PD traits differentially correlating with CU and CUD. For example, Paranoid PD was associated with CU but not CUD, whereas Avoidant and Dependent PD traits are more strongly linked to CUD.

We estimate that 66% [48/(48+25)] and 86% [60/(60+10)] of the total genetic variance in CU and CUD respectively was explained by the Borderline PD trait. This is consistent with reports linking Borderline personality features to cannabis use and misuse via common genetic risks (17, 46). Our measure of Antisocial PD likewise explained large proportions of the total genetic risks in CU (56%) and CUD (43%). This is lower than estimates reported by Fu (18), who found that Antisocial PD explained 58% of the total genetic risks in DSM-IV cannabis dependence. In Szoke's review (12) and Davis' (11) analysis of the NESARC data,

CU was associated with increased schizotypy scores. Another report identified Paranoid, Schizotypal, and Narcissistic PDs as significant predictors of cannabis abuse or dependence (5). Hasin (6) also found that Schizotypal PD predicted three-year persistence of cannabis, alcohol and nicotine use disorders. In our results, neither Schizotypal nor Narcissistic were related to CU or CUD. Paranoid and Schizoid PDs were significantly linked to CU in the linear mixed effects model, but neither explained significant genetic covariance with CU. A notable absence was the lack of cannabis associations with either Paranoid or Schizotypal PD traits in the multivariate mixed linear effects models. Despite links between cannabis use and psychosis (47), coupled with reports demonstrating how Schizotypal and Paranoid PDs are both phenotypically and genetically linked to a spectrum of schizophrenic disorders (48-51), there was no significant genetic or environmental association between CU or CUD and Schizotypal or Paranoid PD trait scores. This could be attributed to psychosis being imprecisely linked to schizophrenia (52), or lack of statistical power stemming from the lower prevalence of lifetime CU (20%) in this Nordic population.

Overall, our results are consistent with the role of PDs in the externalising disorders spectrum, which is highly heritable (53), and characterised by conduct and substance use disorders including CUD (54) and Antisocial or Borderline PDs (16). We have shown that correlations between these two PDs can be attributable to common and longitudinally stable genetic risk factors (55). Antisocial and Borderline are among the PDs most consistently linked to CU and the CUD (14, 56, 57) (15, 46) which together account for high rates of comorbid substance use disorders (5-7, 58). Although twin studies provide compelling evidence that PDs are heritable (59-63) very few have explored the genetic and environmental risks in PDs linked to CU or CUD. After adjusting for normative personality,

Few (46) observed that correlations between Borderline PD and CUD could be attributed to shared genetic risks.

In terms of novel findings, our results link two PDs to reduced risk of CU and CUD. Schizoid and Dependent PD traits were associated with lower risk of CU. Hasin's (6) analysis of NESARC data found no association between Schizoid PD and persistent cannabis abuse-dependence. It should be emphasised however that Schizoid and Dependent PD traits each explained very little genetic variance in CU.

Limitations

Our results should be interpreted in the context of six potential limitations.

First, some sample attrition occurred from the original birth registry through to the 1999-2004 study. In longitudinal studies, attrition reduces statistical power but introduces bias only if it is non-random with respect to critical dependent variables (64). Multiple lines of evidence indicate that the sample remained broadly representative with respect to our key areas of interest (64). Demographic but not psychiatric and substance use measures significantly predicted cooperation (64). No psychiatric variables predicted cooperation assessed during an earlier study in 1998. Instead, the strongest effects seen were for sex, zygosity and education. Based on examination of 45 variables potentially predictive of cooperation from a 1998 survey, including 22 indicators of mental health, only 2 of 45 variables – age and zygosity – significantly predicted cooperation at the interview study, whereas none of the psychiatric variables predicted cooperation. Using the 1998 data, we also fitted standard twin models to 25 variables (including proxies for all ten PDs and alcohol abuse) to determine if results

differed between non-subjects and subjects for the interview study. No parameters differed significantly.

Second, there were 91 complete and 164 incomplete (singletons) opposite-sex DZ twin pairs with cannabis data, meaning the sample was underpowered to detect qualitative and quantitative sex differences. Plausibly, the etiology of the genetic and environmental covariance between the PD traits and CU or CUD varies across sex. We have shown that variation in CU and CUD can be explained by a single liability across sex (39), and where tests of measurement invariance have identified sex differences, the effect is to lower mean CU and misuse among females, but not overall variation (40). Since our modelling included sex as a covariate on the item thresholds, we tested the effect of removing the sex effects on the thresholds in the bivariate twin analyses involving the Antisocial and Borderline PD traits. Equating the thresholds across sex for CU, CUD and Borderline PD caused no significant deterioration in model fit. In contrast, equating the Antisocial PD thresholds in the bivariate analyses involving CU ($\Delta\chi^2$=108.60, Δdf=1) and CUD ($\Delta\chi^2$=105.64, Δdf=1, $p<0.001$) caused significant deterioration, such that Norwegian males reported significantly more symptoms of Antisocial PD.

Third, the study relied on Norwegian adults. The prevalence of lifetime cannabis use and the frequency of the PD criteria were low compared to other developed nations (1). Consequently, we emphasize that variation and replication are required to determine if our results generalize to different age and ethnic groups.

Fourth, the administration of the substance use items was contingent upon response to, "*Are you prepared to speak openly about this subject?*". CU and CUD criteria were significantly

higher among twins who were prepared to speak openly about their substance use. The Antisocial and Borderline bivariate analyses were, therefore, re-run in which CU and CUD scores were contingent upon 'speaking openly' (see Figure S1). As shown in Table S4, there were minimal declines in the phenotypic and additive genetic correlations. We conclude that this contingency had minimal impact.

Fifth, cannabis and nicotine use are frequently comorbid (65), which might confound the observed PD-cannabis associations. Nicotine use was not assessed during the 1999-2004 interview. However, a measure of 'current nicotine use' was assessed in a 1998 survey (see Supplement). Among subjects reporting lifetime CU, 71% also reported current nicotine use. The correlation between current smoking status in 1998 and lifetime CU reported between 1999-2004 was 0.36. The correlation with CUD was 0.26. We re-ran the bivariate twin models with smoking status as a covariate. Except for Antisocial PD, the inclusion of nicotine use resulted in significant, but relatively small changes in the phenotypic and additive genetic correlations (see Table S5). For Antisocial PD, the phenotypic and additive correlations with CU decreased from 0.50 to 0.39 and from 0.75 to 0.56 respectively. This is consistent with results showing how common variants linked to lifetime CU are highly correlated with nicotine use loci (66). Another potential confound is that in Nordic countries, nicotine use is comorbid with snus consumption (67), which is a moist powder tobacco product originating from a variant of dry snuff. Consequently, the degree to which covariance between the PD traits and CU or CUD can be explained by comorbid snus use remains an empirical question.

Finally, although our twin analyses identified significant common genetic variation between PD traits and cannabis use and misuse, our modelling was not exhaustive. We did not test causal hypotheses, which may provide clinical implications. Causal modelling was beyond

the scope of this report. Bornovalova (68) reported that associations between Borderline PD traits and the frequency of tobacco, alcohol, and cannabis use could be best explained by correlated liabilities. This is consistent with our models in which associations between personality pathology and CU are largely driven by correlated genetics mechanisms as opposed to any direct causal influences.

Conclusion

When comparing all ten DSM-IV PD traits, the liability to CU and CUD is strongly linked to genetic risk factors shared with Borderline and Antisocial PD traits.

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Table 1. Standardized beta regression coefficients (including 95% confidence intervals) for the *univariate* and *multivariate* linear mixed effects models predicting lifetime Cannabis Use and Cannabis Use Disorder.

	Cannabis Use				Cannabis Use Disorder			
	Univariate		Multivariate		Univariate		Multivariate	
	ß	(95%CI)	ß	(95%CI)	ß	(95%CI)	ß	(95%CI)
Sex	0.05	(0.00 0.11)	-0.01	(-0.06 0.04)	0.02	(-0.03 0.07)	-0.04	(-0.09 0.02)
Age at interview	**-0.19**	**(-0.24 -0.14)**	**-0.16**	**(-0.21 -0.11)**	**-0.09**	**(-0.14 -0.03)**	**-0.06**	**(-0.11 -0.01)**
Paranoid	**0.17**	**(0.11 0.22)**	**0.09**	**(0.03 0.15)**	**0.15**	**(0.10 0.20)**	0.05	(-0.01 0.11)
Schizoid	-0.01	(-0.06 0.04)	**-0.09**	**(-0.14 -0.04)**	0.04	(-0.01 0.09)	-0.04	(-0.09 0.01)
Schizotypal	**0.11**	**(0.06 0.16)**	0.02	(-0.04 0.08)	**0.13**	**(0.08 0.18)**	0.02	(-0.04 0.08)
Antisocial	**0.29**	**(0.25 0.34)**	**0.23**	**(0.19 0.28)**	**0.29**	**(0.25 0.34)**	**0.26**	**(0.21 0.31)**
Borderline	**0.28**	**(0.23 0.33)**	**0.20**	**(0.14 0.26)**	**0.24**	**(0.19 0.29)**	**0.12**	**(0.06 0.18)**
Histrionic	**0.11**	**(0.06 0.16)**	0.00	(-0.06 0.05)	**0.10**	**(0.05 0.15)**	0.00	(-0.05 0.06)
Narcissistic	**0.12**	**(0.07 0.17)**	0.00	(-0.05 0.06)	**0.09**	**(0.04 0.14)**	-0.05	(-0.10 0.01)
Avoidant	**0.08**	**(0.03 0.13)**	0.05	(-0.01 0.10)	**0.12**	**(0.07 0.17)**	**0.08**	**(0.02 0.13)**
Dependent	0.03	(-0.02 0.08)	**-0.10**	**(-0.16 -0.05)**	**0.09**	**(0.04 0.14)**	-0.03	(-0.09 0.03)
Obsessive Compulsive	0.03	(-0.02 0.08)	-0.05	(-0.10 0.00)	0.05	(0.00 0.10)	-0.03	(-0.08 0.03)

Table 2. Phenotypic (r_P), additive genetic (r_A) and environmental (r_E) correlations between significant personality disorder trait predictors and lifetime Cannabis Use. Results include standardized proportions of genetic and environmental variance (including 95% CIs) explained by each predictor.

				Proportions of Variance in Lifetime Cannabis Use			
	Correlations			Genetic Variance		Environmental Variance	
	r_P	r_A	r_E	Shared (95%CI)	Unique to CU (95%CI)	Shared (95%CI)	Unique to CU (95%CI)
Paranoid	0.26	0.25 (-0.05-0.54)	0.36 (-0.13-0.57)	4% (0-21%)	68% (48-80%)	4% (0-10%)	24% (13-39%)
Schizoid	0.01	0.11 (-0.15-0.40)	-0.09 (-0.35-0.19)	1% (0-11%)	72% (53-84%)	0% (0-4%)	27% (16-42%)
Antisocial	0.50	0.75 (-0.53-0.99)	0.28 (-0.00-0.55)	40% (20-68%)	31% (0-54%)	0% (0-6%)	27% (14-43%)
Borderline	0.44	0.81 (-0.63-0.99)	0.05 (-0.19-0.28)	48% (29-71%)	25% (0-45%)	0% (0-2%)	28% (17-43%)
Dependent	0.06	0.39 (-0.15-0.66)	-0.24 (-0.47-0.00)	11% (2-30%)	61% (36-78%)	2% (0-7%)	26% (15-41%)
Antisocial (trimmed)	0.42	0.66 (-0.42-0.94)	0.21 (-0.08-0.50)	32% (13-63%)	41% (8-63%)	1% (0-4%)	26% (14-42%)
Borderline (trimmed)	0.35	0.66 (-0.45-0.85)	0.05 (-0.19-0.30)	32% (15-55%)	41% (15-61%)	0% (0-2%)	27% (16-43%)

Notes: Results based on best fitting 'additive genetic (A) + unique environment' (E) bivariate model; trimmed=Borderline PD excluded diagnostic criterion '*Failure to conform to social norms with respect to lawful behavior as indicated by repeatedly performing acts that are grounds for arrest*', Antisocial PD score excluded diagnostic criterion '*Impulsivity in at least two areas that are potentially self-damaging (e.g., spending, sex, substance abuse, reckless driving, binge eating)*'

Table 3. Phenotypic (r_P), additive genetic (r_A) and environmental (r_E) correlations between significant personality disorder trait predictors and lifetime Cannabis Use Disorder criteria. Results include standardized proportions of genetic and environmental variance (including 95% CIs) explained by each predictor.

				Proportions of Variance in Lifetime Cannabis Use Disorder			
	Correlations			Genetic Variance		Environmental Variance	
	r_P	r_A	r_E	Shared (95%CI)	Unique to CU (95%CI)	Shared (95%CI)	Unique to CU (95%CI)
Antisocial	0.62	0.66 (-0.39-0.93)	0.69 (-0.31-0.91)	32% (10-66%)	42% (9-62%)	12% (2-29%)	13% (2-36%)
Borderline	0.51	0.92 (-0.69-0.99)	0.10 (-0.22-0.40)	60% (32-84%)	10% (0-40%)	0% (0-5%)	30% (14-53%)
Avoidant	0.23	0.47 (-0.17-0.78)	0.00 (-0.33-0.34)	16% (2-41%)	56% (23-78%)	0% (0-3%)	28% (13-53%)
Antisocial (trimmed)	0.22	0.64 (-0.33-0.98)	0.46 (-0.03-0.84)	31% (8-70%)	44% (37-51%)	5% (0-19%)	20% (6-44%)
Borderline (trimmed)	0.42	0.81 (-0.43-0.99)	0.05 (-0.29-0.37)	45% (19-78%)	25% (0-55%)	0% (0-4%)	30% (14-55%)

Notes: Results based on best fitting 'additive genetic (A) + unique environment' (E) bivariate model; trimmed=Borderline PD excluded diagnostic criterion '*Failure to conform to social norms with respect to lawful behavior as indicated by repeatedly performing acts that are grounds for arrest*', Antisocial PD score excluded diagnostic criterion '*Impulsivity in at least two areas that are potentially self-damaging (e.g., spending, sex, substance abuse, reckless driving, binge eating)*'. [1]Lower bound 95%CI is approximate due to computational difficulties.

Table 4. Multivariate Cholesky Decomposition model fitting comparisons between Paranoid, Schizoid, Antisocial, Borderline, and Dependent PD trait scores* and lifetime Cannabis Use.

Model	-2LL	df	AIC
ACE	28973	18093	-7213
AE	28986	18121	-7256
CE	29038	18121	-7204

Notes: ACE=additive genetic (A) + shared environment (C) + unique environmental (E) risks; -2LL=-2 x Log Likelihood; AIC=Akaike Information Criteria. All models included age as a covariate. *PD traits scores significantly linked to CU in the multivariate linear mixed effects model. To facilitate convergence and maintain computational efficiency sex and age were not included as covariates.

Table 5. Additive genetic (below diagonal) and non-shared environmental (*italics*) latent factor correlations between Paranoid, Schizoid, Antisocial, Borderline, and Dependent PD trait scores and Cannabis Use (CU).

	1.	2.	3.	4.	5.	6.
1. Paranoid	1	*0.30*	*0.31*	*0.39*	*0.32*	*0.16*
2. Schizoid	0.60	1	*0.16*	*0.31*	*0.24*	*-0.09*
3. Antisocial	0.19	0.39	1	*0.47*	*0.27*	*0.10*
4. Borderline	0.84	0.40	0.60	1	*0.44*	*0.05*
5. Dependent	0.66	0.45	0.18	0.62	1	*-0.20*
6. Cannabis Use	0.36	0.13	0.68	0.69	0.35	1

Table 6. Multivariate Cholesky Decomposition model fitting comparisons between Antisocial, Borderline, and Avoidant PD trait scores* and Cannabis Use Disorder.

Model	-2LL	df	AIC
ACE	18771.44	12546	-6320.56
AE	**18774.53**	**12561**	**-6347.47**
CE	18805.08	12561	-6316.92

Notes: ACE=additive genetic (A) + shared environment (C) + unique environmental (E) risks; -2LL=-2 x Log Likelihood; AIC=Akaike Information Criteria. *PD traits scores significantly linked to CUD in the multivariate linear mixed effects model. To facilitate convergence and maintain computational efficiency sex and age were not included as covariates.

Table 7. Additive genetic (below diagonal) and non-shared environmental (*italics*) latent factor correlations between Antisocial, Borderline, and Avoidant PD trait scores and Cannabis Use Disorder (CUD).

	1.	2.	3.	4.
1. Antisocial	1	*0.46*	*0.22*	*0.76*
2. Borderline	0.60	1	*0.36*	*0.08*
3. Avoidant	0.09	0.42	1	*0.01*
4. CUD	0.55	0.88	0.46	1

All models include the full-scale untrimmed Antisocial and Borderline PD trait scores.