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Associations between personality disorders and cannabis use and cannabis use disorder: a population-based twin study

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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 1419 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. Life-time CU and CUD were based on DSM-IV abuse and dependence criteria, including withdrawal and craving. **Findings** After adjusting for age and sex, antisocial [β = 0.23, 95% confidence interval (CI) = 0.19–0.28] and borderline PDs (β = 0.20, 95% CI = 0.14–0.26) were associated strongly with CU. Antisocial (β = 0.26, 95% CI = 0.21–0.31) and borderline PDs (β = 0.12, 95% CI = 0.06–0.18) were also linked strongly 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, environment, genes, personality disorder traits, twin.

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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 10 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 that antisocial PD, when compared to borderline, is the stronger phenotypical indicator of the liability to externalizing disorders that includes cannabis and other SUDs [16].

We are unaware of any study that has jointly analyzed all 10 PDs to identify which PDs are linked most strongly 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 PD traits [18]. We addressed this gap with two specific aims. First, we determined which PDs are associated most strongly with the liability to CU and CUD. Secondly, 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 1967–79 identified through the Norwegian National Medical Birth Registry (see Supporting information, Methods). Data came from an interview study (1999–2004) assessing DSM-IV Axis I and Axis II disorders. Among 3221 eligible twin pairs, 1391 complete pairs (43.2%) and 19 single twins (0.6% pairwise) totaling 2801 twins participated (43.4%) (63% female). The average age at interview was 28.2 years [standard deviation (SD) = 3.9 years, range = 19–36].

Ethical standards

Interviewers were advanced psychology students or psychiatric nurses, who received standardized 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

Life-time DSM-IV [13] Axis II personality disorders were assessed using a Norwegian version of the Structured Interview for DSM-IV Personality PD traits (SIDP-IV) [21] comprising: paranoid (seven criteria); schizoid (eight criteria); schizotypal (nine criteria); histrionic (eight criteria); borderline (nine criteria); obsessive–compulsive (eight criteria); dependent (eight criteria), avoidant (seven criteria); narcissistic (nine criteria); and antisocial (seven criteria; conduct disorder criterion before age 15 not included). The SIDP-IV used non-pejorative questions organized 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 behaviors from temporary states resulting from Axis I disorders. Each criterion was scored on a four-point scale (absent, subthreshold, present or strongly present), then dichotomized (0 = absent, 1 = subthreshold or greater) and summed for each PD. As few participants endorsed most criteria, each PD sum score was recoded onto a three-point scale (0 = no criteria, 1 = one to two criteria, 2 = three or more than three 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 10 PDs [23–25].

Outcomes

Life-time 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 inter-rater reliability [28–30]. Of the sample, 21% reported life-time CU. Life-time 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 three-point scale (0 = never tried, 1 = one to four times and 2 = five or more than five 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 1116 twins with both PD and cannabis data following listwise deletion. For the bivariate twin analyses, there were 1419 twins with combined cannabis and PD data.

Statistical analyses

Overview

We used linear mixed-effects models to identify which PD traits predict life-time 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 predicted CU and CUD significantly 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 version 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 10 PDs; and (ii) the regression of CUD onto all 10 PDs. Having recoded each PD trait onto a common ordinal scale enabled direct comparison of beta regression coefficients (see Supporting information, 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 version 20 package [32] in R version 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 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 associated significantly and positively with life-time 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

Table 1 Standardized beta regression coefficients [including 95% confidence intervals (CIs)] for the univariate and multivariate linear mixed-effects models predicting life-time cannabis use and cannabis use disorder.

	Cannabis use				*Cannabis use disorder*			
	Univariate		*Multivariate*		*Univariate*		*Multivariate*	
	β	*(95% CI)*	*β*	*(95% CI)*	*β*	*(95% CI)*	*β*	*(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 (years)	−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)

negative beta coefficients. In the univariate model predicting CUD, eight of the 10 PD traits were associated significantly with CUD. In the multivariate model for CUD, the standardized beta coefficients for antisocial, borderline and avoidant PD traits were associated significantly and positively with CUD.

Twin analyses

Bivariate Cholesky decompositions

PD traits that were associated significantly 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 Supporting information, Tables S2–3 for model fit comparisons.

Cannabis use

The phenotypical (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 phenotypical association between CU and either schizoid or dependent PD traits. The phenotypical correlation between paranoid and CU was modest. However, the genetic correlation was non-significant. The highest phenotypical and genetic correlations with CU were with antisocial and borderline PD traits.

Table 2 summarizes 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 shared significantly with CU. In terms of genetic covariance, the genetic risks in paranoid and schizoid PD traits were unrelated to CU, whereas the dependent PD trait explained 11% of the additive genetic risks in CU. In contrast, the genetic risks in the antisocial and borderline PD traits were correlated significantly and positively and explained 40–48% 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 PD traits. For antisocial PD traits, the change was smaller, with a

Table 2 Phenotypical (r_P), additive genetic (r_A) and environmental (r_E) correlations between significant personality disorder (PD) trait predictors and life-time cannabis use (CU). Results include standardized proportions of genetic and environmental variance [including 95% confidence intervals (CIs)] explained by each predictor.

	Correlations			*Proportions of variance in life-time cannabis use*			
				Genetic variance		*Environmental variance*	
	r r_P	r_A	r_E	*Shared (95% CI)*	*Unique to CU (95% CI)*	*Shared (95% CI)*	*Unique to CU (95% CI)*
Paranoid	00.26	0.25 (−0.05–0.54)	0.36 (0.13–0.57)	4% (0–21%)	68% (48–80%)	4% (0–10%)	24% (13–39%)
SSchizoid	00.01	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	00.50	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	00.44	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	00.06	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)	00.42	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)	00.35	0.66 (0.45–0.85)	0.05 (−0.19–0.30)	32% (15–55%)	41% (15–61%)	0% (0–2%)	27% (16–43%)

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)'.

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

Cannabis use disorder

Table 3 shows the phenotypical, additive genetic and environmental bivariate correlations between each of the three significant PD traits and CUD. Phenotypical correlations ranged from small (0.23) to modest (0.52–0.62). The additive correlation between avoidant PD and CUD was 0.47 but, given the small phenotypical 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 PD traits and CUD were higher. Commensurate with their phenotypical and additive genetic correlations, genetic risks in these PD traits explained 32–60% of the total variance in CUD.

After removing the substance use criteria from the antisocial and borderline PD traits, the phenotypical 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 the borderline PD trait, 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 (0.68–0.69).

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 10 personality disorders and to explore associations with CU and CUD within a genetically informative design. Among all 10 PD traits, individual differences in borderline and antisocial PD traits emerged as the strongest phenotypical and genetic correlates of both life-time use and misuse of cannabis.

Table 3 Phenotypical (r_P), additive genetic (r_A) and environmental (r_E) correlations between significant personality disorder (PD) trait predictors and life-time cannabis use (CU) disorder criteria. Results include standardized proportions of genetic and environmental variance [including 95% confidence intervals (CIs)] explained by each predictor.

	Correlations			*Proportions of variance in life-time cannabis use disorder*			
				Genetic variance		*Environmental variance*	
	r r_P	r_A	r_E	*Shared (95% CI)*	*Unique to CU (95% CI)*	*Shared (95% CI)*	*Unique to CU (95% CI)*
Antisocial	00.62	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	00.51	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	00.23	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)	00.22	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)	00.42	0.81 (−0.43–0.99)	0.05 (−0.29–0.37)	45% (19–78%)	25% (0–55%)	0% (0–4%)	30% (14–55%)

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)'. 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 personality disorder (PD) trait scores* and life-time cannabis use (CU).

Model	*−2LL*	*d.f.*	*AIC*
ACE	228 973	118 093	−7213
AE	28986	18121	−7256
CE	29038	18121	−7204

ACE = additive genetic (A) + shared environment (C) + unique environmental (E) risks; −2LL = −2 × log-likelihood; AIC = Akaike information criteria. All models included age as a covariate. *PD traits scores linked significantly 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 (in italic type) latent factor correlations between paranoid, schizoid, antisocial, borderline and dependent personality disorder (PD) trait scores and cannabis use (CU).

	11	*22*	*3*	*4*	*5*	*6*
1. Paranoid	1	*00.30*	*0.31*	*0.39*	*0.32*	*0.16*
2. Schizoid	00.60	1	*0.16*	*0.31*	*0.24*	*−0.09*
3. Antisocial	00.19	00.39	1	*0.47*	*0.27*	*0.10*
4. Borderline	00.84	00.40	0.60	1	*0.44*	*0.05*
5. Dependent	00.66	00.45	0.18	0.62	1	*−0.20*
6. Cannabis use	00.36	00.13	0.68	0.69	0.35	1

Table 6 Multivariate Cholesky decomposition model-fitting comparisons between antisocial, borderline and avoidant personality disorder (PD) trait scores* and cannabis use disorder (CUD).

Model	*−2LL*	*d.f.*	*AIC*
ACE	18771.44	112 546	−6320.56
AE	18774.53	112 561	−6347.47
CE	18805.08	112 561	−6316.92

ACE = additive genetic (A) + shared environment (C) + unique environmental (E) risks; −2LL = −2 × log-likelihood; AIC = Akaike information criteria. *PD traits scores linked significantly to CUD in the multivariate linear mixed-effects model. To facilitate convergence and maintain computational efficiency, sex and age were not included as covariates.

Our results are consistent with the known PD correlates of alcohol use and misuse. In findings reported recently 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 phenotypical and genotypical liability to life-time alcohol use and alcohol use disorder [35]. This suggests that life-time 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 phenotypical correlations between life-time alcohol and cannabis use (0.55), as well as alcohol and cannabis use disorders (0.64) assessed at the same interview. As shown in Supporting information, 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 probably being captured in part by the same genetic risks in borderline and antisocial PD trait scores.

Table 7 Additive genetic (below diagonal) and non-shared environmental (in italic type) latent factor correlations between antisocial, borderline and avoidant personality disorder (PD) trait scores and cannabis use disorder (CUD).

	11	*22*	*3*	*4*
10. Antisocial	1	*00.46*	*0.22*	*0.76*
20. Borderline	00.60	1	*0.36*	*0.08*
30. Avoidant	00.09	00.42	1	*0.01*
40. CUD	00.55	00.88	0.46	1

All models include the full-scale untrimmed antisocial and borderline 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 correlated genetically 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 correlating differentially with CU and CUD. For example, paranoid PD was associated with CU but not CUD, whereas avoidant and dependent PD are linked more strongly 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]. Similarly, our measure of antisocial PD 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 3-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 linked significantly 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 linked genetically 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 linked imprecisely to schizophrenia [52] or lack of statistical power stemming from the lower prevalence of life-time CU (20%) in this Nordic population.

Overall, our results are consistent with the role of PDs in the externalizing disorders spectrum, which is highly heritable [53], and characterized 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 linked most consistently to CU and the CUD [14,15,46,56,57], 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 emphasized, 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 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 two of 45 variables—age and zygosity—predicted cooperation significantly 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 10 PDs and alcohol abuse) to determine if results differed between non-subjects and subjects for the interview study. No parameters differed significantly.

Secondly, there were 91 complete and 164 incomplete (singletons) opposite-sex DZ twin pairs with cannabis data, meaning that 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 between sexes. 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]. As 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 ($\Delta\chi^2 = 108.60$, Δd.f. = 1) and CUD ($\Delta\chi^2 = 105.64$, Δd.f. = 1, $P < 0.001$) caused significant deterioration, such that Norwegian males reported significantly more symptoms of antisocial PD.

Thirdly, the study relied upon Norwegian adults. The prevalence of life-time 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.

Fourthly, 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. Therefore, the antisocial and borderline bivariate analyses were re-run, in which CU and CUD scores were contingent upon 'speaking openly' (see Supporting information, Fig. S1). As shown in Supporting information, Table S4, there were minimal

declines in the phenotypical and additive genetic correlations. We conclude that this contingency had minimal impact.

Fifthly, cannabis and nicotine use are frequently comorbid [5], 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 Supporting information). Among subjects reporting life-time CU, 71% also reported current nicotine use. The correlation between current smoking status in 1998 and life-time CU reported between 1999 and 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 phenotypical and additive genetic correlations (see Supporting information, Table S5). For antisocial PD, the phenotypical 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 life-time CU are correlated highly with nicotine use loci [65]. Another potential confound is that, in Nordic countries, nicotine use is comorbid with snus consumption [66], 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 [67] 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 driven largely by correlated genetics mechanisms, as opposed to any direct causal influences.

Conclusion

When comparing all 10 DSM-IV PD traits, the liability to CU and CUD is linked strongly to genetic risk factors shared with borderline and antisocial PD traits.

Declaration of interests

None.

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References

1. Degenhardt L., Ferrari A. J., Calabria B., Hall W. D., Norman R. E., McGrath J. *et al.* The global epidemiology and contribution of cannabis use and dependence to the global burden of disease: results from the GBD 2010 study. *PLOS ONE* 2013; **8**: e76635.
2. Bidwell L. C., Knopik V. S., Audrain-McGovern J., Glynn T. R., Spillane N. S., Ray L. A. *et al.* Novelty seeking as a phenotypic marker of adolescent substance use. *Subst Abuse* 2015; **9**: 1–10.
3. Verdejo-Garcia A., Lawrence A. J., Clark L. Impulsivity as a vulnerability marker for substance-use disorders: review of findings from high-risk research, problem gamblers and genetic association studies. *Neurosci Biobehav Rev* 2008; **32**: 777–810.
4. Lejuez C. W., Magidson J. F., Mitchell S. H., Sinha R., Stevens M. C., de Wit H. Behavioral and biological indicators of impulsivity in the development of alcohol use, problems, and disorders. *Alcohol Clin Exp Res* 2010; **34**: 1334–45.
5. Peters E. N., Schwartz R. P., Wang S., O'Grady K. E., Blanco C. Psychiatric, psychosocial, and physical health correlates of co-occurring cannabis use disorders and nicotine dependence. *Drug Alcohol Depend* 2014; **134**: 228–34.
6. Hasin D., Fenton M. C., Skodol A., Krueger R., Keyes K., Geier T. *et al.* Personality disorders and the 3-year course of alcohol, drug, and nicotine use disorders. *Arch Gen Psychiatry* 2011; **68**: 1158–67.
7. Wu L. T., Gersing K., Burchett B., Woody G. E., Blazer D. G. Substance use disorders and comorbid Axis I and II psychiatric disorders among young psychiatric patients: findings from a large electronic health records database. *J Psychiatr Res* 2011; **45**: 1453–62.
8. Few L. R., Miller J. D., Rothbaum A. O., Meller S., Maples J., Terry D. P. *et al.* Examination of the Section III DSM-5 diagnostic system for personality disorders in an outpatient clinical sample. *J Abnorm Psychol* 2013; **122**: 1057–69.
9. Lopez-Quintero C., Perez de los Cobos J., Hasin D. S., Okuda M., Wang S., Grant B. F. *et al.* Probability and predictors of transition from first use to dependence on nicotine, alcohol, cannabis, and cocaine: results of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). *Drug Alcohol Depend* 2011; **115**: 120–30.
10. Harford T. C., Chen C. M., Kerridge B. T., Grant B. F. Self- and other-directed forms of violence and their relationship with lifetime DSM-5 psychiatric disorders: Results from the National Epidemiologic Survey on Alcohol Related Conditions —III (NESARC-III). *Psychiatry Res* 2017; https://doi.org/10.1016/j.psychres.2017.09.012.

11. Davis G. P., Compton M. T., Wang S., Levin F. R., Blanco C. Association between cannabis use, psychosis, and schizotypal personality disorder: findings from the National Epidemiologic Survey on Alcohol and Related Conditions. *Schizophr Res* 2013; **151**: 197–202.
12. Szoke A., Galliot A. M., Richard J. R., Ferchiou A., Baudin G., Leboyer M. *et al*. Association between cannabis use and schizotypal dimensions—a meta-analysis of cross-sectional studies. *Psychiatry Res* 2014; **219**: 58–66.
13. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders: DSM-IV*. Washington DC: American Psychiatric Association; 1994.
14. Compton W. M., Conway K. P., Stinson F. S., Colliver J. D., Grant B. F. Prevalence, correlates, and comorbidity of DSM-IV antisocial personality syndromes and alcohol and specific drug use disorders in the United States: results from the national epidemiologic survey on alcohol and related conditions. *J Clin Psychiatry* 2005; **66**: 677–85.
15. Trull T. J., Sher K. J., Minks-Brown C., Durbin J., Burr R. Borderline personality disorder and substance use disorders: a review and integration. *Clin Psychol Rev* 2000; **20**: 235–53.
16. Eaton N. R., Krueger R. F., Keyes K. M., Skodol A. E., Markon K. E., Grant B. F. *et al*. Borderline personality disorder comorbidity: relationship to the internalizing-externalizing structure of common mental disorders. *Psychol Med* 2011; **41**: 1041–50.
17. Distel M. A., Trull T. J., de Moor M. M., Vink J. M., Geels L. M., van Beek J. H. *et al*. Borderline personality traits and substance use: genetic factors underlie the association with smoking and ever use of cannabis, but not with high alcohol consumption. *J Pers Disord* 2012; **26**: 867–79.
18. Fu Q., Heath A. C., Bucholz K. K., Nelson E., Goldberg J., Lyons M. J. *et al*. Shared genetic risk of major depression, alcohol dependence, and marijuana dependence: contribution of antisocial personality disorder in men. *Arch Gen Psychiatry* 2002; **59**: 1125–32.
19. Harris J. R., Magnus P., Tambs K. The Norwegian Institute of Public Health Twin Panel: a description of the sample and program of research. *Twin Res* 2002; **5**: 415–23.
20. Nilsen T. S., Knudsen G. P., Gervin K., Brandt I., Roysamb E., Tambs K. *et al*. The Norwegian Twin Registry from a public health perspective: a research update. *Twin Res Hum Genet* 2013; **16**: 285–95.
21. Pfohl B., Blum N., Zimmerman M. *Structured Interview for DSM-IV Personality (SIDP-IV)*. Iowa City: University of Iowa: Department of Psychiatry; 1995.
22. Wittchen H. U. Reliability and validity studies of the WHO--Composite International Diagnostic Interview (CIDI): a critical review. *J Psychiatr Res*. 1994; **28**: 57–84.
23. Kendler K. S., Czajkowski N., Tambs K., Torgersen S., Aggen S. H., Neale M. C. *et al*. Dimensional representations of DSM-IV cluster A personality disorders in a population-based sample of Norwegian twins: a multivariate study. *Psychol Med* 2006; **36**: 1583–91.
24. Torgersen S., Czajkowski N., Jacobson K., Reichborn-Kjennerud T., Roysamb E., Neale M. C. *et al*. Dimensional representations of DSM-IV cluster B personality disorders in a population-based sample of Norwegian twins: a multivariate study. *Psychol Med* 2008; **38**: 1617–25.
25. Reichborn-Kjennerud T., Czajkowski N., Neale M. C., Orstavik R. E., Torgersen S., Tambs K. *et al*. Genetic and environmental influences on dimensional representations of DSM-IV cluster C personality disorders: a population-based multivariate twin study. *Psychol Med* 2007; **37**: 645–53.
26. Landheim A. S., Bakken K., Vaglum P. Gender differences in the prevalence of symptom disorders and personality disorders among poly-substance abusers and pure alcoholics. Substance abusers treated in two counties in Norway. *Eur Addict Res* 2003; **9**: 8–17.
27. Kringlen E., Torgersen S., Cramer V. A Norwegian psychiatric epidemiological study. *Am J Psychiatry* 2001; **158**: 1091–8.
28. Wittchen H. U., Lachner G., Wunderlich U., Pfister H. Test–retest reliability of the computerized DSM-IV version of the Munich-Composite International Diagnostic Interview (M-CIDI). *Soc Psychiatry Psychiatr Epidemiol* 1998; **33**: 568–78.
29. Wittchen H. U. Reliability and validity studies of the WHO—Composite International Diagnostic Interview (CIDI): a critical review. *J Psychiatr Res* 1994; **28**: 57–84.
30. Rubio-Stipec M., Peters L., Andrews G. Test–retest reliability of the computerized CIDI (CIDI-Auto): substance abuse modules. *Subst Abuse* 1999; **20**: 263–72.
31. R Development Core Team. R: a language and environment for statistical computing. R Foundation for Statistical Computing. Vienna, Austria; 2008. Available at: http://www.r-project.org/(accessed 14 February 2018) (Archived at http://www.webcitation.org/6xEIQRxyz on 14 February 2018).
32. Neale M. C., Hunter M. D., Pritikin J. N., Zahery M., Brick T. R., Kirkpatrick R. M. *et al*. OpenMx 2.0: extended structural equation and statistical modeling. *Psychometrika* 2016; **81**: 535–49.
33. Neale M. C., Cardon L. R. *Methodology for genetic studies of twins and families*. Dordrecht: Kluwer Academic Publishers; 1992.
34. Akaike H. Factor analysis and AIC. *Psychometrika* 1987; **52**: 317–32.
35. Long E. C., Aggen S. H., Neale M. C., Knudsen G. P., Krueger R. F., South S. C. *et al*. The association between personality disorders with alcohol use and misuse: a population-based twin study. *Drug Alcohol Depend* 2017; **174**: 171–80.
36. Kendler K. S., Jacobson K. C., Prescott C. A., Neale M. C. Specificity of genetic and environmental risk factors for use and abuse/dependence of cannabis, cocaine, hallucinogens, sedatives, stimulants, and opiates in male twins. *Am J Psychiatry* 2003; **160**: 687–495.
37. Tsuang M. T., Lyons M. J., Meyer J. M., Doyle T., Eisen S. A., Goldberg J. *et al*. Co-occurrence of abuse of different drugs in men: the role of drug-specific and shared vulnerabilities. *Arch Gen Psychiatry* 1998; **55**: 967–72.
38. Kendler K. S., Myers J., Prescott C. A. Specificity of genetic and environmental risk factors for symptoms of cannabis, cocaine, alcohol, caffeine, and nicotine dependence. *Arch Gen Psychiatry* 2007; **64**: 1313–20.
39. Gillespie N. A., Kendler K. S., Neale M. C. Psychometric modeling of cannabis initiation and use and the symptoms of cannabis abuse, dependence and withdrawal in a sample of male and female twins. *Drug Alcohol Depend* 2011; **118**: 166–72.
40. Gillespie N. A., Neale M. C., Legrand L. N., Iacono W. G., McGue M. Are the symptoms of cannabis use disorder best accounted for by dimensional, categorical, or factor mixture models? A comparison of male and female young adults. *Psychol Addict Behav* 2012; **26**: 68–77.
41. Kubarych T. S., Aggen S. H., Estabrook R., Edwards A. C., Neale M. C., Clark S. L. *et al*. Comparing factor, class and mixture models of cannabis initiation and DSM cannabis use disorder (CUD) criteria, including craving, in the

Brisbane Longitudinal Twin Study. *Twin Res Hum Genet* 2014; **17**: 89–98.
42. Gillespie N. A., Neale M. C., Prescott C. A., Aggen S. H., Kendler K. S. Factor and item–response analysis DSM-IV criteria for abuse of and dependence on cannabis, cocaine, hallucinogens, sedatives, stimulants and opioids. *Addiction* 2007; **102**: 920–30.
43. Agrawal A., Neale M. C., Prescott C. A., Kendler K. S. A twin study of early cannabis use and subsequent use and abuse/dependence of other illicit drugs. *Psychol Med* 2004; **34**: 1227–37.
44. Agrawal A., Neale M. C., Jacobson K. C., Prescott C. A., Kendler K. S. Illicit drug use and abuse/dependence: modeling of two-stage variables using the CCC approach. *Addict Behav* 2005; **30**: 1043–8.
45. Gillespie N. A., Neale M. C., Kendler K. S. Pathways to cannabis abuse: a multi-stage model from cannabis availability, cannabis initiation and progression to abuse. *Addiction* 2009; **104**: 430–8.
46. Few L. R., Grant J. D., Trull T. J., Statham D. J., Martin N. G., Lynskey M. T. *et al.* Genetic variation in personality traits explains genetic overlap between borderline personality features and substance use disorders. *Addiction* 2014; **109**: 2118–27.
47. Murray R. M., Englund A., Abi-Dargham A., Lewis D. A., Di Forti M., Davies C. *et al.* Cannabis-associated psychosis: neural substrate and clinical impact. *Neuropharmacology* 2017124–4.
48. Kendler K. S., Gruenberg A. M., Strauss J. S. An independent analysis of the Copenhagen sample of the Danish adoption study of schizophrenia. II. The relationship between schizotypal personality disorder and schizophrenia. *Arch Gen Psychiatry* 1981; **38**: 982–4.
49. Baron M., Gruen R., Rainer J. D., Kane J., Asnis L., Lord S. A family study of schizophrenic and normal control probands: implications for the spectrum concept of schizophrenia. *Am J Psychiatry* 1985; **142**: 447–55.
50. Kendler K. S., Gruenberg A. M., Kinney D. K. Independent diagnoses of adoptees and relatives as defined by DSM-III in the provincial and national samples of the Danish Adoption Study of Schizophrenia. *Arch Gen Psychiatry* 1994; **51**: 456–68.
51. Kendler K. S., McGuire M., Gruenberg A. M., O'Hare A., Spellman M., Walsh D. The Roscommon Family Study. III. Schizophrenia-related personality disorders in relatives. *Arch Gen Psychiatry* 1993; **50**: 781–8.
52. Chan V. Schizophrenia and psychosis: diagnosis, current research trends, and model treatment approaches with implications for transitional age youth. *Child Adolesc Psychiatr Clin North Am* 2017; **26**: 341–66.
53. Krueger R. F., Hicks B. M., Patrick C. J., Carlson S. R., Iacono W. G., McGue M. Etiologic connections among substance dependence, antisocial behavior, and personality: modeling the externalizing spectrum. *J Abnorm Psychol* 2002; **111**: 411–24.
54. Markon K. E., Krueger R. F., Watson D. Delineating the structure of normal and abnormal personality: an integrative hierarchical approach. *J Pers Soc Psychol* 2005; **88**: 139–57.
55. Reichborn-Kjennerud T., Czajkowski N., Ystrom E., Orstavik R., Aggen S. H., Tambs K. *et al.* A longitudinal twin study of borderline and antisocial personality disorder traits in early to middle adulthood. *Psychol Med* 2015; **45**: 3121–31.
56. Regier D. A., Farmer M. E., Rae D. S., Locke B. Z., Keith S. J., Judd L. L. *et al.* Comorbidity of mental disorders with alcohol and other drug abuse. Results from the Epidemiologic Catchment Area (ECA) Study. *JAMA* 1990; **264**: 2511–8.
57. Compton W. M. III, Cottler L. B., Ben Abdallah A., Phelps D. L., Spitznagel E. L., Horton J. C. Substance dependence and other psychiatric disorders among drug dependent subjects: race and gender correlates. *Am J Addict* 2000; **9**: 113–25.
58. Lopez-Quintero C., Hasin D. S., de Los Cobos J. P., Pines A., Wang S., Grant B. F. *et al.* Probability and predictors of remission from life-time nicotine, alcohol, cannabis or cocaine dependence: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Addiction* 2011; **106**: 657–69.
59. Distel M. A., Trull T. J., Willemsen G., Vink J. M., Derom C. A., Lynskey M. *et al.* The five-factor model of personality and borderline personality disorder: a genetic analysis of comorbidity. *Biol Psychiatry* 2009; **66**: 1131–8.
60. Kendler K. S., Myers J., Torgersen S., Neale M. C., Reichborn-Kjennerud T. The heritability of cluster A personality disorders assessed by both personal interview and questionnaire. *Psychol Med* 2007; **37**: 655–65.
61. Torgersen S., Myers J., Reichborn-Kjennerud T., Roysamb E., Kubarych T. S., Kendler K. S. The heritability of Cluster B personality disorders assessed both by personal interview and questionnaire. *J Pers Disord* 2012; **26**: 848–66.
62. Kendler K. S., Aggen S. H., Patrick C. J. A multivariate twin study of the DSM-IV criteria for antisocial personality disorder. *Biol Psychiatry* 2012; **71**: 247–53.
63. Livesley W. J., Jang K. L., Jackson D. N., Vernon P. A. Genetic and environmental contributions to dimensions of personality disorder. *Am J Psychiatry* 1993; **150**: 1826–31.
64. Tambs K., Ronning T., Prescott C. A., Kendler K. S., Reichborn-Kjennerud T., Torgersen S. *et al.* The Norwegian Institute of Public Health twin study of mental health: examining recruitment and attrition bias. *Twin Res Hum Genet* 2009; **12**: 158–68.
65. Stringer S., Minică C. C., Verweij K. J. H., Mbarek H., Bernard M., Derringer J. *et al.* Genome-wide association study of lifetime cannabis use based on a large meta-analytic sample of 32 330 subjects from the International Cannabis Consortium. *Transl Psychiatry* 2016; **6**: e769.
66. Kvaavik E., Lund I., Nygard M., Hansen B. T. Lifestyle correlates of female snus use and smoking: a large population-based survey of women in Norway. *Nicotine Tob Res* 2016; **18**: 431–6.
67. Bornovalova M. A., Hicks B. M., Iacono W. G., McGue M. Longitudinal twin study of borderline personality disorder traits and substance use in adolescence: developmental change, reciprocal effects, and genetic and environmental influences. *Pers Disord* 2013; **4**: 23–32.

Supporting Information

Additional Supporting Information may be found online in the supporting information tab for this article.

Figure S1 Path diagram illustrating a trivariate Cholesky decomposition to estimate the genetic covariance between a PD trait and life-time cannabis use when life-time cannabis use is contingent upon the response to: 'Are you prepared to speak openly about this subject?'

Table S1 Descriptive summary of the ordinal measures of life-time cannabis use and cannabis use disorder and DSM-IV personality disorder traits.

Table S2 Bivariate model fitting comparisons between significant personality disorder trait scores and life-time cannabis use.

Table S3 Bivariate model fitting comparisons between significant personality disorder trait scores and cannabis use disorder.

Table S4 Phenotypical (r_P) and additive genetic (r_A) bivariate correlations in which the personality disorder and cannabis correlations were contingent upon 'speaking openly'.

Table S5 Phenotypical (r_P), additive genetic (r_A) and environmental (r_E) correlations between personality disorder trait scores* and life-time cannabis use and cannabis use disorder while adjusting for smoking status.[1]

Table S6 Phenotypical (r_P) additive genetic (r_A) and non-shared environmental (r_E) latent factor correlations between life-time alcohol use (AU) and cannabis use (CU), and between alcohol use disorder (AUD) and cannabis use disorder (CUD).